No.

IN THE
Supreme Court of the United States

Ninth Circuit. Case No. 19-17565

STEVEN BRUCE,

Petitioner,

v.

ALEX AZAR II,
Secretary of the U.S. Dept. of Health and
Human Services, BLUE SHIELD INSURANCE CO., and ENVISION
INSURANCE Co.,

Respondents.

**On Petition for a Writ of Certiorari to
the United States Court of Appeals
for the Ninth Circuit**

PETITION FOR WRIT OF CERTIORARI

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Certiorari Questions

This is Compendia case, a case of first impression under *Shalala v. Illinois Council*, 529 U.S. 1 (2000).

1. Can the U.S. Court of Appeals for the Ninth Circuit ("9th Circuit") sidestep all issues under Medicare, Part D by not looking behind a compendium's Medically Acceptable Indications ("MAI") also known as 'on or off label' when the evidence leads to an underlying false and misleading premise for a prescription, i.e., no rational basis also under Fifth Amendment, Due Process and Section 504 of the Rehabilitation Act of 1973 ("Sec. 504")? The medication, Serostim, as listed in a compendium requires that the patient also have HIV an unrelated condition that does not treat HIV, only lipodystrophy, a life-threatening condition which prevents Petitioner from retaining lipids.

2.a Does *Shalala v. Illinois Council*, 529 U.S. 1 (2000), an exhaustion case, preclude Due Process and/or Sec. 504? Was it an abuse of discretion not to allow Petitioner to amend the Complaint as to a Sec. 504 claim or constitutional due process?

b. Does 42 U.S.C. § 405(h) - if it arises under the Social Security Act, mean that a beneficiary cannot pursue his Due Process and Sec. 504 rights when there is a false and fraudulent premise in HHS policy? Or does § 405(h) only bar actions under 28 U.S.C. §§ 1331 and 1346?

3. Can insurance carriers which are Medicare contractors, be sued for not making statutory exceptions under Medicare, Part D? Can HHS not permit statutory peer reviewed articles from the National Institutes of Health (NIH) into account and can the 9th Circuit prevent this evidence favorable to Petitioner to be considered in cross motions for summary judgment?

LIST OF ALL PROCEEDINGS[1]

1. In re Steven Bruce, Enrollee/Beneficiary. Office of Medicare Hearings and Appeals, ALJ Appeal Number 1-5125326621 (Myles, ALJ), issued March 30, 2018 (AR 720-727), after remand.

2. In re Steven Bruce, Enrollee/Beneficiary. Departmental Appeals Board Docket ("Doc.") No. M-17-7463. Remand order issued December 20, 2017 (AR 320-24).

3. In re Steven Bruce, Enrollee/Beneficiary. Office of Medicare Hearings and Appeals, ALJ Appeal Number 1-6176167691R1 (Gulin, ALJ), issued March 15, 2018 (AR 49-566), after remand.

4. Objections to Agency for not making findings on Sec. 504 of the Rehabilitation Act of 1973 (Sec. 504), due process and regarding non-development of record (AR 0007-0009); In re Steven Bruce, Enrollee/Beneficiary. Departmental Appeals Board Doc. No. M-18-4059. Order issued December July 12, 2018 (AR 12-17).

5. In re Steven Bruce, Enrollee/Beneficiary. Departmental Appeals Board Doc. No. M-18-5595; Order issued September 7, 2018 (AR 2-6).

6. *Bruce v. Alex M. Azar II, et al.* U.S. District Court ("D.C.") for the Northern District of California, Matter No. 18-cv-05022-HSG. Order Granting Motions to Dismiss and Administrative Motion to File Under Seal, and Denying Motions to Supplement the Record, filed June 18, 2019.

7. Order on Cross Motions for Summary Judgment by U.S. D.C., Northern District of California, filed December 16, 2019. (D.C. Doc. No. 110)

8. *Bruce v. Alex M. Azar II, et al.* 9th Circuit Court of Appeals No. 19-17565. Memorandum Disposition. 9th Circuit Court of Appeals, filed October 20, 2020.

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[1] The two administrative law judge decisions after remand and the three appeals council decisions are in a sealed Excerpts of Record, Vol. 3, ordered sealed by the agency, the D.C. and by the 9th Circuit Court of Appeals.

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I. JURISDICTION

The unpublished opinion of the court of appeals was entered on October 20, 2020. This Court has jurisdiction pursuant to 28 U.S.C. § 1254, 42 U.S.C. § 405(g) of the Social Security Act; 21 U.S.C. §§ 360aa-360dd, as amended and the Modernization and Improvement Act of 2003 (MMA), 42 U.S.C.S. § 1395w-101 et seq. U.S. Const., Fifth Amend., Due Process Clause; Sec. 504; Food, Drug, and Cosmetic Act ("FDCA"), 21 U.S.C. § 301, *et seq.,* the Orphan Drug Act of 1983 (ODA), 21 U.S.C. §§ 360aa-360dd as amended.

II. STATEMENT OF THE CASE

A. Introduction

Exhaustion took over two years with three Administrative Law Judges (ALJ) Decisions and three Medicare Appeals Council (MAC) Decisions.[2] This is an issue of first impression under Medicare, Prescription Drug Modernization and Improvement Act of 2003 (MMA), 42 U.S.C.S. § 1395w-101 *et seq.* That is, should Medically Acceptable Indications (MAIs) be broadly interpreted with medical equivalence and should federal courts take into account underlying false and/or fraudulent underlying rational for Compendia MAIs by U.S. Department of Health and Human Services ("HHS") and insurance companies. Petitioner has argued this basis for false HHS premises based on 5 HHS/NIH peer review documents because of a false premise given by HHS in not permitting coverage. Regrettably, both lower courts have denied admitting these material and relevant documents into evidence. Had they been admitted, the D.C. could not have granted HHS' Motion for Summary Judgment (MSJ).App. No. 2

Petitioner, Steven Bruce ("Mr. Bruce" or "Bruce") was diagnosed with lipodystrophy, a life-threatening, auto-immune metabolic disease which can result in death in July 2016. Symptoms include wasting syndrome aka cachexia causing him to undergo a dramatic weight loss to 132 lbs. He is 5'11" tall (AR 82, 54), organ failure and life spans are estimated to be significantly shorter. The primary organs affected are the liver, kidneys and pancreas (App. ("App.") Nos. 9 and 10, not admitted into the record but two motions with "5 HHS NIH documents" were filed

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[2] HHS's administrative record ("AR") of approximately 1,500 pages was and is not in chronological order. HHS required duplicate exhibits for each of two ALJs. The AR was kept separate because HHS does not consolidate ALJ cases even for the same issues. Two duplicate post remand ALJ decisions were removed leaving two ALJ decisions, Myles and Gulin. The AR is sealed and there would be too many numbers with E.R. numbers added since each page filed in the D.C. had two page numbers. The sealed AR is in E.R. Vol. 3.

in D.C. See App. No. 5, Order on Cross Motions for Summary Judgment (MSJs)). At all relevant times Mr. Bruce was/is a Medicare, Part D (prescription drug) beneficiary.

The only medication which allowed Mr. Bruce to gain weight back, notwithstanding severe side-effects, is Serostim (Somatropin). (AR 33, 134, 330, 628.) Its retail price is $18,000 per month in 2020. Two Medicare contractors, Blue Shield of California and Envision, denied coverage. The reason given by HHS for affirming the insurance carriers was that Bruce had to prove he had another, unrelated auto-immune disease (HIV) based on a false premise - that HIV caused his lipodystrophy. (AR 184-85, 297-98, 630-31.) He has non-HIV lipodystrophy.

At no time did HHS disclose they knew HIV was unrelated to lipodystrophy. All they had to do is look at their own components; NIH, and the Food and Drug Administration ("FDA") or look at Myalept (Metreleptin), a replacement hormone for anyone who has lipodystrophy, which the FDA approved in 2014. See Request to take Judicial Notice Request pursuant to Fed. R. Evid. 201 filed in D.C., the 9th Circuit. (App. Nos. 3, 4.) HHS states its position is not law but its own policy; that this lipodystrophy medication, Serostim, will only be available to people who also have HIV knowing it does not treat HIV.

B. Procedural History

1. The Administrative Proceedings

1. After two ALJs' noticed[3] hearings the Medicare Appeals Council ("MAC") remanded both ALJ decisions to so the administrative record (AR) includes the

[3] All Notices of Hearing stated overly vague generic issues; e.g., "The issues before the ALJ include all of the issues brought out initially; by redetermination; that were not decided in a party's favor, specified in the request for hearing." (AR 73, 756, 1059, 1203-04); Mr. Bruce objected to this notice. (AR 66.)

"Medicare-approved Compendia," which HHS relies on, and the insurance companies' formularies. (AR 1031-32.) ALJ Gulin did not conduct a hearing until the MAC ordered him to do so. After the next appeal to the MAC, it affirmed the ALJ decisions on 7/12/18 (AR 10-17.)

2. Both of the ALJ decisions (Myles, AR 720-27 and Gulin- AR 49-56) were appealed a third time (AR 8-9) to the MAC, which stated this result is required because it is on the compendium list that way. The MAC further stated after Mr. Bruce complained about not receiving the three Compendia, that he 'should have challenged it harder.' (AR 5, 15.) But the first two MAC remands already required the ALJs to include the compendia and formularies. The ALJs and MAC do not recognize the statutory "exception" for this prescription as both insurance companies desired the most restrictive definition of a MAI. See all MAC decisions, generally. (AR 2-6, AR 12-17 AR 320-24 and AR 1030-1032.)

3. In response to an objection letter to the MAC (AR 8-9) based on absence of Due Process and Sec. 504 findings after having raised it, the MAC stated HHS had no jurisdiction over Due Process or Sec. 504. (AR 4.) HHS is correct regarding Due Process and incorrect about Sec. 504. See 45 C.F.R. Pt. 85 for federal agencies and Part 84 for federal contractors (the insurance companies.)

4. After the double remand for the two ALJs (AR 320-24, 1030-32), Mr. Bruce first became aware that HHS had known for over 20 years that the population with HIV had their lipodystrophy cured by changing the HIV anti-retroviral therapy ("ART") which apparently is the actual cause of lipodystrophy in HIV patients according to 5 HHS/NIH documents submitted to the D.C. as evidence. (App. Nos. 9, 10. At the second ALJ hearing, Mr. Bruce argued HHS violated his Due Process and Sec. 504 rights. HHS was applying a known false causation theory without ever telling Mr. Bruce, who had to do considerable independent research into HHS' NIH peer review articles. Myalept was approved for lipodystrophy treatment in February 2014, but not known to Mr. Bruce and never mentioned by HHS or the

two insurance carriers as evidence that HHS does provide research and medication for generalized lipodystrophy.

2. The D.C.

The D.C. over-controlled[4] the case by erroneously dismissing **with prejudice** Due Process, Sec. 504, denying Mr. Bruce's Motion to Supplement the AR which includes access to Compendia evidence other than the two pages put in the AR, and dismissed Blue Shield and Envision Insurance as parties. (App. Nos. 3, 5.) Plaintiff filed objections to this Order (E.R. Vol. 2, Doc. 84.) Although the D.C. stated, at oral argument on the MSJs (TR DC MSJ[5] at 7:8), that the D.C. understood Plaintiff's allegations of bad faith, intrinsic fraud, and misrepresentations under the Due Process Clause and Sec. 504 precluding Mr. Bruce equal [meaningful] access to its Medicare, Part D program, the D.C. did not consider this gravamen of the case by not mentioning this substantially nonpublic criteria which Plaintiff spent hours talking to patients, doctors and then researching the HHS/NIH online to find the agency's relevant evidence, HHS' documents relating to non-HIV lipodystrophy.

3. The Court of Appeals

The 9th Circuit affirmed the D.C. with little or no analysis, did not apply its own *de novo* legal review standard and did not look at any of the underlying issues regarding HHS's lack of rational basis in the compendium for Serostim which to be a MAI required that one have another unrelated auto-immune condition, HIV in addition to lipodystrophy. Accordingly, that court glossed over constitutional due

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[4] A reading of the transcript on the motion to dismiss (Transcript of Proceedings, Bruce v. Alex M. Azar, II, et al., 4:18-cv-05022-HSG (Feb. 28, 2019), (E.R. Vol. 1)) reveals a D.C. anxious to dismiss most of the complaint without taking into account any facts from the approx. 1500 pages of the (AR), which was not filed until 2/5/19, because the D.C. did not mention any detail or findings of the two ALJ and three MAC decisions in this Order. (App. No. 5.)

[5] Reporter's Transcript of Proceedings, *Bruce v. Alex M. Azar, II, et a*l., 4:18-cv-05022-HSG (Dec. 5, 2019) (E.R. Vol. 1).

process, Sec. 504 and the Medicare, Part D statute as it speaks to peer review bases for statutory exceptions, statutory consumer protections or any other primary disputed issue in this case. It issued a short 4-page, unpublished decision.

Mr. Bruce is requesting this Court take into account the "5 HHS/NIH documents," App. Nos. 9 and 10 (App. No. 9 has one attachment and App. No. 10 has four attachments) into evidence. Under Fed. R. Civ. P. 56, summary judgment could not have been granted for HHS if the D.C. had granted Bruce's motion to allow the 5 HHS/NIH documents into evidence, evidence that HIV is not relevant for covering Serostim for his life-threatening condition. Nor did it grant Bruce's motion to take Judicial Notice of Myalept the only other medication for generalized lipodystrophy approved by the FDA. It made no mention of the FDCA, 21 U.S.C. 301 *et seq.* or the Orphan Drug Act of 1983 (ODA), 21 U.S.C. §§ 360aa-360dd, as amended.

C. Statement of Facts

The 9th Circuit stated that the parties agree with the facts and; therefore, omitted any recitation of facts. Mr. Bruce generally agrees with the facts in the two ALJ decisions (Gulin and Myles) after MAC remand (AR 49-56 and 720-27), summarized as follows (and disagrees with some facts including that HHS has no Sec. 504 jurisdiction and the facts in the 5 NIH articles):

1. A Medicare Part D drug is either FDA approved or supported by being listed in or having citation(s) in Compendia or being a statutory **exception**, or based on peer review (AR 52-55.) Plaintiff's primary care physician, Dr. Cubba, and Eveline Stock, M.D., a doctor from the University of California at San Francisco Medical Center's Lipid Clinic, diagnosed Mr. Bruce with a rare metabolic autoimmune disorder, lipodystrophy, which produces severe weight loss (wasting syndrome).

2. The only treatment is human growth hormone, Somatropin (brand name, Serostim). lipodystrophy can result in death. (AR 22, 36, 82 *et. seq.*) An NIH web

source is cited[6] in ALJ's Myles decision containing a link to the Compendia (AR 726) and in ALJ Gulin's decision. (AR 55.)

> "A 'medically accepted indication' is any use for a covered outpatient drug which is approved under the Food, Drug, and Cosmetic Act [21 U.S.C. 301 et seq.] or the use of which is supported by one or more citations included or approved for inclusion in any of the compendia described in subsection (g)(1)(B)(i) of this section. (Title XVIII, § 1927(k)(6) of the Act)." (AR 54.)

3. According to ALJ Gulin, Serostim is FDA approved with a condition that it is for HIV patients who need it for wasting syndrome to increase body mass. This is the same use as Petitioner's need. (AR 55.)

4. Petitioner moved the D.C. to Order the Compendia (App. No. 3), relied on by the MAC by decision dated 7/12/18 (AR 14-15), produced including the introduction relating to how it is used. Without the three Compendia, which are not provided to Medicare [or apparently to Medicaid] beneficiaries, the statutory requirement of an MAI or citation is unclear as to, e.g., benefits of "off label" prescriptions or similar drugs.

ALJ Gulin declined coverage because ALJs are bound by the implementing regulations (AR 54-55) and twice states at the hearing he cannot/will not follow case law but will research Mr. Bruce's position that the ART, not HIV, causes lipodystrophy. (AR 704, 707.)

ALJ Myles stated:

> "**… Petitioner argued that HIV drug treatment, rather than the HIV, causes weight loss or cachexia. Therefore, Serostim should be considered a treatment for weight loss and wasting rather than one for HIV. This view is supported by medical literature from the NIH.…**" (AR 725.)

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[6] www.nihlibrarycampusguides.com.ezproxyhhsnihlibbrary.nih.gov/c.php?g=38325&p=245138 It is not available to public; apparently this is an agency intranet. See Declarations of the AUSA and Ann Marie Chandler, attachments to Plaintiff's MSJ Reply brief, which both state this Compendia evidence is not publicly available. (App. No. 8.)

ALJ Myles stated he is not permitted to follow law but can only apply HHS policies and regulations. (AR 726-27.) ALJ Myles found that if that NIH literature supports the conclusion argued by Plaintiff; i.e., that **it is the ART that causes lipodystrophy, not HIV,** there is nothing he can do - he is bound by what is exactly printed in the Compendia…. he has no authority but to affirm the insurance carrier. (AR 727.) Also "see" which is not a Compendium but an FDA list cited by the ALJs: http://www.accessdata.fda.gov/scripts/cder/daf. Per HHS, there are no additional off-label uses for Serostim included in the American Hospital Formulary Service (AHFS-DI) database. (AR 726.) Access to AHFS-DI was requested, but not provided.

HHS stated "…a court cannot waive the Part D requirements simply because an enrollee's condition is rare…." (E.R. Vol. 2, Doc. 94 at 13:11, citing a 2015 D.C. in Ohio.) HHS, in the same listing in the two pages of the DrugDex compendia (in ALJ Myles decision), lists *short bowel syndrome.*

5. In February 2014, Myalept was FDA approved for people with generalized lipodystrophy.

6. The ALJs and D.C. declined to discuss any law relating to the false requirement (causal condition), agency misrepresentation and/or intrinsic fraud on the public. Both ALJs concur that Serostim has been the only prescription drug that works with Mr. Bruce's lipodystrophy symptomatology - wasting syndrome. (AR 50, 724-26.)

7. ALJ Myles states Mr. Bruce was entirely credible and further, that he is sympathetic to his life-threatening predicament. (AR 55, AR 726.)

8. In D.C., Mr. Bruce relied on HHS/NIH documents. There is no clear cause and effect and treatment for people with non-HIV lipodystrophy and severe weight loss and those with HIV and "wasting" syndrome. In fact, if one has both HIV and lipodystrophy caused lipid loss it is treated [cured] by changing the anti-viral HIV compounds, historically. Treatment for lipodystrophy cachexia is treated by

Serostim. There are no HIV compounds to change.[7]

9. HHS stated in D.C. that an approximately $400.00 outdated 2016 compendium should be purchased by Mr. Bruce on Amazon.com rather than provide access to the current electronic Compendia. (E.R. Vol. 2, Doc. 77 at 4:n 3.) Recently, HHS represented to another D.C. that the same (or 2015) compendium HHS told Mr. Bruce to buy through Amazon.com was too outdated to be relied upon. *Aloi v. Azar*, 337 F. Supp. 3d 105 (D.C. RI, Oct. 2018).

10. The MAC, at AR 7-17, knew Mr. Bruce's position was that there was no difference between the wasting symptoms of lipodystrophy and that changing the HIV ART is a cure for lipodystrophy. The 5 HHS/NIH documents, are specific evidence in support of the false premise known and utilized by HHS; i.e., that it is not the Compendia-required HIV that causes life-threatening wasting syndrome. (See App. Nos. 9 and 10.) The D.C. denied Mr. Bruce's two administrative motions to admit this evidence in its Order granting HHS' MSJ (App. No. 2), App. No. 9 with one attachment, App. No. 10 with four attachments, and ignored this merit argument. I.e., that the Compendia, at least those DrugDex pages Mr. Bruce was permitted to see, did not reference the true underlying facts, that HHS has known for over 20 years that HIV was not the cause or related to the cause, ART, of lipodystrophy. The "5 HHS/NIH documents" are dated September and November 2019, September 2015, March 2010, and October 2008 and are examples of NIH evidence relating to non-HIV lipodystrophy. The first NIH document (App. No. 9, article 1) is a fact sheet, which states "…Lipodystrophy will not be a concern for

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[7] The primary therapy for severe lipodystrophy, particularly lipoatrophy, is a change in Anti-Retroviral Therapy (ART). Finkelstein, Julia L *et al.* "HIV/AIDS and lipodystrophy: implications for clinical management in resource-limited settings." *Journal of the International AIDS Society* vol. 18, 1 19033. 15 Jan. 2015, doi:10.7448/IAS.18.1.19033, *available at* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4297925/ (last visited Mar. 4, 2020) from the U.S. National Library of Medicine National Institutes of Health website.

most people who start HIV treatment now." ("HIV and Lipodystrophy.")[8] The D.C. said, *inter alia*, that since the Court was going to give HHS a judgment it did not matter that it denied Bruce's motions to admit the 5 HHS/NIH documents. (App. No. 2 at 6:n 4.) If HIV was a cause of lipodystrophy HHS' position would not be irrational. The MAC, like the two ALJs, does not dispute the facts presented by Mr. Bruce. The MAC states that off-label uses are from Medicare Compendia known as AHFS-DI, or DrugDex, or USP-DI or its successor. No Compendia has been produced except for a partial Micro-DrugDex entry for Serostim and a formulary which is used by Envision (AR 738-49; AR 787-88.) In December 2019 Mr. Bruce checked the costs of DrugDex now owned by IBM and found each year online subscription was $2,000 to $3,000.[9]

11. HHS, in its opposition to Mr. Bruce's motion to add one document (E.R. Vol. 2, Doc. 101 and App. No. 9) to the record, states and generally Mr. Bruce agrees, that there is no causation requirement for prescription medications; however, that is not what HHS is doing. The Agency requires a patient to have HIV in order to receive Serostim, notwithstanding this requirement is based on a false premise. According to the 5 HHS/NIH documents, another medication, Myalept (generic Metreleptin), has been approved since 2014 only for generalized lipodystrophy.

12. The third MAC Judge omitted the AHFS-DI and USP-DI Compendia for Serostim and stated Mr. Bruce 'did not challenge the ALJs hard enough' (AR 5.) To

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[8] HIVinfo.NIH.gov, "Side Effects of HIV Medicines, HIV and Lipodystrophy Last Reviewed: September 19, 2019" *available at* https://aidsinfo.nih.gov/understanding-hiv-aids/fact-sheets/22/61/hiv-and-lipodystrophy (last visited Mar. 12, 2020).

[9] Multiple year subscriptions are requested (per the IBM business development person on the phone Dec. 2019.)

the contrary, the MAC in its first Remand Order required ALJ Myles to obtain the Compendia and Formularies as exhibits; but only a few pages of one Compendium, DrugDex, were produced by ALJ Myles. (AR 320-24, AR 1030-32.)
On 2/5/2019 HHS filed the AR with the D.C. Petitioner is only appealing not receiving the three compendia or access thereto in his Motion to Supplement the AR.

13. Request to Take Judicial Notice and Relevant and Material Evidence in Favor of Petitioner: The 9th Circuit affirmed the DC's 1. denial of Petitioner's request to take judicial notice of Myalept, a synthetic hormone produced by lipids and the only other lipodystrophy treatment in addition to Serostim (see App. No. 4) and 2. The 5 HHS/NIH documents in support of petitioner. (App. Nos. 9 and 10.)

D. Bases for Federal Jurisdiction

The bases for federal jurisdiction in the D.C. are pursuant to 42 U.S.C. § 405(g) of the Social Security Act; U.S. Const., Fifth Amend., Due Process Clause; Sec. 504; FDCA, 21 U.S.C. § 301, *et seq.,* and the (ODA), as amended and MMA, 42 U.S.C.S. § 1395w-101 *et seq.*

III. ARGUMENT

A. Nonpublic Criteria (Procedures, Practices and/or Policies) Are Illegal when Used Under the Social Security Act, 42 U.S.C. § 400 et seq. The HIV Requirement "Rationale" Is Contradicted by HHS/NIH Documents Erroneously Not Admitted into Evidence. There is Medical Equivalence in Medically Acceptable Indications.

Nonpublic criteria (procedures, practices and/or policies) are illegal when used under the Social Security Act. Fundamental rights such as Due Process are cognizable under *Smith v. Berryhill*, 139 S. Ct. 1765 (2019) at 1717, which states "…Congress wanted more oversight by the courts rather than less under § 405(g) and that "Congress designed [the statute as a whole] to be 'unusually protective' of claimants."

> "…Where the Government's secretive conduct prevents plaintiffs from knowing of a violation of rights, statutes of limitations have been tolled until such time as plaintiffs had a reasonable opportunity to learn the facts concerning the cause of action…." *Bowen v. City of New York*, 476 U.S. 467 (1986) at 481.

The underlying truth about the HIV [non causation] was not known to Bruce until after the administrative exhaustion process started. "…it has not suggested that it intended for the SSA (previously Appellee, HHS) to be the unreviewable arbiter of whether claimants have complied with those procedures…." *Smith* at 1770.

The underlying purpose of 42 U.S.C. §§ 405(g) and 405(h) is to develop a factual record. See *Weinberger v. Salfi,* 422 U.S. 749 (1975), not to keep out material facts. Also see *Mathews v. Eldridge*, 424 U.S. 319 (1976) for applicable due process, affirmed in *Smith*.

42 U.S.C. § 1396r-8(k)(6), states: The term "medically accepted indication" means any use for a covered outpatient drug which is approved under the Federal Food, Drug, and Cosmetic Act ("FDCA") or the use of which is supported by one or more citations included or approved for inclusion in any of the compendia described in subsection (g)(1)(B)(i).

The MMA, Part D, 42 U.S.C. § 1395 *et seq.* has consumer protections built in:

Sec. 1860D-2. [42 U.S.C. 1395w-102] (a) Requirements. —

> "…(C) Update.—For purposes of applying subparagraph (A)(ii), the **Secretary shall revise the list of compendia** (emphasis added) described in section 1927(g)(1)(B)(i) **as is appropriate for identifying medically accepted indications for drugs**. Any such revision shall be done in a manner consistent with the process for revising compendia under section 1861(t)(2)(B) Sec. 1860D-2. [42 U.S.C. 1395w-102] (a) Requirements. — "… (II) the carrier involved determines, **based upon guidance provided by the Secretary to carriers for determining accepted uses of drugs**, **that such use is medically accepted based on supportive clinical evidence in peer reviewed medical literature appearing in publications** which have been identified for purposes of

> this subclause by the Secretary. (emphasis added) …The Secretary may revise the list of compendia in clause (ii)(I) as is appropriate for identifying medically accepted indications for drugs. On and after January 1, 2010, **no compendia may be included on the list of compendia under this subparagraph unless the compendia have a publicly transparent process for evaluating therapies** and for identifying potential conflicts of interests (emphasis added.)

HHS has not followed this Congressional mandate, but continues to utilize a false premise with regard to HHS' known findings that HIV is unrelated to lipodystrophy which can be treated and cured by those afflicted with HIV by changing the ART used to treat HIV. Serostim does not treat HIV. In 2014 HHS' FDA component approved Myalept (generic-Metreleptin), a synthetic hormone to replace Leptin produced by lipids, which lipodystrophy patients do not have.

B. On Remand Expert Opinion Should Have Been Required Given the Lower Courts Refused to Consider Material and Relevant Evidence in NIH Peer Review Articles

In *United States v. King-Vassel*, 728 F.3d 707, 716 (7th Cir. 2013) the Court stated about compendia that an expert may be required: "They seem to be intended primarily for an audience of health care professionals, but again, were specifically incorporated by Congress into the statutory standard for a 'medically accepted indication.' 42 U.S.C. § 1396r-8(k)(6)…."

Here applying the same rationale, the ALJs (stated they had no authority) and the 9th Circuit should have decided on a biochemist expert since this case concerns metabolic areas of specialization.

If the 9th Circuit and the D.C. admitted the 5 HHS/NIH document evidence, there would be a dispute as to material facts and the D.C. could not have granted HHS' MSJ. The D.C. Order on cross MSJs (App. No. 2) relates back to the Order to Dismiss and Motion to Supplement Administrative Record (App. No. 5), and states in part:

> "…Plaintiff failed to rebut with clear evidence the presumption that the record is complete, or present any evidence that an exception applies to allow the Court to consider extra-record evidence. *See* Dkt. No. 83 at 10–11. Accordingly, the Court **DENIES** Plaintiff's administrative motions to file additional documents. *See* Dkt. Nos. 100, 102. And even were the Court to consider the additional materials Plaintiff seeks to introduce, the Court finds that these materials would not change its analysis." (App. No. 2 at 6:n 4.)

This is plain legal error in that this material and relevant evidence should not have been omitted under Fed. R. Civ. P. 56. Had it been discovered later, Fed. R. Civ. P. 60 would have required the judgment be set aside.

The D.C and 9th Circuit relied on a misinterpreted exhaustion case, *Shalala v. Illinois Council*, 529 U.S. 1 (2000). (App. Nos. 1, 5 at 7.) Moreover, it is unlikely that the D.C. considered any facts from the two ALJ and three MAC decisions in the 1500-page AR filed on 2/5/19, E.R. Vol. 3, sealed since the D.C. did not mention any details or findings from them in its Order issued on 6/18/2019. (App. No. 5.)

Not to admit material and relevant evidence (App. Nos. 9 and 10) before judgment is an affront to basic conceptions of fundamental fairness. *Lands Council v. Forester of Region One of the United States Forest Serv.*, 395 F.3d 1019, 1030 (9th Cir. 2004) which states:

> "…a reviewing court may consider extra-record evidence where admission of that evidence (1) is necessary to determine 'whether the agency has considered all relevant factors and has explained its decision,' (2) is necessary to determine whether 'the agency has relied on documents not in the record,' (3) 'when supplementing the record is necessary to explain technical terms or complex subject matter,' or (4) 'when plaintiffs make a showing of agency bad faith.'…"

In the HHS' MSJ (E.R. Vol. 2, Doc. 94 7:8-10), HHS argued the FDA does not have to approve treatment for rare disorders like lipodystrophy, but in truth it does. (In 2014 the FDA approved Myalept.) Lipids, which people like Petitioner cannot retain, produce a hormone called Leptin which helps people with generalized lipodystrophy. It helps against the metabolic consequences of

lipodystrophy which according to NIH second abstract attached to App. 10 causes insulin resistance and organ failure (liver, kidney and pancreas) and; therefore, can result in death. Along with HIV, the approx. two pages of the DrugDex compendium in the AR state Serostim is also for short bowel syndrome, another rare disorder. The HIV limitation has no rational basis. The HIV causation requirement was before both ALJs and HHS had a duty to develop this record and inform any Medicare (or Medicaid) beneficiary that Myalept was approved for lipodystrophy without HIV. ALJ Gulin stated at the hearing his staff would research this; there is no evidence that it happened. (Tr., AR 704.) ALJ Myles said because of the insurance carrier determination, the reconsideration, and the MAC remand, he has to affirm.[10] (ALJ Decision at AR 727.) Historically, the ALJ has a duty to develop the factual record. *Weinberger,* 422 U.S. at 758-60.

> "Social Security proceedings are inquisitorial rather than adversarial… It is the ALJ's duty to investigate the facts and develop the arguments both for and against granting benefits, see *Richardson* v. *Perales,* 402 U. S. 389, 400-401 (1971), and the Council's review is similarly broad. *Sims v. Apfel*, 530 U.S. 103, 111–12 (2000). An ALJ has a duty to develop the record further "when there is ambiguous evidence or when the record is inadequate to allow for proper evaluation of the evidence."

In *Smith* at 1770*,* 1777 this Court held that:

> "…Congress wanted more oversight by the courts rather than less under §405(g)… "Congress designed [the statute as a whole] to be 'unusually protective' of claimants….Congress has not suggested that it intended for the SSA to be the unreviewable arbiter…" (Internal citations omitted).

The 9th Circuit affirmed the D.C. in its judgment for HHS, declining to rule on the merits by not applying its legal review standard (*de novo)*, and leaving HHS as the final arbiter. The D.C.'s rationale in its Order on the MSJs is legal error, factually wrong and inherently discriminatory based on disability (non-HIV

[10] ALJ hearings are *de novo*.

lipodystrophy). The D.C. erroneously found and the 9th Circuit affirmed "…Whether Part D *should* cover Plaintiff's use of Serostim to treat his condition because it has similar symptoms to those of patients with covered conditions is a policy matter not within the Court's competence to decide…." (App. No. 2 at 7:14-16.) ALJ Gulin stated:

> "… NIH studies lead to the conclusion that it is not the HIV that leads to lipodystrophy, but the anti-viral agents used to treat HIV… Mr. Bruce cited to the National Institutes of Health ("NIH") study included in the record in response to Ms. Lester [Blue Shield]. Current research leads to the conclusion it is not really the HIV, but the agents used for HIV, that cause lipodystrophy. There is federal case law describing how the statute, rather than the compendia is read more inclusively for the beneficiary. Simply citing the compendia is not always enough .to deny coverage. (Hearing CD) …." (AR 54-55.)

ALJ Myles states he cannot use statutory interpretation but cites a contradictory regulation, 42 C.F.R. § 423.2063(a) *Applicability of laws, regulations, CMS Rulings, and precedential decisions*. (AR 726-27.)

This ALJ also stated:

> "…Petitioner argued that HIV drug treatment, rather than the HIV, causes weight loss or Cachexia. Therefore, Serostim should be considered a treatment for Cachexia or wasting rather than one for HIV…." (AR 725.)

The D.C.'s rationale that resolution of the underlying issue is "**beyond the competence of the D.C**." is not based on substantial evidence and is clear legal error. (App. No. 2.) The D.C. should have reversed based on the 5 HHS/NIH documents evidence and FDA approval of Myalept or granted a "sentence four" or "sentence six" remand of a § 405(g) judgment for Bruce remanding the case to HHS to use a biochemist M.D. expert or just reversed for payment of benefits.

C. HHS Suppressed Evidence (App. Nos. 9 and 10)

All of the exceptions; e.g., see *Lands Council, infra* to supplement an AR apply to the earlier motion to supplement the record filed and rejected in the Order

dismissing them. See App. Nos. 3 and 5. HHS knew the HIV population had a cure for lipodystrophy by changing the ART used to treat HIV; The metabolic effects of lipodystrophy, including insulin resistance and failure of liver, kidney, and pancreas which apply to Mr. Bruce's condition, is a technical and complex metabolic subject matter; (4) There is a showing of "bad faith" in that the Compendium requirement of HIV is based on a false premise that may have been believed in the 1980s, but since then the HHS/NIH documents make clear that requiring a patient with a lipid auto-immune disorder to have another irrelevant auto-immune disorder (HIV) is in reckless disregard of the truth.[11]

This court made it clear that building a factual record is the underlying purpose of administrative exhaustion. 42 U.S.C. §§ 405(g) and 405(h) are to develop a factual record, see *Weinberger,* 422 U.S. 749; not to keep out material facts. Other appellate courts; e.g., *Thompson v. United States Dep't of Labor,* 885 F.2d 551, 555 (9th Cir. 1989) established that a court may look beyond the administrative record to determine whether the agency considered all relevant factors, to determine whether the agency's "course of inquiry" was sufficient or inadequate. Courts often require medical experts in the correct area of specialization. See *Biestek v. Berryhill,* 139 S. Ct. 1148 (2019), *Bragdon v. Abbott,* 524 U.S. 624 (1998). Mr. Bruce's lipid doctors from UCSF's Lipid Clinic are experts who recommended Serostim be used in this non HIV lipodystrophy case.

The Court of Appeals' affirmation of the D.C.'s two orders (App. Nos. 1, 5, 2), including the Motion to Supplement the record with the Compendia, is legal error. (App. No. 3). The "5 HHS/NIH document evidence" are inextricably intertwined with Mr. Bruce's position that there is a showing of bad faith in that the Compendium requirement of HIV is based on a false premise. The D.C. rationale

[11] The Order to Dismiss (Doc. 83) covers Due Process (Count B), Sec. 504 (Count C), the two insurance carriers and the motion to supplement the record with compendia access.

that Mr. Bruce's evidence is "…nowhere close to showing 'clear evidence" (App. No. 2 refers to App. No. 5) at that point in the litigation is highly regrettable because HHS claims three Compendia, citations, references and peer reviewed literature can be the basis for coverage. See First Amended Complaint and Opposition to HHS, motion to dismiss containing that evidence. (App. Nos. 6, 7, Again, had the D.C. taken into account the two ALJ and three MAC decisions it referenced; the "clear evidence" would have been even more apparent.

HHS falsely represented the Compendia is publicly available. See HHS Opposition to Motion to Supplement. (E.R. Vol. 2, Doc. 77 at 5.) The Agency states it is public through a link; however, the link referred to is not a Compendium link. The NIH library used by HHS's lawyer is not open to the public. See the Declaration of Kimberly Robertson, AUSA, who only mentioned one compendium on March 6, 2019, and Anne Marie Chandler, Legal Assistant, both filed concurrently herewith as App. No. 8. The HHS tried to conceal the information from a Medicare beneficiary.

D. Constitutional Due Process

The 9th Circuit affirmed the D.C. striking the Due Process Clause count with prejudice (App. Nos. 1, 5.) Mr. Bruce filed Objections (E.R. Vol. 2, Doc. 84) which were never ruled upon and then stated in his MSJ that due process is applicable whether through § 405(g) or not. (E.R. Vol. 2, Doc. 90.) This Court has consistently ruled for the past 44 years that Due Process applies without exhaustion under the Social Security Act so long as there is a colorable claim which is collateral. *Smith v. Berryhill, supra*, *Lopez v. Heckler*, 753 F.2d 1464 (9th Cir. 1985), revered on other grounds 469 U.S. 1082), and *Mathews v. Eldridge,* collaterality required, 424 U.S. 319 (1976). Moreover, notice is constitutionally defective where it was not reasonably calculated, under all the circumstances, to apprise interested parties of the pendency of the action and afford them an opportunity to present meaningful objections thereto. *Mullane v. Central Hanover Bank & Trust Co.*, 339 U.S. 306,

314, 319 (1950). Bruce did not know using this standard; i.e., MAI, that HIV was really **not** the cause of lipodystrophy. This is not the first time this Agency has acted surreptitiously and in bad faith.[12] The 9th Circuit erred in relying on *Shalala* v. *Illinois Council*, 529 U.S. 1 (2000), an exhaustion case.

The 9th Circuit also erred by dismissing the insurance carriers as parties, and Sec. 504 of the complaint **with prejudice** contrary to its own case law requiring leave to amend a complaint: *Morongo Band of Mission Indians v. Rose*, 893 F.2d 1074, 1079 (9th Cir. 1990); *DCD Programs, Ltd. v. Leighton*, 833 F.2d 183, 186 (9th Cir. 1987).

E. Meaningful Program Access Under Sec. 504 Is Cognizable and Should Not Have Been Dismissed by the D.C. and Affirmed by the 9th Circuit.

Cases that arise under the Social Security Act do not override a Congressional mandate applying Sec. 504 to federal agencies especially when an agency has no rational basis for disparate treatment of individuals with a disability, non-HIV lipodystrophy. It is also legal error to dismiss this cause of action with prejudice. It was pled in the first amended Complaint alleging that Mr. Bruce stated he did not have equal meaningful program access under 45 C.F.R. § 85.21. Surprisingly, the 9th Circuit affirmed the D.C., finding that *Shalala v. Illinois Council,* a Social Security Act Title XVIII exhaustion case overruled a Rehabilitation Act of 1973 exhaustion case, *J.L. v. Soc. Sec. Admin.*, 91 F.2d 260 (9th Cir. 1992) even though this judicially created exhaustion in *J.L.* is not under the same statute (Social Security Act) and required filing an administrative Sec. 504 complaint with the Agency and in 6 months appealing it back to the agency, without ALJs. (App. No. 5 at 8).

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[12] Samuel Estreicher & Richard L. Revesz, Professor of Law, New York University, *Nonacquiescence by Federal Administrative Agencies*, 98 Yale L.J. 679 (1989).

Moreover, the 9th Circuit stated the parties are familiar with the facts, so there is no need to recite them. A regrettable statement as to Sec. 504. Petitioner did allege sufficient facts and Respondents alleged the opposite. The complaint, first amended, states "… By providing coverage for Serostim only to individuals who have HIV, Envision and Blue Shield denied Plaintiff, as an individual with a disability ([l]ipodystrophy), the opportunity to participate in, or benefit from, Envision's and Blue Shield's aids, benefits, or services afforded to those with HIV. There is no rational basis for providing Serostim to treat cachexia, wasting syndrome or lipodystrophy only to individuals who have been also diagnosed with HIV…. Defendants provided no evidence to the contrary." ¶¶ 49, 50. Opposition to HHS' Motion to Dismiss Sec. 504 states in pertinent part "… – there is no rational basis to deny coverage for Plaintiff's wasting syndrome/cachexia because it is not also accompanied by HIV… Plaintiff challenges the arbitrary classification requiring HIV as it does not provide meaningful access to individuals with disabilities such as Plaintiff, who has the underlying condition that Serostim was envisioned to treat…."

The Court of Appeals should have applied its *de novo* review standard and found either there were sufficient facts based on the opposition to HHS' Motion to Dismiss and found the Complaint could be amended or there was sufficient evidence as quoted herein under 9th Circuit law. The Court of Appeals' lack of analysis on disputed issues is regrettable. Again, the underlying purpose of 42 U.S.C. §§ 405(g) and 405(h) is to develop a factual record, see *Weinberger,* 422 U.S. 749, not to keep out material facts.

As an individual with non-HIV lipodystrophy, Mr. Bruce has no meaningful program access to the medication needed because it is based on a false and misleading premise - that HIV is required in order to receive Serostim for lipodystrophy. The 5 HHS/NIH evidence show knowledge of HHS that people with HIV can be cured of lipodystrophy. (App. Nos. 9 and 10.) Petitioner does

not have any further burden of proof having found this conflicting evidence from HHS.

F. The Two Insurance Carriers, Blue Shield and Envision, Are Proper Defendants and Should Not Have Been Dismissed with Prejudice

1. The insurance companies are proper defendants and Congress has mandated that they perform a pivotal role in initiating exceptions when listings are not in the Compendia. See Section E – An Exception Should Have Been Granted.

> Sec. 1860D-2. [42 U.S.C. 1395w-102] (a) Requirements. — "…(C) Update.—… the Secretary shall revise the list of compendia described in section 1927(g)(1)(B)(i) as is appropriate for identifying medically accepted indications for drugs. Any such revision shall be done in a manner consistent with the process for revising compendia under section 1861(t)(2)(B) Sec. 1860D-2. [42 U.S.C. § 1395w-102] (a) Requirements. — "… (II) **the carrier involved determines**, **based upon guidance provided by the Secretary to carriers** for determining accepted uses of drugs, that such use is medically accepted based on supportive clinical evidence **in peer reviewed medical literature** (emphasis added) appearing in publications which have been identified for purposes of this subclause by the Secretary." Emphasis added

The claim is not a derivative claim, which the D.C. states is the primary reason for there being no jurisdiction under *Shalala v. Illinois Council, supra* at 14 (App. No. 5 at 5-7.)

It is true that under 42 U.S.C. § 405(g) HHS is a proper defendant (see App. No. 5 at 5-7) under 42 C.F.R. § 423.2136(d)(1). Because HHS is a proper defendant does not lead to the conclusion that the two federal contractors are not. The Sec. 504 regulations that cover federal contractors are found at 45 C.F.R. Pt. 84. It cannot be presumed that the insurance contractors have no knowledge that lipodystrophy is not caused by HIV or that not covering this population on the basis of this disability violates the requirement of equal meaningful program participation in the

Medicare prescription drug program. Blue Shield and Envision Insurance employ doctors and had one testify, Dr. Watson, an internist (the wrong area of specialization). Blue Shield lists Serostim in its formulary and should also be presumed to have and seek medical opinions. The lower courts cite no binding authority except purportedly, *Shalala v. Illinois Council, supra* at 14 (App. No. 5 at 5-7) and *Do Sung Uhm v. Humana, Inc.*, 620 F.3d 1134 (9th Cir. 2010), an exhaustion case in its Order dismissing two insurance carriers with prejudice. (App. No. 5)

45 C.F.R. § 85.61(l) provides that the agency may delegate its authority for conducting complaint investigations to a component agency or other federal agencies, except that the authority for making the final determination may not be delegated. Here HHS has an incurable conflict of interests to enforce compliance with Blue Shield and Envision since HHS' own policy, being based on a false premise, cannot enforce compliance under 45 C.F.R. Pt. 84.

If it is true that the lower Courts believed there was insufficient evidence pled under Sec. 504, it was an abuse of discretion to dismiss with prejudice without leave to amend.

HHS did not refer the administrative cases to the DOJ or elsewhere for Sec. 504 compliance and enforcement. The only realistic process for remedies under both Sec. 504 and Due Process violations[13] are federal courts which dismissed the two insurance companies lacking the same substantial evidence and including the same legal errors.

Finally, by dismissing Sec. 504, Due Process and the two HHS insurance contractors, there is no process to adjudicate the violations of Blue Shield and

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[13] As with HHS, *Mathews* requires a colorable claim and collaterality which exists by legal definition since, as HHS states, it has no jurisdiction under Fifth Amendment's Due Process and benefits under the Social Security Act are "property" under the Due Process Clause. -(*Mathews v. Eldridge*, 424 U.S. 319.)

Envision under Sec. 504 and it is unlikely that Due Process violations would ever be rectified.

G. An Exception Should Have Been Granted

An exception to obtain coverage was "denied" by the MAC under 42 C.F.R. § 423.578 *Exceptions process* which requires the prescribing physician to state why it is necessary, which he did; but both carriers denied they had to cover the medication. 42 C.F.R. § 423.578(e) "formulary process cannot be used to cover a drug that does not meet the definition of a Part D drug."

The MAC uses circular reasoning; i.e., using the most restrictive definition instead of a broader definition which is indicated under rules of construction. (AR 5, 17.) The Blue Shield carrier references it at AR 399, 400, and 402, *et seq.*, but to no avail. "…You and your provider can ask the plan to make an exception…" which was done and it should not have been rejected by HHS. 42 U.S.C. § 1395x(t)(2)(B) applies even if not on a compendia list: "…that such use is medically accepted based on supportive clinical evidence **in peer reviewed medical literature** (emphasis added) appearing in publications which have been identified for purposes of this subclause by the Secretary"

Indeed, the 5 HHS/NIH evidence kept out of the record are peer reviewed literature. See 42 U.S.C. § 289a - Peer review requirements. It does meet the statutory exception requirements. The insurance companies argued before the ALJs that it is not coverable except if HIV is present (presumably as a cost-saving mechanism). HHS, like Blue Shield and Envision, wanted to restrict the definition only as to the written version in DrugDex even though HHS and the carriers knew or should have known that conclusion has a false premise and presumably as such would make large profits.

H. The FDCA and Therefore a MAI Requires Safety and Effectiveness as a Matter of Law

The FDCA, 21 U.S.C. § 301 *et seq.* is the applicable statute being violated here and this Court states that "…FDCA requires premarket approval of any new drug, and further that the Food and Drug Administration (FDA) shall issue an order refusing to approve an application of a new drug if it is not **safe and effective** for intended purpose. 21 U.S.C. §§ 355(a)(b). If the FDA discovers after approval that a drug is unsafe or ineffective (emphasis added), …." 21 U.S.C.S. §§ 355(d)(1)-(2), (4)-(5), 21 U.S.C.S. §§ 355(e)(1)-(3). See *FDA v. Brown Williamson Tobacco Corp.,* 529 U.S. 120 (2000).[14]

This case concerns a false theory sometimes referred to as "implied or false certification." HHS, Blue Shield and Envision, in circular reasoning, ask Medicare beneficiaries and the federal judiciary to believe that the HIV requirement is based on FDA's current scientific reasoning based on trials. This is more accurately described as based on a false premise. In *Sekhar v. United States*, 570 U.S. 729 (2013) this Court holds that claims or, by logical extension, misrepresentation which omit critical information; i.e., that having HIV is required to qualify for Serostim for non-HIV lipodystrophy is actionable misrepresentation. This is analogous to the present case wherein the 5 NIH documents are evidence that HHS is intentionally misrepresenting to the public. This could not be for "safety and effectiveness" under the FDCA because Serostim is not a HIV treatment according to NIH research documents filed with the D.C.

I. HHS' POSITION

HHS' position is an irrational agency policy: specifically, that it wants to keep the lipodystrophy medication, Serostim only within the HIV-lipodystrophy population and not in the non-HIV lipodystrophy population. The agency further states that since Congress allows broader MAI for cancer patients, it should not allow the Medicare statutory language to apply peer review literature to this

[14] Superseded by statute in 2005, Tobacco Control Act, 21 U.S.C.S. § 387 et seq.

orphan drug. In 2013, 42 U.S.C. § 1395w-102(e)(4) allowed prescriptions to be used to treat epilepsy, cancer, or a chronic mental health disorder and Benzodiazepines. Peer review, the mission statement of NIH is a basis for broadening MAIs. Also see the (ODA) as amended, provides incentives to drug manufacturers to research treatment for diseases which affect a small portion of the population and, as such, is a Congressional mandate to provide prescription drugs for disorders affecting usually under 200,000 people such as non-HIV lipodystrophy, Huntington's disease, ALS (Lou Gehrig's disease), Tourette syndrome, and muscular dystrophy and/or other conditions as set forth in the ODA. Myalept which Petitioner requests this court take judicial notice (See App. No. 7) and Serostim, both FDA approved, fall under these categories.

IV. CONCLUSION

Based on the foregoing, Petitioner requests that his Petition be granted.

Dated: November 23, 2020

Respectfully submitted,
/s/ Steven Bruce

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V. APPENDIX

Appendix Table of Contents

Opinions, Orders & Findings of Fact (or Absence Thereof) Sought to be Reviewed

Publications Essential to Understand the Petition

NOT FOR PUBLICATION

FILED

OCT 20 2020

MOLLY C. DWYER, CLERK
U.S. COURT OF APPEALS

UNITED STATES COURT OF APPEALS

FOR THE NINTH CIRCUIT

STEVEN BRUCE, Plaintiff-Appellant, v. ALEX M. AZAR II, Secretary of the U.S. Department of Health and Human Services; et al., Defendants-Appellees.	No. 19-17565 D.C. No. 4:18-cv-05022-HSG MEMORANDUM*

Appeal from the United States District Court
for the Northern District of California
Haywood S. Gilliam, Jr., District Judge, Presiding

Submitted October 15, 2020**
San Francisco, California

Before: McKEOWN and NGUYEN, Circuit Judges, and VITALIANO,*** District Judge.

Steven Bruce appeals from the district court's orders granting motions to

* This disposition is not appropriate for publication and is not precedent except as provided by Ninth Circuit Rule 36-3.

** The panel unanimously concludes this case is suitable for decision without oral argument. *See* Fed. R. App. P. 34(a)(2).

*** The Honorable Eric N. Vitaliano, United States District Judge for the Eastern District of New York, sitting by designation.

dismiss filed by Blue Shield, Envision, and the Department of Health and Human Services ("DHHS") and granting DHHS's summary judgment motion on the remaining claim against it. Bruce claims that DHHS's denial of coverage under Medicare Part D for Serostim—a drug he was prescribed to treat his lipodystrophy and wasting syndrome—was not supported by substantial evidence and violated the Fifth Amendment Due Process Clause and Section 504 of the Rehabilitation Act. The parties are familiar with the facts, so we do not repeat them here. We affirm.

The Medicare Appeals Council's decision that Serostim was not a covered Part D drug is supported by substantial evidence and not based on legal error. *See Magallanes v. Bowen*, 881 F.2d 747, 750 (9th Cir. 1989). For purposes of the Medicare Act, a "covered part D drug" includes "any use of a covered part D drug for a medically accepted indication." *See* 42 U.S.C. § 1395w-102(e)(1)(B). A "medically accepted indication" is, in turn, defined as "any use for a covered outpatient drug" which is approved by the FDA or supported by citations in one of three pharmaceutical compendia. *See id.* §§ 1396r-8(k)(6), 1396r-8(g)(1)(B)(i). Serostim is FDA-approved for wasting syndrome in individuals with HIV and short bowel syndrome. There is no evidence that any of the compendia list non-HIV-related wasting syndrome—the condition Bruce suffers from—as an approved use of Serostim. Because Bruce was not prescribed Serostim for a

"medically accepted indication," the prescribed Serostim does not satisfy the Medicare Act's definition of a "covered part D drug."

Bruce argues that a "medically accepted indication" may also be supported by peer reviewed medical literature. *See* 42 U.S.C. § 1395x(t)(2)(B). However, the broader definition of "medically accepted indication" contained in § 1395x(t)(2)(B) applies only to drugs used in anticancer chemotherapeutic regimens and thus is not applicable here. *See id.* § 1395x(t)(2)(A). Bruce's argument that he is entitled to a medical necessity exception pursuant to 42 C.F.R. § 423.578 also fails because this section does not "allow an enrollee to . . . request or be granted coverage for a prescription drug that does not meet the definition of a Part D drug." 42 C.F.R. § 423.578(e).

The district court lacked jurisdiction over Bruce's due process and Rehabilitation Act claims against DHHS under 42 U.S.C. § 405(h). That section, which "purports to make exclusive the judicial review method set forth in [42 U.S.C.] § 405(g)," *Shalala v. Ill. Council on Long Term Care, Inc.*, 529 U.S. 1, 10 (2000), provides that "[n]o action against the United States, the Commissioner of Social Security, or any officer or employee thereof shall be brought under section 1331 or 1346 of title 28 to recover on any claim *arising under* [the Medicare Act]," 42 U.S.C. § 405(h) (emphasis added). "[O]ur case law establishes that where, at bottom, a plaintiff is complaining about the denial of Medicare benefits—[such as]

drug benefits under Part D—the claim 'arises under' the Medicare Act." *Do Sung Uhm v. Humana, Inc.*, 620 F.3d 1134, 1142–43 (9th Cir. 2010). Because Bruce's due process and Rehabilitation Act claims are, at bottom, about the denial of Medicare benefits, these claims "arise under" the Medicare Act and § 405(h) bars judicial review of them.

Bruce's claims against Envision and Blue Shield, the insurers that administered Bruce's Medicare Part D prescription drug plan, are also about the denial of Medicare benefits and arise under the Medicare Act. As such, those claims, too, are subject to 42 U.S.C. §§ 405(h) and (g) and related Medicare regulations. Pursuant to these statutes and regulations, Envision and Blue Shield were not properly named as defendants in this action. *See* 42 C.F.R. § 423.2136(d)(1) (providing that in a civil action seeking court review of a Medicare Appeals Council decision, the Secretary of DHHS is "*the* proper defendant" (emphasis added)); *Do Sung Uhm*, 620 F.3d at 1145 ("[Appellants] cannot circumvent § 405(h)'s requirements by suing [the Part D prescription drug provider].").

Finally, the district court did not abuse its discretion in denying Bruce's motion to supplement the administrative record. The administrative record is presumed to be complete, and Bruce did not present "clear evidence to the contrary" rebutting this presumption. *See In re United States*, 875 F.3d 1200, 1206

(9th Cir. 2017), *cert. granted, judgment vacated on other grounds*, 138 S. Ct. 443 (2017). Nor did Bruce demonstrate that any of the narrow exceptions allowing the reviewing court to consider extra-record evidence applied. *See San Luis & Delta–Mendota Water Auth. v. Locke*, 776 F.3d 971, 992–93 (9th Cir. 2014).

AFFIRMED.[1]

[1] Bruce's motions to take judicial notice (Dkt. 7) and supplement the record on appeal (Dkt. 29) are denied.

UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

STEVEN BRUCE,

Plaintiff,

v.

ALEX M. AZAR,

Defendant.

Case No. 18-cv-05022-HSG

ORDER ON CROSS MOTIONS FOR SUMMARY JUDGMENT

Re: Dkt. Nos. 90, 94

Pending before the Court are the parties' cross motions for summary judgment. Dkt. Nos. 90 ("Pl. Mot"), 94 ("Def. Mot"). The Court held a hearing on the motions on December 5, 2019. After carefully considering the papers and the parties' arguments, the Court **DENIES** Plaintiff's motion for summary judgment and **GRANTS** Defendant's motion for summary judgment.

I. BACKGROUND

Plaintiff Stephen Bruce filed this action on August 16, 2018, seeking judicial review of the final decision by the Medicare Appeals Council ("MAC") denying Plaintiff coverage for the drug Serostim. Dkt. No. 1. The Court provides the relevant statutory framework and facts below.

A. Part D of the Medicare Act

The Medicare Act, established under Title XVIII of the Social Security Act, 42 U.S.C. § 1395 *et seq.*, provides coverage for certain medical services to eligible aged and disabled individuals. *Maximum Comfort Inc. v. Sec'y of Health & Human Servs.*, 512 F.3d 1081, 1083 (9th Cir. 2007). At issue here is Part D of the program, which is a voluntary prescription drug benefit program established by the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 ("Medicare Modernization Act"). Pub. L. No. 108–173, 117 Stat. 2066 (2012). Part D provides coverage for certain types of drugs: (1) prescription drugs; (2) biological products;

(3) insulin and insulin supplies used to inject insulin; and (4) vaccines. *See* 42 U.S.C. § 1395w-102(e).

Under the statute, the term "covered part D drug" includes "any use of a covered part D drug for a medically accepted indication." *Id.* § 1395w-102(e)(1). The definition of "medically accepted indication" depends on whether the medication is used in an "anticancer chemotherapeutic regimen." *Id.* § 1395w-102(e)(4). If not, as is the case here, "medically accepted indication" is defined by cross-reference to 42 U.S.C. § 1396r-8(k)(6), which states:

> The term "medically accepted indication" means any use for a covered outpatient drug which is approved under the Federal Food, Drug, and Cosmetic Act or the use of which is supported by one or more citations included or approved for inclusion in any of the compendia described in subsection (g)(1)(B)(i).

Id. § 1396r-8(k)(6). The "compendia described in subsection (g)(1)(B)(i)" consist of: (1) the American Hospital Formulary Service Drug Information ("AHFS-DI"); (2) United States Pharmacopeia-Drug Information ("USPDI") (or its successor publication); and (3) the DRUGDEX Information System. *Id.* § 1396r-8(g)(1)(B)(i).

B. Plaintiff's Requests for Coverage of Serostim

Plaintiff is a Medicare beneficiary enrolled in Part D, administered by Envision in 2016 and Blue Shield in 2017. AR 49, 720.[1] In July 2016, he was diagnosed with lipodystrophy or wasting syndrome (used interchangeably in Plaintiff's case), a rare disorder which causes Plaintiff to suffer from severe and progressive weight loss. AR 82. To halt this weight loss, his primary physician, Dr. Louis J. Cubba, M.D., prescribed Serostim, which Dr. Cubba said was the only medication "that was able to successfully halt his progressive, life threatening, weight loss." *Id.*

Plaintiff submitted a request for coverage of Serostim to his insurers, Envision in 2016 and Blue Shield in 2017. *See* AR 184–85, 192–94, 630–31. Both insurers denied coverage because Plaintiff's use of Serostim for lipodystrophy was not prescribed for a "medically accepted indication." *See id.*

[1] References to AR refer to the certified administrative record filed and attached as exhibits to the Declaration of Kimberly A. Robinson. Dkt. Nos. 64-7, 64-8, 64-9, 64-10.

i. Plaintiff's Appeal in 2016

In September 2016, Plaintiff filed a reconsideration request with the independent review entity ("IRE"). AR 1217–18. The physician reviewer found that the "Part D Plan was correct in denying the request for Serostim," because it was prescribed for "off-label (non-FDA) approved uses," and the Medicare-approved compendia "do not contain any citations to support the use of this drug for these conditions." AR 1217.

Plaintiff requested a hearing before an administrative law judge ("ALJ"). AR 997. ALJ James Myles held a telephone hearing with Plaintiff on October 21, 2016, and on November 15, 2016, ALJ Myles issued a decision against Plaintiff. AR 997–1003. ALJ Myles stated that while he was "sympathetic to Mr. Bruce's situation," he was bound by Medicare Part D coverage requirements, which state that the "proposed used of Medication must be supported by approved on label use by the FDA or Medicare-recognized compendia." AR 1002. Based on the record and evidence presented, ALJ Myles found that Plaintiff was requesting coverage of Serostim for "off-label, non-FDA approved uses which are not 'medically accepted indications' as defined by Medicare law." AR 1002–03. Therefore, he concluded that Plaintiff's Plan was not required to provide coverage for Serostim. AR 1003.

Plaintiff appealed ALJ Myles's decision to the MAC. AR 1031–32. The MAC remanded the case back to ALJ Myles, because the claim file did not include a copy of "either the FDA label or the Medicare-approved compendia." AR 1032. The MAC instructed the ALJ to obtain a copy of the Plan's "Evidence of Coverage and formulary for 2016, the FDA label, and the Medicare-approved compendia." *Id.*

On remand, ALJ Myles issued another unfavorable decision on March 30, 2018. AR 720–27. He did not dispute Plaintiff's credibility, or that Serostim is helpful for Plaintiff to maintain his weight. AR 726–27. However, he concluded that "[g]iven the information found on the FDA's label and the Medicare approved compendia, Serostim is not prescribed for a medically accepted indication." AR 727. Plaintiff again appealed the decision. *See* AR 12.

ii. Plaintiff's Appeal in 2017

After Blue Shield denied coverage in 2017, Plaintiff filed a reconsideration request with

the IRE. *See* AR 619. The IRE, after conducting a "new and independent review of the appeal," concluded that Plaintiff's Part D Plan was not required to cover Serostim. *Id.* The physician reviewer determined that there "are no citations in the Medicare approved compendia that support the use of Serostim for the diagnosed condition," and as a result, "the drug is not being prescribed for a medically accepted indication as defined by Medicare law." AR 620.

Plaintiff then requested an ALJ hearing on May 1, 2017. AR 660. ALJ Jeffrey Gulin dismissed the request because he found that ALJ Myles's decision was based "on the same facts and on the same issues" as the appeal before him and thus binding. *Id.* The MAC remanded the case back to ALJ Gulin, because it found that the facts in the decision by ALJ Myles were "not the same as the facts at issue here," given Plaintiff was seeking coverage under two different Medicare Part D prescription drug plans (in other words, under Envision in 2016 and Blue Shield in 2017). AR 323. After a telephone hearing, ALJ Gulin issued an unfavorable decision on March 15, 2018. AR 49–56. Based on the evidence and record presented, he found that Serostim was not being used for a medically accepted indication. AR 56. Plaintiff appealed the decision. *See* AR 12–17.

iii. MAC Decision

The MAC reviewed and adopted both ALJs' decisions. *Id.* In its July 12, 2018 order, the MAC acknowledged Plaintiff's argument "that there is no realistic difference between the Human Immunodeficiency Virus and the virus which the appellant asserts has caused the autoimmune disease that is the basis for his condition." AR 16. However, the MAC found that "the similarity of a diagnosis to a covered diagnosis is simply not a basis on which we direct Part D coverage." *Id.* Because the FDA label and Medicare compendia did not list Plaintiff's prescribed use, the MAC concluded that Part D did not cover Serostim in Plaintiff's case.[2] *Id.*

C. This Action

Following the MAC's decision, Plaintiff filed this civil action challenging the July 2018

[2] Plaintiff also sent a letter to the Administrative Appeals Judge, requesting that the MAC "make findings on the Section 504 of the Rehabilitation Act of 1973, the due process clause of the Fifth Amendment, and offer a reason for why [the MAC] remanded these cases without including the above copy of the 'FDA label or the AHFS-DI' for Serostim." AR 8–9. The MAC construed the letter as a request to reopen its July 2018 decision and held that Plaintiff did not show good cause for reopening. AR 2.

MAC decision. Dkt. No. 1. He named Blue Shield, Envision, and Alex M. Azar II, Secretary of the United States Department of Health and Human Services ("DHHS"), as Defendants. *Id.* Defendants filed motions to dismiss, which the Court granted on June 18, 2019. Dkt. No. 83. Currently, the only remaining Defendant is DHHS, and the only remaining cause of action is Plaintiff's first cause of action, which seeks review of the final decision by the MAC.[3] *See id.*

II. STANDARD OF REVIEW

A Medicare beneficiary may obtain judicial review of the MAC's final decision denying Part D coverage under 42 U.S.C. § 405(g). *See* 42 U.S.C. § 1395w-104(h) (incorporating Part C's judicial review provision, § 1395w–22(g), which provides for judicial review under § 405(g)). The governing regulations specify that a Part D beneficiary may obtain court review if the amount in controversy meets the threshold requirement estimated annually by the Secretary of DHHS. 42 C.F.R. § 423.2136(a).

Under the Administrative Procedure Act, the district court may set aside an agency decision that is "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." *Palomar Med. Ctr. v. Sebelius*, 693 F.3d 1151, 1159 (9th Cir. 2012) (citation and quotations omitted). A district court may disturb the decision to deny benefits only if the decision is either not supported by substantial evidence, or is based on legal error. *Burch v. Barnhart*, 400 F.3d 676, 679 (9th Cir. 2005). "Substantial evidence means such relevant evidence as a reasonable mind might accept as adequate to support a conclusion. The evidence must be more than a mere scintilla, but may be less than a preponderance." *Molina v. Astrue*, 674 F.3d 1104, 1110–11 (9th Cir. 2012) (quotations and citations omitted). The court must consider the administrative record as a whole, weighing both the evidence that supports the decision and the evidence that detracts from it. *McAllister v. Sullivan*, 888 F.2d 599, 602 (9th Cir. 1989). If the evidence can rationally

[3] The Court dismissed Plaintiff's second and third causes of action, which alleged that Defendants violated Plaintiff's due process rights and Section 504 of the Rehabilitation Act of 1973, because the Court determined that it did not have subject matter jurisdiction over those two claims under *Shalala v. Ill. Council on Long Term Care, Inc.*, 529 U.S. 1 (2000). Dkt. No. 83 at 5–8. Plaintiff attempts to relitigate those issues in his motion for summary judgment. Pl. Mot. at 13–15. But the Court declines to do so, and will not consider Plaintiff's arguments as to those two causes of action.

be interpreted in more than one way, the court must uphold the agency's decision. *Mayes v. Massanari*, 276 F.3d 453, 459 (9th Cir. 2001).

III. DISCUSSION

A. Plaintiff's Prescription for Serostim Is Not For a "Medically Accepted Indication"

As already discussed, Plaintiff's use of Serostim is covered by Part D only if it is used for a "medically accepted indication," meaning it is prescribed for an FDA-approved use or listed in one of the approved compendia. *See* 42 U.S.C. § 1396r-8(k)(6). Upon review of the record presented, the Court finds that Serostim was not used for a medically accepted indication.

The FDA label included in the record states that Serostim is "indicated for the treatment of HIV patients with wasting or cachexia to increase lean body weight, and improve physical endurance." AR 317; *see also* AR 16 (MAC decision citing to the FDA website and finding the same). Plaintiff does not dispute this, nor does he dispute that he does not have HIV-related wasting syndrome. As to the compendia requirement, the DRUGDEX compendium included in the administrative record lists the following uses for Serostim: cachexia associated with AIDs, growth hormone deficiency, and short bowel syndrome. AR 787–88. It also lists fat maldistribution for HIV infection as a non-FDA (or off-label) use. AR 788. ALJ Gulin noted that the AHFS-DI compendium did not identify any uses for Serostim outside the FDA approved indications.[4] AR 25. Based on the administrative record, there is no suggestion that any of the relevant compendia list non-HIV-related lipodystrophy as a use for Serostim.

Plaintiff argues that the phrase "medically accepted indication" is merely "illustrative, not definitional." Dkt. No. 98 at 5. But as DHHS notes, district courts in this circuit have rejected

[4] Plaintiff, in his reply brief, again seeks to supplement or complete the administrative record, a request the Court previously denied. Dkt. No. 98 at 6. He also filed two administrative motions requesting to file extra-record evidence. Dkt. Nos. 100, 102. The Court incorporates its prior analysis finding that Plaintiff failed to rebut with clear evidence the presumption that the record is complete, or present any evidence that an exception applies to allow the Court to consider extra-record evidence. *See* Dkt. No. 83 at 10–11. Accordingly, the Court **DENIES** Plaintiff's administrative motions to file additional documents. *See* Dkt. Nos. 100, 102. And even were the Court to consider the additional materials Plaintiff seeks to introduce, the Court finds that these materials would not change its analysis.

that very same argument. *See, e.g.*, *Nievod v. Sebellius*, No. C 11-4134 SBA, 2013 WL 503089, at *10 (N.D. Cal. Feb. 8, 2013); *United States v. Celgene Corp.*, 226 F. Supp. 3d 1032, 1047 (C.D. Cal. 2016) ("We note, however, that CMS and a clear majority of district courts have read this clause to incorporate the medical acceptance limitation, while only one district court has read it differently." (collecting cases)); *Broome v. Burwell*, No. 6:14-CV-01248-MC, 2015 WL 1526532, at *4 (D. Or. Apr. 1, 2015); *Rickhoff v. U.S. Sec'y ex rel. Dep't of Health & Human Servs.*, No. CV-11-2189-PHX-DGC, 2012 WL 6177411, at *4 (D. Ariz. Dec. 11, 2012). The Court agrees with the reasoning of these decisions, and finds it clear under the plain terms of the statute that a covered Part D drug must satisfy the medically accepted indication requirement.[5]

According to Plaintiff, providing coverage only to those who have HIV-related lipodystrophy, and not to those who have non-HIV-related lipodystrophy, is "unreasonable based on the lack of [a] relevant connection." Pl. Mot. at 12; *see also* Dkt. No. 98 at 8 (arguing it is "irrational and violative of substantive due process" to require Plaintiff to have HIV with lipodystrophy to qualify for coverage). Whether Part D *should* cover Plaintiff's use of Serostim to treat his condition because it has similar symptoms to those of patients with covered conditions is a policy matter not within the Court's competence to decide. The Court echoes the sentiments expressed by the MAC and ALJs, and is sympathetic to Plaintiff's situation. But the only issue before the Court is whether the MAC's decision to deny coverage either was not supported by substantial evidence or constituted legal error. Based on the record and for the reasons already discussed, the Court finds the MAC's decision to be supported by substantial evidence and not based on legal error.

B. 42 C.F.R. § 423.578 Exception

Plaintiff also argues that the MAC failed to apply an exception under 42 C.F.R. § 423.578.[6] Pl. Mot. at 14. Contrary to Plaintiff's argument, the MAC did consider this exception and held that Plaintiff did not qualify. AR 6. To qualify for a formulary exception under 42

[5] The Court finds Plaintiff's out-of-circuit cases inapposite or not persuasive. *See* Dkt. No. 98 at 5, 9 (citing cases).

[6] Plaintiff appears to invoke 42 C.F.R. § 421.2112(a) as another exception, Pl. Mot. at 14, but this regulation outlines the requirements for requesting review of an ALJ action.

C.F.R. § 423.578(b), the drug must be "medically necessary, consistent with the physician's or other prescriber's statement under paragraph (b)(5) of this section, and that the drug would be covered but for the fact that it is an off-formulary drug." 42 C.F.R. § 423.578(b). However, "[n]othing in this section may be construed to allow an enrollee to use the exceptions process set out in this section to request or be granted coverage for a prescription drug that does not meet the definition of a Part D drug." *Id.* § 423.578(e).

The MAC found that the "formulary process cannot be used to cover a drug that does not meet the definition of a Part D drug." AR 6. Because Serostim in Plaintiff's case "does not meet the definition of a Part D drug," the MAC concluded that "there is no basis on which a formulary exception for Serostim can be granted." *Id.* As already discussed, Plaintiff has not shown that his prescribed use of Serostim meets the definition of a Part D drug. Thus, the Court does not find the MAC's determination to be arbitrary, capricious, or not in accordance with the law.

IV. DISCUSSION

The Court **DENIES** Plaintiff's motion for summary judgment, **GRANTS** Defendant's motion for summary judgment, and **DENIES** Plaintiff's administrative motions to file additional documents. Dkt. Nos. 90, 94, 100, 102. The MAC's decision is affirmed. The Court directs the Clerk to enter judgment in Defendant's favor and close the case. No further filings will be accepted in this closed case.

IT IS SO ORDERED.

Dated: 12/16/2019

Haywood S. Gilliam, Jr.

HAYWOOD S. GILLIAM, JR.
United States District Judge

United States District Court
Northern District of California

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Attorneys for Plaintiff

UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

STEVEN BRUCE,

Plaintiff,

vs.

ALEX M. AZAR II, Secretary of the Department of Health and Human Services, ENVISION INSURANCE COMPANY, BLUE SHIELD OF CALIFORNIA, and DOES 1-50,

Defendants.

Case No. 4:18-cv-05022 HSG

PLAINTIFF'S NOTICE OF MOTION, MOTION, AND MEMORANDUM OF POINTS AND AUTHORITIES IN SUPPORT OF MOTION TO SUPPLEMENT THE ADMINSITRATIVE RECORD

Date: November 8, 2018 [Requested]
Time: 2:00 PM
Judge: Hon. Haywood S. Gilliam, Jr., Crtrm 2
Location: 1301 Clay St., Floor 4, Oakland, California 94612

NOTICE OF MOTION AND MOTION

TO ALL PARTIES AND THEIR ATTORNEYS OF RECORD:

PLEASE TAKE NOTICE that on _____, at 2:00 PM, or as soon thereafter as the matter may be heard before the Honorable Judge Haywood S. Gilliam, Jr., in the United States District Court for the Northern District of California, Courtroom 2, located on the 4th Floor of the United States Courthouse, at 1301 Clay Street, Oakland, California, Plaintiff Steven Bruce will, and hereby does move this Court for an order compelling Defendant U.S. Department of Health and

Human Services (DHHS), Alex M. Azar, III, in his official capacity as Secretary of the DHHS to supplement the Administrative Record (AR) in this action with the following documents:

1. Copy of the FDA label for Serostim; and
2. Copy of the AHFS-DI compendium for Serostim.

This motion is based on this Notice of Motion and Motion, the Memorandum of Points and Authorities, and the Declaration of Zoya Yarnykh (Yarnykh Decl.) filed concurrently herewith.

MEMORNADUM OF POINTS AND AUTHORITIES IN SUPPORT OF MOTION TO SUPPLEMENT THE ADMINISTRATIVE RECORD

I. INTRODUCTION

Plaintiff Steven Bruce filed the Complaint in this action on August 16, 2018 (Doc. 1) and First Amended Complaint on September 20, 2018 (Doc. 19) seeking reversal of the decision of the Medicare Appeals Council's (MAC) decision to deny coverage for Serostim under Title XVIII of the Social Security Act, and alleging violations of the due process clause of Fifth Amendment to the United States Constitution, violation of Section 504 of the Rehabilitation Act of 1973, and violation of Title III of Americans with Disabilities Act.

Plaintiff now brings this motion to compel Defendant DHHS to supplement the AR with documents which were noted to be missing from it, specifically the FDA label for Serostim and the AHFS-DI compendium for Serostim. Defendant has refused to voluntarily supplement the record or state in writing that these documents, which are not part of the AR according to the HHS/Medicare's final decision by an Appeals Council Judge, are irrelevant to their FRCP 12(b)(6) motion necessitating the filing of this motion. True and correct copies of emails between counsel discussing this matter are attached as Ex. B to the Yarnykh Decl.

Plaintiff and Defendants stipulated to extend the time to file a dispositive motion to November 13, 2018, with the answer and the AR due on December 19, 2018 (Doc. 20). Plaintiff does not have access to the AR. Plaintiff's response to the motion would be November 27, 2018.

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II. ARGUMENT

A. Applicable Law

The Administrative Procedure Act (APA) provides for judicial review of agency action based on the adversarial review of the administrative record. 5 U.S.C. § 706. A complete and thorough administrative record is necessary so that the Court can decide whether the agency "failed to consider an important aspect of the problem," or failed to "explain the evidence which is available." *Motor Vehicle Manufacturers Ass'n v. State Farm Mutual Automobile Insurance Co.*, 463 U.S. 29, 43 (1983). Before the district court can review the parties' dispositive motions and merits briefs, a court must base its review of a final agency action under the APA on the "whole record." 5 U.S.C. § 706. The "whole record" consists of "everything that was before the agency pertaining to the merits of its action." *Portland Audubon Soc. v. Endangered Species Comm.*, 984 F.2d 1534, 1548 (9th Cir. 1993).

Generally speaking, judicial review of informal agency actions is confined to a review of the record that was before the agency at the time it made its decision. This basic precept of administrative law is often called the "record rule." This rule, as established by the United States Supreme Court in *Citizens to Preserve Overton Park, Inc. v.* Volpe, 401 U.S. 402 (1971) serves a valuable function. It ensures that courts do not engage in free-roaming de novo review of agency decisions, instead leaving to the expert agencies the difficult task of scientific and policy assessment for which they were created in the first place. However, several exceptions exist, including a situation where the agency has considered or relied on documents, yet has failed to include such documents in its administrative record. In such a situation, the court should nonetheless consider those documents during judicial review. *Id.* at 420.

In *Thompson v. Department of Labor*, 885 F. 2d 551 (9th Cir. 1989), for example, the Ninth Circuit explained: "The whole administrative record . . . is not necessarily those documents that the agency has compiled and submitted as 'the' administrative record. The 'whole' administrative record, therefore, consists of all documents and materials directly or indirectly considered by agency decision-makers and includes evidence contrary to the agency's position."

Id., at 555 (citation and some internal quotation marks omitted).

B. The Medicare Appeals Council Considered the FDA Label and the Compendia for Serostim in Reaching Its Decision and Therefore It Must Be Included in the Administrative Record.

The MAC issued its final decision denying coverage to Plaintiff for Serostim on July 12, 2018. A true and correct copy of that decision is attached as Exhibit A to the Yarnykh Decl. On page four of the decision, the MAC Judge noted that "the administrative record does not contain a copy of the FDA label or the AHFS-DI compendium for Serostim". Thereafter on page five of the decision, the MAC stated: "[a]according to the record before the Council . . . the FDA has approved Serostim for treatment of 'HIV patients with wasting or cachexia. . .' as well as 'for short bowel syndrome'". The Council went on to state that "[t]he ALJ also found that the Medicare-approved compendia cited off-label use of Serostim for 'fat misdistribution from HIV infection'".

It is unclear how the MAC could have obtained this information without considering the information contained on the FDA label or the compendia for Serostim[1]; yet, the label and the AHFS-DI compendium are not part of the AR according to the final decision of DHHS.

Where the agency has considered or relied on documents, yet has failed to include such documents in its administrative record, the court should nonetheless consider those documents during judicial review. This is consistent with *Citizens to Preserve Overton Park, Inc. v. Volpe*, 401 U.S. 402 (1971) because of the Supreme Court's admonition that judicial review is to be based upon the full record that was before the decision maker when the decision was made. Courts have consistently rejected attempts by agencies to look only to that record compiled and submitted by the agency, to the exclusion of other documents that were clearly considered. As the D.C. Circuit Court of Appeals has explained, "[t]o review less than the full administrative record might

[1] The MAC referenced additional Medicare-approved compendia in addition to the AHFS-DI, including DRUGDEX and USP-DI, which are not at issue in this motion, as only the AHFS-DI was noted as not being part of the record.

allow a party to withhold evidence unfavorable to its case, and so the APA requires review of 'the whole record.'" The Ninth Circuit recognizes this important exception to the "record rule." *Thompson v. U. S. Dep't of Labor*, 885 F.2d 551, 555–56 (9th Cir. 1989).

Therefore, Plaintiff respectfully asks that this Court order Defendant DHHS to supplement the AR with the FDA label and the AHFS-DI compendium for Serostim. Pursuant to Federal Rule of Evidence 102 requires administering every proceeding fairly, eliminating unjustifiable expense and delay, and promoting the development of evidence law, to the end of ascertaining the truth and securing a just determination. There is substantial prejudice to Plaintiff if Defendant relies on documents not made available to Plaintiff.

CONCLUSION

Based on the above, Plaintiff respectfully asks that this Court order Defendant DHHS/Secretary Azar to supplement the AR with the FDA label and the AHFS-DI compendium for Serostim, and produce these documents to Plaintiff no later than November 13, 2018.

In the alternative, Plaintiff requests that this Court ordered DHHS not to file any dispositive motion until after discovery is closed.

Dated: 10/25/18

PEOPLE WITH DISABILITIES FOUNDATION

By: /s/ Zoya Yarnykh
ZOYA YARNYKH
Attorneys for Plaintiff

No. 19-17565

UNITED STATES COURT OF APPEALS
FOR THE NINTH CIRCUIT

STEVEN BRUCE,
Plaintiff-Appellant,
v.
ALEX AZAR, II,
SECRETARY OF HEALTH AND HUMAN SERVICES, *Et Al*
Defendant-Appellee

APPEAL FROM THE
UNITED STATES DISTRICT COURT
FOR THE
NORTHERN DISTRICT OF CALIFORNIA

MOTION TO TAKE JUDICIAL NOTICE PURSUANT TO FEDERAL RULES OF EVIDENCE 201

STEVEN BRUCE, SBN 70300
People With Disabilities Foundation
507 Polk Street, Suite 430
San Francisco, CA 94102
Phone: (415) 931-3070
Facsimile: (415) 931-2828
Email: steveb@pwdf.org

I. INTRODUCTION

Appellant ("Bruce") argued a FDCA approved prescription Drug, Myalept (generic, Metreleptin) in the District Court ("D.C.") and now moves this Court to take Judicial Notice of its 2014 approval and the population for which it is approved. The D.C. did not include this in its Order(s).

II. REQUEST

A. Pursuant to Federal Rules of Evidence 201, Bruce now requests this Court take Judicial Notice that Myalept was approved in February 2014 for anyone with generalized Lipodystrophy and cautioned if an individual has HIV.

It is relevant and material to the underlying issue in the present case, whether Serostim can be denied coverage under Medicare, Part D if a patient does not have HIV. In D.C. HHS argued they do not have to approve medications because they are rare conditions and Lipodystrophy is too rare to for the FDA to be bothered with. (HHS Cross MSJ (Doc.94 at 11.) In Bruce's MSJ Reply Brief (Doc. 98 at 8-9) he states HHS omits the FDA approved Myalept for treatment of Generalized Lipodystrophy in 2014 (https://nordiclifescience.org/fda-approves-myalept-to-treat-rare-metabolic-disease. (Last visited October 13, 2019.)

As stated in the attached Myalept label under "Indications and usage", "Patients with Generalized Lipodystrophy – Myalept (generic - metreleptin) for

injection is indicated as an adjunct to diet as replacement therapy to treat the complications of leptin deficiency in....."

Mr. Bruce is aware that Lymphoma is a significant side effect of Myalept; however, that decision, will be decided by him at the appropriate time. He is also aware that Myalept is cautioned for use by people with HIV.

III. CONCLUSION

Based on the foregoing Bruce requests this Court take notice thereof.

/s/
Dated: March 23, 2020 Steven Bruce, Appellant, Attorney

No. 19-17565

UNITED STATES COURT OF APPEALS
FOR THE NINTH CIRCUIT

STEVEN BRUCE,
Plaintiff-Appellant,
v.
ALEX AZAR, II,
SECRETARY OF HEALTH AND HUMAN SERVICES, *Et Al*
Defendant-Appellee

APPEAL FROM THE
UNITED STATES DISTRICT COURT
FOR THE
NORTHERN DISTRICT OF CALIFORNIA

DECLARATION STEVEN BRUCE IN SUPPORT OF MOTION TO TAKE JUDICIAL NOTICE PURSUANT TO FEDERAL RULES OF EVIDENCE 201

STEVEN BRUCE, SBN 70300
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507 Polk Street, Suite 430
San Francisco, CA 94102
Phone: (415) 931-3070
Facsimile: (415) 931-2828
Email: steveb@pwdf.org

DECLARATION

I, Steven Bruce hereby DECLARE as follows:

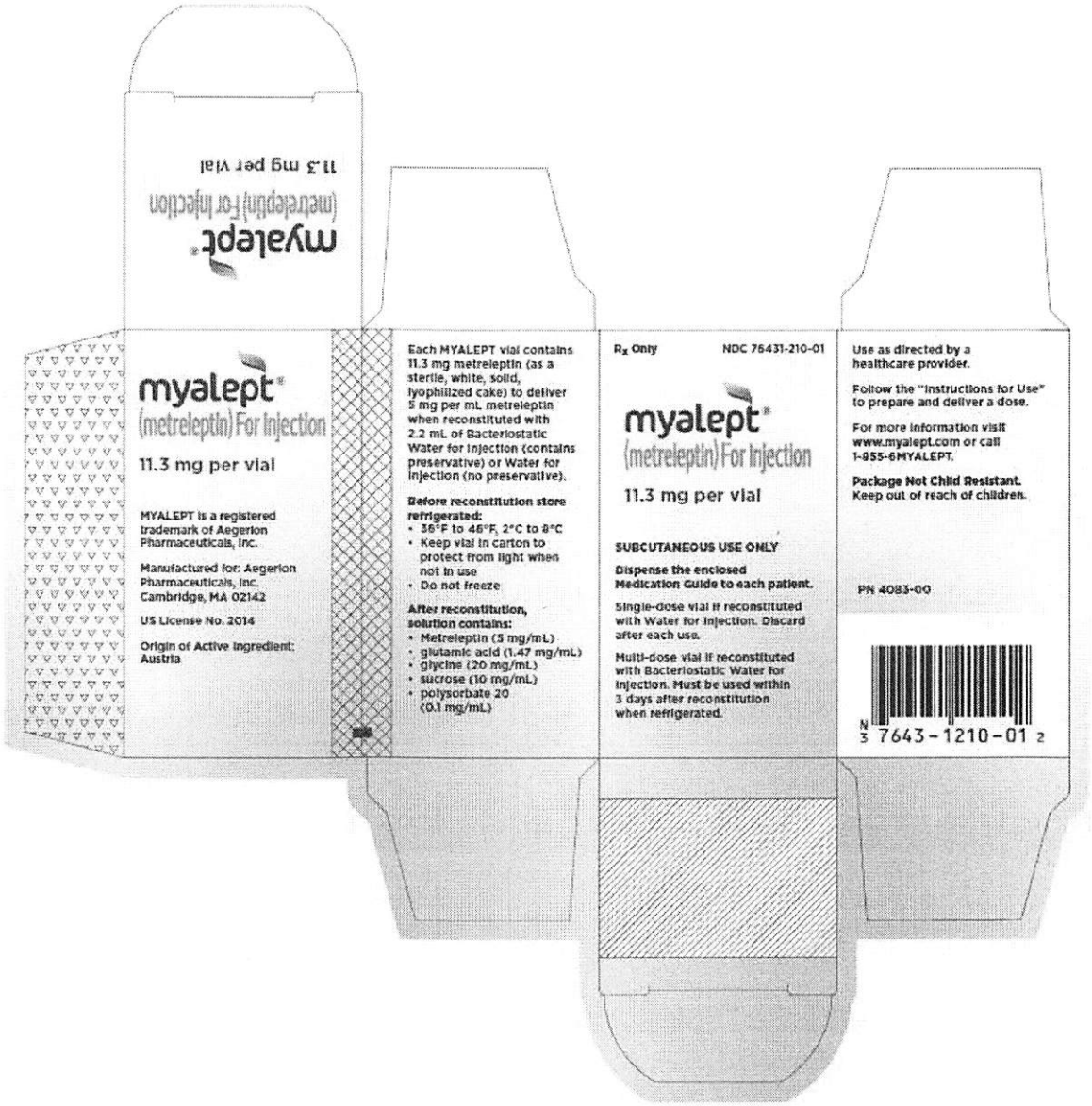
1. I, am the APPELLANT herein and an employee of People With Disabilities Foundation based in San Francisco, California.
2. Federal Food, Drug and Cosmetic Act, Section 201(k) defines label as a: 'display of written, printed, or graphic matter upon the immediate container of any article....' A FDA label is part of the FDA approval process.
3. I declare under penalty of perjury that the facts on the Motion to Take Judicial Notice are true based on my knowledge and belief and that this declaration was executed in NY., NY on March 7, 2020

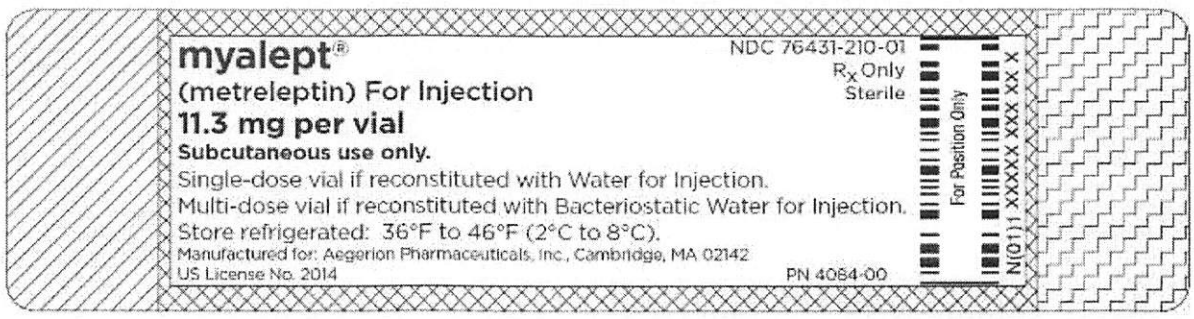
/Steven Bruce/

Steven Bruce

Label: MYALEPT- metreleptin injection, powder, lyophilized, for solution

View Package Photos


myalept
(metreleptin) For Injection
11.3 mg per vial
myalept
(metreleptin) For Injection
11.3 mg per vial
MYALEPT is a registered trademark of Aegerion Pharmaceuticals, Inc.
Manufactured for: Aegerion Pharmaceuticals, Inc. Cambridge, MA 02142
US License No. 2014
Origin of Active Ingredient: Austria
Each MYALEPT vial contains 11.3 mg metreleptin (as a sterile, white, solid, lyophilized cake) to deliver 5 mg per mL metreleptin when reconstituted with 2.2 mL of Bacteriostatic Water for Injection (contains preservative) or Water for Injection (no preservative).
Before reconstitution store refrigerated:
• 36°F to 46°F, 2°C to 8°C
• Keep vial in carton to protect from light when not in use
• Do not freeze
After reconstitution, solution contains:
• Metreleptin (5 mg/mL)
• glutamic acid (1.47 mg/mL)
• glycine (20 mg/mL)
• sucrose (10 mg/mL)
• polysorbate 20 (0.1 mg/mL)
Rx Only
NDC 76431-210-01
myalept
(metreleptin) For Injection
11.3 mg per vial
SUBCUTANEOUS USE ONLY
Dispense the enclosed Medication Guide to each patient.
Single-dose vial if reconstituted with Water for Injection. Discard after each use.
Multi-dose vial if reconstituted with Bacteriostatic Water for Injection. Must be used within 3 days after reconstitution when refrigerated.
Use as directed by a healthcare provider.
Follow the "Instructions for Use" to prepare and deliver a dose.
For more information visit www.myalept.com or call 1-855-6MYALEPT.
Package Not Child Resistant.
Keep out of reach of children.
PN 4083-00
N 3 7643-1210-01 2


myalept®
(metreleptin) For Injection
11.3 mg per vial
Subcutaneous use only.
Single-dose vial if reconstituted with Water for Injection.
Multi-dose vial if reconstituted with Bacteriostatic Water for Injection.
Store refrigerated: 36°F to 46°F (2°C to 8°C).
Manufactured for: Aegerion Pharmaceuticals, Inc., Cambridge, MA 02142
US License No. 2014
PN 4084-00
NDC 76431-210-01
Rx Only
Sterile
For Position Only
N(01)1 XXXXX XXX XX X

Safety

- Boxed Warnings
- Report Adverse Events
- FDA Safety Recalls
- Presence in Breast Milk

Related Resources

- Medline Plus
- Clinical Trials
- PubMed
- Biochemical Data Summary

More Info For This Drug

- View Label Archives
- RxNorm
- Get Label RSS Feed
- View NDC Code(s)NEW!

- **NDC Code(s):** 76431-210-01
- **Packager:** Aegerion Pharmaceuticals, Inc.

- **Category:** HUMAN PRESCRIPTION DRUG LABEL
- **DEA Schedule:** None
- **Marketing Status:** Biologic Licensing Application

Drug Label Information

Updated December 20, 2019

If you are a consumer or patient please visit this version.

- Download DRUG LABEL INFO: PDF XML
- Medication Guide: HTML
- Official Label (Printer Friendly)

View All Sections

- HIGHLIGHTS OF PRESCRIBING INFORMATION

  These highlights do not include all the information needed to use MYALEPT safely and effectively. See full prescribing information for MYALEPT. MYALEPT® (metreleptin) for injection for subcutaneous ...

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Table of Contents

WARNING: RISK OF ANTI-METRELEPTIN ANTIBODIES WITH NEUTRALIZING ACTIVITY AND RISK OF LYMPHOMA

Anti-metreleptin antibodies with neutralizing activity have been identified in patients treated with MYALEPT. The consequences of these neutralizing antibodies are not well characterized but could include inhibition of endogenous leptin action and/or loss of MYALEPT efficacy. Severe infection and/or worsening metabolic control have been reported. Test for anti-metreleptin antibodies with neutralizing activity in patients who develop severe infections or show signs suspicious for loss of MYALEPT efficacy during treatment. Contact Aegerion Pharmaceuticals, Inc. at 1-866-216-1526 for neutralizing antibody testing of clinical samples [see Contraindications (4.1) and Warnings and Precautions (5.1)].

T-cell lymphoma has been reported in patients with acquired generalized lipodystrophy, both treated and not treated with MYALEPT. Carefully consider the benefits and risks of treatment with MYALEPT in patients with significant hematologic abnormalities and/or acquired generalized lipodystrophy [see Warnings and Precautions (5.2)].

Because of these risks associated with the development of anti-metreleptin antibodies that neutralize endogenous leptin and/or MYALEPT and the risk for lymphoma, MYALEPT is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the MYALEPT REMS PROGRAM [see Warnings and Precautions (5.3)].

Close

1.1 Patients with Generalized Lipodystrophy - MYALEPT (metreleptin) for injection is indicated as an adjunct to diet as replacement therapy to treat the complications of leptin deficiency in ...

2.1 Recommended Dosing - See Table 1 for the recommended daily dose and maximum recommended daily dose in adults and pediatric patients. Based on clinical response (e.g., inadequate metabolic ...

- 3 DOSAGE FORMS AND STRENGTHS

  For Injection: 11.3 mg of metreleptin supplied in a vial as a sterile, white, solid, lyophilized cake (delivers 5 mg per mL of metreleptin when reconstituted with 2.2 mL of BWFI or WFI).

- 4 CONTRAINDICATIONS

  4.1 General Obesity - MYALEPT is contraindicated in patients with general obesity not associated with congenital leptin deficiency. MYALEPT has not been shown to be effective in treating general ...

- 5 WARNINGS AND PRECAUTIONS

  5.1 Risk for Development of Antibodies that Neutralize Endogenous Leptin and/or MYALEPT - Anti-metreleptin antibodies with in vitro neutralizing activity to leptin associated with adverse events ...

- 6 ADVERSE REACTIONS

  6.1 Clinical Trials Experience - Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly ...

- 7 DRUG INTERACTIONS

  No formal drug interaction studies were performed. Leptin is a cytokine and may have the potential to alter the formation of cytochrome P450 (CYP450) enzymes. This should be taken into account ...

- 8 USE IN SPECIFIC POPULATIONS

  8.1 Pregnancy - Pregnancy Category C - There is a program that monitors outcomes in women exposed to MYALEPT during pregnancy. Women who become pregnant during MYALEPT treatment are encouraged ...

- 10 OVERDOSAGE

  In one post-marketing case, a dose miscalculation resulted in an infant being exposed to a 10-fold overdose of metreleptin for 8 months. In this case, prolonged overdose was associated with severe ...

- 11 DESCRIPTION

  MYALEPT (metreleptin) for injection is a recombinant human leptin analog for injection that binds to and activates the leptin receptor. Metreleptin (recombinant methionyl-human leptin) is produced ...

- 12 CLINICAL PHARMACOLOGY

  12.1 Mechanism of Action - Adipocytes store lipids to meet the fuel requirements of non-adipose tissues during fasting. In patients with generalized lipodystrophy, the deficiency of adipose ...

- 13 NONCLINICAL TOXICOLOGY

  13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility - Two-year carcinogenicity studies in rodents have not been conducted with metreleptin. No proliferative or preneoplastic lesions were ...

- 14 CLINICAL STUDIES

  14.1 Open-Label, Single-Arm Study - An open-label, single-arm study evaluated MYALEPT treatment in patients with congenital or acquired generalized lipodystrophy and diabetes mellitus ...

- 16 HOW SUPPLIED/STORAGE AND HANDLING

  16.1 How Supplied - MYALEPT (metreleptin) for injection for subcutaneous administration is supplied in a single carton containing one vial for reconstitution (NDC 76431-210-01). Each vial ...

- 17 PATIENT COUNSELING INFORMATION

  See FDA-approved Patient Labeling (Medication Guide). Risk of Neutralizing Antibodies - Advise patients that neutralizing antibodies may result in loss in activity of endogenous leptin or loss of ...

- SPL UNCLASSIFIED SECTION

  Manufactured for: Aegerion Pharmaceuticals, Inc. Cambridge, MA 02142 - MYALEPT is a registered trademark of Aegerion Pharmaceuticals, Inc. PN 4085-03

UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

STEVEN BRUCE,

Plaintiff,

v.

ALEX M. AZAR, et al.,

Defendants.

Case No. 18-cv-05022-HSG

ORDER GRANTING MOTIONS TO DISMISS AND ADMINISTRATIVE MOTION TO FILE UNDER SEAL, AND DENYING MOTIONS TO SUPPLEMENT THE RECORD

Re: Dkt. Nos. 24, 36, 39, 40, 64, 70

Pending before the Court are three motions to dismiss, filed separately by Defendant California Physicians' Service d/b/a Blue Shield of California ("Blue Shield"), Dkt. No. 36; Defendant Envision Insurance Company ("Envision"), Dkt. No. 40; and Defendant Alex M. Azar II, Secretary of the United States Department of Health and Human Services ("DHHS"), Dkt. No. 39. DHHS also filed a motion to file the administrative record under seal, Dkt. No. 64, and Plaintiff Steven Bruce filed two motions to supplement the administrative record, Dkt. Nos. 24, 70. For the reasons articulated below, the Court **GRANTS** the motions to dismiss without leave to amend. The Court also **GRANTS** DHHS's motion to file the administrative record under seal, and **DENIES** Plaintiff's motions to supplement the administrative record.

I. BACKGROUND

Plaintiff brought this action against Defendants on August 16, 2018, seeking judicial review of the final decision by the Medicare Appeals Council ("MAC") denying Plaintiff coverage for the drug Serostim. Dkt. No. 1. Plaintiff is a Medicare beneficiary enrolled in the Part D prescription drug plan, administered by Envision in 2016 and Blue Shield in 2017. Dkt. No. 19 ("FAC") ¶¶ 1, 11, 23. In early 2016, Plaintiff was diagnosed with lipodystrophy, an auto-immune disease, and wasting syndrome. *Id.* ¶ 12. To treat his conditions, his primary care physician

prescribed the drug Serostim. *Id.* ¶ 13. Both Envision and Blue Shield denied coverage for Serostim in 2016 and 2017, respectively, because Serostim was not prescribed to Plaintiff for a use approved by the Food and Drug Administration ("FDA") or supported by a Medicare-approved drug compendium. *Id.* ¶¶ 14, 24.

Plaintiff appealed both Envision and Blue Shield's denials of coverage. *Id.* ¶¶ 15–21, 25–30. The appeals went through timely reconsideration requests with the Independent Review Entity and hearings in front of Administrative Law Judges ("ALJs") Myles and Gulin. *Id.* Both ALJs denied coverage, and Plaintiff appealed those decisions to the MAC. *Id.* ¶¶ 17–21, 27–30. The MAC related and consolidated both appeals and issued a final decision on July 12, 2018, denying coverage of Serostim. *Id.* ¶ 30.

Plaintiff now brings this action against his insurers, Blue Shield and Envision, and DHHS, to "appeal a final decision of the DHHS that denied coverage for Serostim." *Id.* ¶ 8. In the FAC, Plaintiff alleges the following four claims against Defendants: (1) "Defendants' decisions denying Plaintiff's claim for Medicare coverage of Serostim is [sic] not supported by substantial evidence and is [sic] incorrect as a matter of law," *id.* ¶ 35; (2) Defendants violated Plaintiff's due process rights "by refusing to provide coverage," *id.* ¶¶ 36–41; (3) Defendants, "[b]y providing coverage for Serostim only to individuals who have HIV," denied Plaintiff benefits in violation of Section 504 of the Rehabilitation Act of 1973, *id.* ¶¶ 42–51; and (4) Defendants Envision and Blue Shield, in refusing to provide coverage, discriminated against Plaintiff due to "his HIV-negative status," in violation of Title III of the Americans with Disabilities Act, *id.* ¶¶ 52–55.[1] Plaintiff requests that the Court reverse the decision of the agency and award Plaintiff benefits, along with any out-of-pocket costs and attorneys' fees and expenses. *Id.*, Prayer for Relief.

II. MOTIONS TO DISMISS

Defendants Envision and Blue Shield move to dismiss the complaint under Federal Rule of Civil Procedure 12(b)(6) for failure to state a claim. Dkt. Nos. 36, 40. Specifically, Envision and

[1] Plaintiff voluntarily withdrew his Title III claim against Defendants Envision and Blue Shield, *see* Dkt. No. 48 at 7; Dkt. No. 49 at 6, and the Court therefore **GRANTS** Defendants' motions to dismiss Plaintiff's fourth cause of action.

Blue Shield assert that they are not the proper defendants in this action, and even if they are, Plaintiff has not alleged sufficient facts to state a claim upon which relief can be granted. *Id.* DHHS moves to dismiss Plaintiff's second and third causes of action for lack of subject matter jurisdiction under Rule 12(b)(1), and, alternatively, for failure to state a claim under Rule 12(b)(6). Dkt. No. 39.

A. Legal Standards

i. Rule 12(b)(1)

A defendant may move for dismissal on grounds that the court lacks subject matter jurisdiction over the action. Fed. R. Civ. P. 12(b)(1). Federal district courts are courts of limited jurisdiction, and "[n]o principle is more fundamental to the judiciary's proper role in our system of government than the constitutional limitation of federal-court jurisdiction to actual cases or controversies." *DaimlerChrysler Corp. v. Cuno*, 547 U.S. 332, 341 (2006) (quotations omitted). It is the plaintiff's burden to establish subject matter jurisdiction. *See Ass'n of Am. Med. Colls. v. U.S.*, 217 F.3d 770, 778-79 (9th Cir. 2000); *Kokkonen v. Guardian Life Ins. Co. of Am.*, 511 U.S. 375, 376-78 (1994). "A Rule 12(b)(1) jurisdictional attack may be facial or factual." *Safe Air for Everyone v. Meyer*, 373 F.3d 1035, 1039 (9th Cir. 2004) (citing *White v. Lee*, 227 F.3d 1214, 1242 (9th Cir. 2000)). A facial attack "asserts that the allegations contained in a complaint are insufficient on their face to invoke federal jurisdiction." *Id.* A factual attack "disputes the truth of the allegations that, by themselves, would otherwise invoke federal jurisdiction." *Id.*

ii. Rule 12(b)(6)

Federal Rule of Civil Procedure 8(a) requires that a complaint contain "a short and plain statement of the claim showing that the pleader is entitled to relief." Fed. R. Civ. P. 8(a)(2). A defendant may move to dismiss a complaint for failing to state a claim upon which relief can be granted under Federal Rule of Civil Procedure 12(b)(6). "Dismissal under Rule 12(b)(6) is appropriate only where the complaint lacks a cognizable legal theory or sufficient facts to support a cognizable legal theory." *Mendiondo v. Centinela Hosp. Med. Ctr.*, 521 F.3d 1097, 1104 (9th Cir. 2008). To survive a Rule 12(b)(6) motion, a plaintiff must plead "enough facts to state a claim to relief that is plausible on its face." *Bell Atl. Corp. v. Twombly*, 550 U.S. 544, 570 (2007).

A claim is facially plausible when a plaintiff pleads "factual content that allows the court to draw the reasonable inference that the defendant is liable for the misconduct alleged." *Ashcroft v. Iqbal*, 556 U.S. 662, 678 (2009).

In reviewing the plausibility of a complaint, courts "accept factual allegations in the complaint as true and construe the pleadings in the light most favorable to the nonmoving party." *Manzarek v. St. Paul Fire & Marine Ins. Co.*, 519 F.3d 1025, 1031 (9th Cir. 2008). Nonetheless, Courts do not "accept as true allegations that are merely conclusory, unwarranted deductions of fact, or unreasonable inferences." *In re Gilead Scis. Sec. Litig.*, 536 F.3d 1049, 1055 (9th Cir. 2008).

If dismissal is appropriate under Rule 12(b)(6), a court "should grant leave to amend even if no request to amend the pleading was made, unless it determines that the pleading could not possibly be cured by the allegation of other facts." *Lopez v. Smith*, 203 F.3d 1122, 1130 (9th Cir. 2000) (quotations and citation omitted).

B. Discussion

i. Envision and Blue Shield Are Not Proper Defendants

Plaintiff's first cause of action against Envision and Blue Shield is an administrative challenge to "Defendants' decisions denying Plaintiff's claim for Medicare coverage of Serostim." FAC ¶¶ 34–35. Blue Shield and Envision maintain that they are not proper defendants for such a claim, because under the statutory review process, the only proper defendant in an appeal of the agency's decision is the Secretary of DHHS. Dkt. No. 36 at 3–4; Dkt. No. 40 at 3.

Under Section 1852 of the Social Security Act, codified in 42 U.S.C. § 1395 and the related sections, a Medicare beneficiary may obtain judicial review of the MAC's final decision pursuant to 42 U.S.C. § 405(g). *See* 42 U.S.C. § 1395w-104(h).[2] The governing regulations specify that a Part D beneficiary may obtain court review of the MAC's decision if the amount in

[2] Section 1395w-104(h) provides for judicial review of appeals Part D beneficiaries bring. 42 U.S.C. § 1395w-104(h). Although § 405(g) is not expressly listed in that section, § 1395w-104(h) incorporates Part C's judicial review provision, § 1395w–22(g), which in turn provides for judicial review under § 405(g). *See id.*; *see also Do Sung Uhm v. Humana, Inc.*, 620 F.3d 1134, 1140 n.9 (9th Cir. 2010).

controversy meets the threshold requirement estimated annually by the Secretary of DHHS. 42 C.F.R. § 423.2136(a). In such a review, the "Secretary of HHS, in his or her official capacity, is the proper defendant." *Id.* § 423.2136(d)(1).

Plaintiff's first cause of action seeks review of the final decision of the MAC. *See* FAC ¶¶ 34–35. By the plain language of 42 C.F.R. § 423.2136(d)(1), DHHS is the only proper defendant for such a claim, and therefore Blue Shield and Envision are not proper defendants. *See Madsen v. Kaiser Found. Health Plan, Inc.*, No. 08CV2236-WQH-JMA, 2009 WL 1537878, at *4 (S.D. Cal. June 2, 2009). As to Plaintiff's two remaining claims, because they are derivative of his claim challenging the MAC's final decision, those too must be dismissed. *See* FAC, Prayer for Relief ¶ 1 (Plaintiff requests the Court "[r]everse and set aside the decision of the DHHS and award such benefits as to which Plaintiff is entitled"); *see also id.* ¶¶ 1 ("This complaint is for judicial review of a final decision of the Department of Health and Human Services"), 41 (second claim alleging that "Defendants Envision and Blue Shield violated Plaintiff's due process rights under the Fifth Amendment [ ] by refusing to provide coverage"), 48 (third claim alleging that Envision and Blue shield, "[b]y providing coverage for Serostim only to individuals who have HIV," denied Plaintiff the opportunity to receive benefits).[3]

The Court therefore **DISMISSES** Plaintiff's action against Defendants Envision and Blue Shield without leave to amend.

ii. With Respect to DHHS, the Court Does Not Have Subject Matter Jurisdiction Over the Second and Third Causes of Action

DHHS does not seek to dismiss Plaintiff's first cause of action in its motion, but only moves to dismiss Plaintiff's second and third causes of action on the basis that the Court, under 42 U.S.C. § 405(h), does not have subject matter jurisdiction over those claims. Dkt. No. 39 at 5, 7. As discussed earlier, a beneficiary may obtain judicial review of the agency's decision through § 405(g). Section 405(h), a related provision, "channels most, if not all, Medicare claims through

[3] Because the Court finds that Envision and Blue Shield are not proper defendants in an administrative challenge and the remaining claims are derivative, the Court need not reach the merits of Defendants' arguments that the second and third causes of action independently fail to state cognizable claims. *See* Dkt. No. 36 at 5–9; Dkt. No. 3–5.

this special review system." *Shalala v. Ill. Council on Long Term Care, Inc.*, 529 U.S. 1, 8 (2000); *see also Do Sung Uhm*, 620 F.3d at 1140 (Section 405(g) is the "sole avenue for judicial review for claims arising under the Medicare Act") (quoting *Heckler v. Ringer*, 466 U.S. 602, 614–15 (1984)) (quotations omitted). Specifically, § 405(h) states that:

> The findings and decision of the Commissioner of Social Security after a hearing shall be binding upon all individuals who were parties to such hearing. No findings of fact or decision of the Commissioner of Social Security shall be reviewed by any person, tribunal, or governmental agency except as herein provided. No action against the United States, the Commissioner of Social Security, or any officer or employee thereof shall be brought under section 1331 or 1346 of Title 28 to recover on any claim arising under this subchapter.

42 U.S.C. § 405(h) (emphasis added). DHHS contends that the statutory language "arising under" includes any action derivative of a denial of benefits review, including Plaintiff's second and third claims, thereby barring judicial review of those claims. Dkt. No. 39 at 8.

The Supreme Court's holding in *Shalala* is dispositive. There, plaintiffs sued DHHS, asserting that certain Medicare-related regulations violated their statutory and constitutional rights. *Shalala*, 529 U.S. at 5–7. The *Shalala* Court held that plaintiffs' anticipatory challenge to the lawfulness of the regulations was precluded from judicial review under § 405(h). *Id.* at 25. In so holding, the Supreme Court reasoned that the language of § 405(h) "purports to make exclusive the judicial review method set forth in § 405(g)." *Id.* 10. Exclusive § 405(g) review applies to any claims "arising under" the Medicare Act, and "clearly appl[ies]" in a "typical [ ] Medicare benefits case, where an individual seeks a monetary benefit from the agency[,] the agency denies the benefit, and the individual challenges the lawfulness of that denial[,] irrespective of whether the individual challenges the agency's denial on evidentiary, rule-related, statutory, constitutional, or other legal grounds." *Id.*

This case falls squarely within the "typical [ ] Medicare benefits case" the *Shalala* Court described as not subject to judicial review. *See id.* Plaintiff's entire action rests on the premise that the agency's decision denying coverage of Serostim was unlawful. *See* FAC ¶¶ 38–40, 48, 50. Thus, "irrespective" of whether Plaintiff is attempting to challenge this denial on "statutory, constitutional or other legal grounds," the statute "plainly bars" judicial review of Plaintiff's

second and third claims. *See Shalala*, 529 U.S. at 10.

Plaintiff argues that his claims are "not essentially a claim for benefits," but rather a challenge to an "arbitrary classification" that denies him "meaningful access" to Serostim. Dkt. No. 47 at 2–3. According to Plaintiff, his claims are related to "plan design [to save money], not to a precise level of care." *Id.* But Plaintiff does not coherently articulate what significance this purported distinction has, and the Supreme Court has found similar arguments unpersuasive. Section 405(h) applies where "both the standing and substantive basis for the presentation of a claim is the Medicare Act," regardless of whether the nature of the challenge is "collateral versus noncollateral." *See Shalala*, 529 U.S. at 12, 14. The Supreme Court has made clear that:

> [c]laims for money, claims for other benefits, claims of program eligibility, and claims that contest a sanction or remedy may all similarly rest upon individual fact-related circumstances, may all similarly dispute agency policy determinations, or may all similarly involve the application, interpretation, or constitutionality of interrelated regulations or statutory provisions. There is no reason to distinguish among them in terms of the language or in terms of the purposes of § 405(h).

Id. at 14. *See also Heckler*, 466 U.S. at 614–16 (Section 405(h) bars jurisdiction over case involving challenge to agency's procedures); *Weinberger v. Salfi*, 422 U.S. 749 (1975) (no jurisdiction under § 405(h) even in case where plaintiffs did not request payment of benefits, but rather challenged agency's procedures and sought declaratory relief); *Marin v. HEW, Health Care Fin. Agency*, 769 F.2d 590, 592 (9th Cir. 1985) (Section 405(h) bars health care providers' claims for reimbursement under the Medicare Act even where claims were brought under the Federal Tort Claims Act for damages "caused by negligent failure," as such claims still "arise under" the Medicare Act). As in those cases, Plaintiff cannot circumvent the bar of § 405(h) by "imbu[ing]" his claims with federal question jurisdiction, as that "would render meaningless the jurisdiction restriction of § 405(h)." *See Marin*, 769 F.2d at 592. Section 405(g) thus provides the proper avenue for resolution of Plaintiff's claims. *See Davis v. Astrue*, 513 F. Supp. 2d 1137, 1145 (N.D. Cal. 2007) ("In sum, this court cannot assume jurisdiction based on Section 1331 over plaintiff's causes of action under the Rehabilitation Act and Due Process Clause").

Plaintiff's reliance on *J.L. v. Soc. Sec. Admin.*, 971 F.2d 260 (9th Cir. 1992) and *Am.*

Council of the Blind v. Astrue, No. C 05-04696 WHA, 2008 WL 1858928 (N.D. Cal. Apr. 23, 2008) is unavailing. *See* Dkt. No. 51 at 7. *J.L.* predates *Shalala* and its holding has since been questioned in light of *Shalala*.[4] And *American Council of the Blind* is fundamentally distinguishable from this action. The court in *American Council* found that plaintiffs' claims were not tied to any benefits. 2008 WL 1858928, at *5. Instead, those claims were premised on the agency's failure to communicate with plaintiffs in an accessible format, thereby depriving plaintiffs of "adequate notice and an opportunity to be heard." *Id.* at *1. Because the plaintiffs were challenging the agency's procedures for communicating with participants, and not the procedures for determining benefits, the court held the plaintiffs' claims did not arise under the Social Security Act and the court therefore had jurisdiction. *Id.* at *5. In contrast, there is no question that what Plaintiff is challenging here is clearly tied to his benefits.

Since the determination that it lacks jurisdiction over Plaintiff's second and third claims is dispositive, the Court need not address DHHS's alternative argument that the claims should be dismissed under Rule 12(b)(6). *See* Dkt. No. 39 at 9–16. Plaintiff's second and third causes of action are **DISMISSED** without leave to amend.

III. MOTIONS TO SUPPLEMENT THE ADMINISTRATIVE RECORD[5]

On October 25, 2018, Plaintiff filed a motion to supplement the administrative record ("AR"), alleging that the AR did not include the FDA label for Serostim and the American-Hospital Formulary Service Drug Information ("AHFS-DI") compendium for Serostim. Dkt. No. 24 at 2. DHHS opposed the motion as premature and subsequently lodged the administrative

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[4] The court in *Davis* stated that *J.L.* appears "inconsistent with the Supreme Court's subsequent holding in [*Shalala*] that legal challenges to agency practices and procedures are subject to the limitations in Section 405(h)." *Davis*, 513 F. Supp. 2d at 1144.

[5] Although Plaintiff moves to "supplement" the record, based on a review of his pleadings, it appears Plaintiff is seeking to compel DHHS to "complete" the record. *See* Dkt. No. 70 at 4 (alleging that the agency considered and relied on the documents and should have included them in the AR); Dkt. No. 79 at 2 ("The materials and information at issue here is [sic] not extra-record evidence."). "Supplementing" and "completing" the AR are two distinct concepts: "completing the record" refers to including "materials which were actually considered by the agency, yet omitted from the administrative record," whereas "supplementing the record" refers to including "materials which were not considered by the agency, but which are necessary for the court to conduct a substantial inquiry." *Ctr. for Native Ecosystems v. Salazar*, 711 F. Supp. 2d 1267, 1274 (D. Colo. 2010). The Court will construe Plaintiff's motion as a motion to complete or, in the alternative, to supplement the AR, and apply both applicable standards.

record with the Court on February 5, 2019, including the FDA label for Serostim. Dkt. No. 34 at 3–4; Dkt. No. 61; Dkt. No. 64 (AR). While DHHS had agreed to supplement the AR with the AHFS-DI compendium for Serostim, DHHS avers that the compendium did not contain Serostim, so it did not include it. Dkt. No. 64-6 ¶ 2. Nonetheless, Plaintiff, in a statement to the court on February 6, 2019, affirmed that he still sought inclusion of the AHFS-DI compendium for Serostim. Dkt. No. 65. He also alleged that DHHS is compelled to provide two additional documents that were not identified before the Court in Plaintiff's initial motion: (1) the AHFS-DI compendium for "somatotropin," which Plaintiff posits is the generic compound of Serostim, and (2) the introductory portions of the AHFS-DI compendium. Dkt. No. 65.

Because the scope of Plaintiff's original motion had changed considerably, the Court directed Plaintiff to file a new motion, addressing the most current documents at issue. Dkt. No. 69. Plaintiff filed his second motion to supplement the administrative record on February 20, 2019.[6] Dkt. No. 70. In the most recent motion, Plaintiff seeks to compel DHHS to complete, or supplement, the AR with the AHFS-DI compendia for Serostim and somatotropin, and the introductory portion of the AHFS-DI compendium, for the years 2016–2018.[7] *Id.* at 2.

A. Legal Standard

Judicial review of an agency decision is limited to "the administrative record already in existence, not some new record made initially in the reviewing court." *Camp v. Pitts*, 411 U.S. 138, 142 (1973). The administrative record is "not necessarily those documents that the agency has compiled and submitted as 'the' administrative record." *Thompson v. U.S. Dept. of Labor*, 885 F.2d 551, 555 (9th Cir. 1989) (citation omitted). Instead, it must be "the whole record," which "includes everything that was before the agency pertaining to the merits of its decision." *Portland Audubon Soc'y v. Endangered Species Comm.*, 984 F.2d 1534, 1548 (9th Cir. 1993) (citation omitted). The "whole record" thus encompasses "all documents and materials directly or

[6] Since the most recent motion to supplement the administrative record supersedes Plaintiff's original motion, the Court **DENIES AS MOOT** the original motion, Dkt. No. 24.

[7] In his reply, Plaintiff seeks documents for the years 2015–2019. Dkt. No. 79 at 2. Because the years 2015 and 2019 were not raised in his motion, the Court will not consider his request to complete the AR with documents from those years. *See* Dkt. No. 70.

indirectly considered by agency decision-makers and includes evidence contrary to the agency's position." *Thompson*, 885 F.3d at 555 (citation omitted).

The administrative record before the agency, however, does not include "every scrap of paper that could or might have been created." *Pinnacle Armor, Inc. v. United States*, 923 F. Supp. 2d 1226, 1237 (E.D. Cal. 2013) (quoting *TOMAC v. Norton*, 193 F. Supp. 2d 182, 195 (D.D.C. 2002)). Also, an agency's designation and certification of the administrative record as complete is entitled to a "presumption of administrative regularity." *McCrary v. Gutierrez*, 495 F. Supp. 2d 1038, 1041 (N.D. Cal. 2007) (citing *Bar MK Ranches v. Yuetter*, 994 F.2d 735, 740 (10th Cir. 1993)). In turn, courts presume administrative records are complete, but plaintiffs can rebut this presumption with "clear evidence to the contrary." *In re United States*, 875 F.3d 1200, 1206 (9th Cir. 2017) (citing *Bar MK Ranches*, 994 F.2d at 740), *vacated on other grounds*, 138 S. Ct. 443 (2017)).

A court generally may not consider extra-record evidence, although the Ninth Circuit has recognized certain exceptions to that rule. *San Luis & Delta-Mendota Water Auth. v. Locke*, 776 F.3d 971, 992 (9th Cir. 2014). These exceptions are when admission of the evidence: "(1) is necessary to determine whether the agency has considered all relevant factors and has explained its decision, (2) is necessary to determine whether the agency has relied on documents not in the record, (3) [ ] is necessary to explain technical terms or complex subject matter, or (4) when plaintiffs make a showing of agency bad faith." *Id.* (citations and quotations omitted). The exceptions are to be "narrowly construed," and the party seeking to supplement with the extra-record evidence "bears the burden of demonstrating that a relevant exception applies." *Id.* at 992–93. Otherwise, "[w]ere the federal courts routinely or liberally to admit new evidence when reviewing agency decisions, it would be obvious that the federal courts would be proceeding, in effect, de novo rather than with the proper deference to agency processes, expertise, and decision-making." *Lands Council v. Powell*, 395 F.3d 1019, 1030 (9th Cir. 2005).

B. Discussion

Plaintiff has not presented any "clear evidence" to overcome the applicable presumption of deference to the agency's judgment that the AR is complete. *See In re United States*, 875 F.3d at

1206. Nor has Plaintiff demonstrated that any of the narrow exceptions to supplement the AR apply in this case. *See San Luis*, 776 F.3d at 992. Plaintiff, in conclusory fashion, argues that "'clearly' the MAC could not have obtained information about the off-label uses of Serostim for HIV" without considering the AHFS-DI compendium. Dkt. No. 79 at 3. As to the introductory portion, according to Plaintiff, it is "preposterous to assume that the decision-makers in this case never relied on something so clearly foundational." *Id.* Plaintiff then asserts that DHHS's objection to providing the documents "is evidence of concealment," and that DHHS propounds an "absurd and condescending reason" for failing to provide the documents. *Id.* at 3, 5.

Plaintiff completely misses the mark. These conclusory pronouncements come nowhere close to showing "clear evidence" that any of the documents should be in the AR. The record reflects that the agency considered DRUGDEX, another Medicare-approved compendium, to determine what the non FDA-approved (or "off-label") use for Serostim is. AR at 0055, 0726. Plaintiff does not dispute that DRUGDEX is in the administrative record. Dkt. No. 70 at 5 n.3. The ALJs, in their opinions, also stated that the AHFS-DI compendium did not include any additional off-label uses for Serostim. AR at 0055, 0726. The record does not reflect any reference to "somatotropin," and Plaintiff presents no evidence that the agency relied on information about this drug. Plaintiff does not present any evidence, let alone "clear evidence," that the agency considered any of the materials whose inclusion he seeks to compel.

Because Plaintiff fails to rebut with clear evidence the presumption that the administrative record is complete, or present any evidence that the documents fall under one of the exceptions allowing the Court to consider extra-record evidence, the Court **DENIES** Plaintiff's second motion to supplement the administrative record.

IV. MOTION TO FILE UNDER SEAL

DHHS filed the entire certified administrative record, approximately 1,500 pages, with the Court, along with a motion requesting to file the record under seal. Dkt. No. 64. Because these records are more than tangentially related to the underlying action, the Court applies the "compelling reasons" standard articulated below.

A. Legal Standard

Courts generally apply a "compelling reasons" standard when considering motions to seal documents. *Pintos v. Pac. Creditors Ass'n*, 605 F.3d 665, 678 (9th Cir. 2010) (quoting *Kamakana v. City & Cty. of Honolulu*, 447 F.3d 1172, 1178 (9th Cir. 2006)). "This standard derives from the common law right 'to inspect and copy public records and documents, including judicial records and documents.'" *Id.* (quoting *Kamakana*, 447 F.3d at 1178). "[A] strong presumption in favor of access is the starting point." *Kamakana*, 447 F.3d at 1178 (quotations omitted). To overcome this strong presumption, the party seeking to seal a judicial record attached to a dispositive motion must "articulate compelling reasons supported by specific factual findings that outweigh the general history of access and the public policies favoring disclosure, such as the public interest in understanding the judicial process" and "significant public events." *Id.* at 1178–79 (quotations omitted). "In general, 'compelling reasons' sufficient to outweigh the public's interest in disclosure and justify sealing court records exist when such 'court files might have become a vehicle for improper purposes,' such as the use of records to gratify private spite, promote public scandal, circulate libelous statements, or release trade secrets." *Id. at 1179* (quoting *Nixon v. Warner Commc'ns, Inc.*, 435 U.S. 589, 598 (1978)). "The mere fact that the production of records may lead to a litigant's embarrassment, incrimination, or exposure to further litigation will not, without more, compel the court to seal its records." *Id.*

The Court must "balance[] the competing interests of the public and the party who seeks to keep certain judicial records secret. After considering these interests, if the court decides to seal certain judicial records, it must base its decision on a compelling reason and articulate the factual basis for its ruling, without relying on hypothesis or conjecture." *Id.* Civil Local Rule 79-5 supplements the compelling reasons standard set forth in *Kamakana*: the party seeking to file a document or portions of it under seal must "establish[] that the document, or portions thereof, are privileged, protectable as a trade secret or otherwise entitled to protection under the law . . . The request must be narrowly tailored to seek sealing only of sealable material." Civil L.R. 79-5(b).

B. Discussion

The Court finds that DHHS has shown a compelling interest in sealing the entire

administrative record, as it contains Plaintiff's medical records and private information. Courts have found a party's privacy interests in such records to outweigh the public's interest in access. *See A.B. v. San Francisco Unified Sch. Dist.*, No. C 07-4738 PJH, 2007 WL 2900527, at *1 (N.D. Cal. Oct. 2, 2007) (granting motion to seal administrative record "which often contains sensitive educational and medical information, and often in references too numerous to redact"); *see also Krysten v. Blue Shield of California*, No. 15-CV-02421-RS, 2016 WL 5934709, at *3 n.3 (N.D. Cal. Oct. 11, 2016); *A.C. v. City of Santa Clara*, No. 13-CV-03276-HSG, 2015 WL 4076364, at *2 (N.D. Cal. July 2, 2015).

V. CONCLUSION

The Court **GRANTS** all three motions to dismiss without leave to amend. Dkt. Nos. 36, 39, 40. The clerk is **DIRECTED** to terminate Defendants Envision and Blue Shield from the case. The Court also **DENIES AS MOOT** Plaintiff's first motion to supplement the administrative record, Dkt. No. 24; **DENIES** Plaintiff's second motion to supplement the administrative record, Dkt. No. 70; and **GRANTS** Defendant's motion to file the administrative record under seal, Dkt. No. 64.

The Court further **SETS** a case management conference for July 23, 2019 at 2:00 p.m., and **DIRECTS** the parties to file on or before July 16, 2019 a joint case management statement including a proposed case schedule for resolution of the remaining claim against DHHS.

IT IS SO ORDERED.

Dated: 6/18/2019

Haywood S. Gilliam, Jr.

HAYWOOD S. GILLIAM, JR.
United States District Judge

United States District Court
Northern District of California

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UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

STEVEN BRUCE,

Plaintiff,

vs.

ALEX M. AZAR II, Secretary of the Department of Health and Human Services, ENVISION INSURANCE COMPANY, BLUE SHIELD OF CALIFORNIA, and DOES 1-50,

Defendants.

Case No. 4:18-cv-05022 HSG

FIRST AMENDED COMPLAINT FOR:

1. **PRESCRIPTION COVERAGE UNDER TITLE XVIII OF THE SOCIAL SECURITY ACT – MEDICARE PART B AND PART D;**
2. **INJUNCTIVE RELIEF;**
3. **DECLARATORY RELIEF;**
4. **MONETARY DAMAGES;**
5. **DUE PROCESS VIOLATION;**
6. **VIOLATION OF SECTION 504 OF THE REHABILITATION ACT OF 1973;**
7. **VIOLATION OF THE AMERICANS WITH DISABILITIES ACT AS TO THE NON-FEDERAL DEFENDANTS**
8. **JURY DEMAND**

I. PRELIMINARY STATEMENT

1. The Plaintiff Steven Bruce is a Medicare beneficiary who is enrolled in Medicare, Part B (42 U.S.C. § 1395w-21 *et seq.*) and a Medicare prescription drug plan, Part D (42 U.S.C. §§1395j-1395w-6) and who sought coverage from his plan for a medically necessary prescribed medication, Serostim. This complaint is for judicial review of a

final decision of the Department of Health and Human Services (DHHS), made by the Medicare Appeals Council (AC) on July 12, 2018, denying coverage for the medication. Plaintiff requires Serostim for treatment of his wasting disease caused by an auto-immune disease, lipodystrophy. The DHHS does not question the efficacy of Serostim in managing Plaintiff's serious life threatening medical condition. The DHHS further agrees that Mr. Bruce has been unable to take other medications to treat his condition. Nonetheless, the DHHS denied coverage based on an overly restrictive interpretation of what constitutes a "medically accepted indication" under the statute.

II. THE PARTIES

2. Plaintiff Steven Bruce is a resident of San Francisco, California. He is, and has been, a Medicare beneficiary at all times relevant to this action.

3. Defendant, Alex M. Azar II, is the Secretary of the United States Department of Health and Human Services, and as such is responsible for the administration of the Social Security Act, Title XVIII, the Medicare program. The Secretary is a proper Defendant in this appeal of the AC decision, and is being served in his official capacity. *See* 42 C.F.R. §423.2136.

4. Defendant Envision Insurance Company, a corporation doing business in California, provides EnvisionRx Plus Silver, a Medicare-approved prescription drug plan providing prescription drug coverage under Medicare Part D.

5. Defendant Blue Shield of California (Blue Shield) is a California corporation and provides Blue Shield of California Enhanced Prescription Drug Plan, a Medicare approved drug plan providing prescription drug coverage under Medicare Part D.

III. VENUE

6. Venue is proper in this District by reason of Plaintiff's residence in San Francisco County, California. See 42 C.F.R § 423.2136(b).

7. Pursuant to Local Rule 3-2(d), this action should be assigned to either the San Francisco or Oakland Division.

IV. JURISDICTION

8. The Plaintiff brings this action pursuant to § 42 U.S.C. § 1395w-104(h)(1) which incorporates the requirements of 42 U.S.C. § 1395w-22(g)(5) and 42 U.S.C. § 405(g), to appeal a final decision of the DHHS that denied coverage for Serostim.

9. The Plaintiff has exhausted his administrative remedies. The Administrative Law Judge (ALJ) Appeal Numbers are 1-5125326621R1 (EnvisionRx Plus Silver) and 1-6176167691R1 (Blue Shield).

V. FACTS AND ADMINISTRATIVE PROCEEDINGS

10. Serostim is approved by the Food and Drug Administration (FDA) for HIV patients with wasting or cachexia to increase lean body mass and body weight and to improve physical endurance, and for short bowel syndrome. Non-FDA approved uses are for fat maldistribution from HIV infection.

A. EnvisionRx Plus Silver

11. Plaintiff is a duly-qualified Medicare beneficiary based on age. In 2016, his Part D drug plan was administered by EnvisionRx Plus Silver through Defendant Envision Insurance Company.

12. Mr. Bruce was diagnosed with lipodystrophy and life-threatening wasting syndrome in on or about March of 2016. Plaintiff does not have HIV.

13. His primary care physician Dr. Louis Cubba prescribed Serostim to halt Plaintiff's severe and dramatic weight loss. Plaintiff's weight dropped to 132 pounds in the beginning of 2016. Plaintiff is 5'11" tall. Plaintiff regained approximately 10lbs after starting Serostim regimen. It is the only drug that helped Plaintiff regain weight.

14. Dr. Cubba requested coverage of Serostim from Plaintiff's Part Medicare plan, EnvisionRx Plus Silver on May 31, 2016. The plan denied coverage on June 3, 2016 on an alleged basis that the requested medication to treat the condition was neither an approved use by the FDA, nor supported by a drug compendia approved by Medicare.

15. The Plaintiff timely filed a reconsideration request with the Medicare Part D Independent Review Entity (IRE). The IRE issued an unfavorable decision on September 16, 2016.

16. Mr. Bruce timely requested a hearing with an ALJ on November 15, 2016. On October 21, 2016, a telephone hearing was held by ALJ James Myles.

17. On November 15, 2016, Judge Myles issued an unfavorable decision. ALJ Gulin erroneously dismissed Plaintiff's request for hearing as to Medicare and Blue Shield by assuming that this appeal was also against Envision when it was against Blue Shield, *see infra*.

18. Plaintiff timely appealed to the ALJ's decision to the AC, which remanded the case back to the ALJ for further development of the record on December 20, 2017.

19. Plaintiff provided an example of how Gabapentin (Neurontin) was prescribed off-label for pain, rather than an anti-seizure medication. Dr. Watson, a medical expert, testified at the hearing about another drug, Lyrica, which, like Gabapentin, was also used off-label purposes and covered under Medicare Part D. This further supports Plaintiff's position that there is no reason to deny him coverage, either under the FDA-approved use for cachexia/wasting because it is unknown whether HIV actually causes this condition, or for an off-label use for lipodystrophy.

20. ALJ Myles issued another unfavorable decision on March 30, 2018.

21. Plaintiff timely appealed again to the AC, which issued an unfavorable decision on July 12, 2018.

B. Blue Shield

22. Plaintiff refers to, and incorporates herein by reference, all preceding paragraphs as though fully set forth herein.

23. For benefit year 2017, Plaintiff's Part D plan was administered by Blue Shield (Blue Shield of California Enhanced Prescription Drug Plan).

24. The plan did not approve Serostim for Plaintiff because his "diagnosis of Lipodystrophy is not a 'medically accepted indication' use of Serostim." Blue Shield argued that Serostim was an off-label use not included in the compendia for Plaintiff's life-threatening condition.

25. Plaintiff timely requested reconsideration from IRE.

26. IRE denied coverage on April 17, 2017. IRE asserted that there were no citations in the Medicare-approved compendia supporting Serostim for Plaintiff's condition, lipodystrophy.

27. Plaintiff timely requested a hearing before an ALJ on May 1, 2017. Following the initial request, ALJ Jeffrey S. Gulin dismissed the case because of the previous decision issued by ALJ Myles. Plaintiff timely appealed the dismissal with the AC, which remanded the case back to the ALJ for further development on December 20, 2017.

28. On February 8, 2018, Plaintiff had a telephonic hearing with Judge Gulin. Plaintiff argued that cachexia is a synonym for wasting syndrome and both are medically equivalent. Plaintiff also cited National Institutes Health (NIH) studies that lead to the conclusion that is was not the HIV that led to lipodystrophy, but the anti-viral agents used to treat HIV. Plaintiff also argued that $2,000 of the $14,000 retail cost of Serostim was covered by Medicare Part B as further proof that Serostim was not being used for an unapproved "off-label" use under to the statute.

29. On March 15, 2018, ALJ Gulin issued an unfavorable decision.

30. Plaintiff timely appealed to the AC, which issued an unfavorable decision on July 12, 2018, relating and consolidating both Administrative Law Judge (ALJ) Appeal Numbers are 1-5125326621R1 (EnvisionRx Plus Silver) and 1-6176167691R1 (Blue Shield).

31. Plaintiff now timely appeals the final July 12, 2018 decision of the AC and is properly before this Court. The amount in controversy exceeds $1,600 and as of the date of filing this Complaint is approximately $70,000.00

32. There is no practical difference between HIV or the anti-viral drugs which may cause the auto-immune disease that Plaintiff has, lipodystrophy. Both are auto-immune diseases which result in a life-threatening wasting syndrome for which Serostim is prescribed. Plaintiff's use of Serostim is for a medically accepted indication within the meaning of § 1927(k)(6) of the Social Security Act, 42 U.S.C. § 1396r-8(k)(6). He is entitled to Medicare coverage for this drug.

33. Medicare Part B covered $2000 of the cost of Serostim, reducing the price to approximately $12,500. *See* 42 U.S.C. § 1395w-21 *et seq.* This further supports Plaintiff's position that his Serostim should be covered by Medicare Part D, and is not used off-label.

VI. CAUSES OF ACTION

A. Medicare Part B (42 U.S.C. § 1395w-21 *et seq.*) and Part D (42 U.S.C. §1395j-1395w-6) Coverage – Title XVIII, Against Defendants DHHS, Envision and Blue Shield

34. Plaintiff refers to, and incorporates herein by reference, all the preceding paragraphs as though fully set forth herein.

35. The Defendants' decisions denying Plaintiff's claim for Medicare coverage of Serostim is not supported by substantial evidence and is incorrect as a matter of law, on the following grounds:

    a. Substantial evidence, when the record is viewed as a whole, supports that Serostim is a covered under both Parts D and B (approximately $2,000.00 of $14,500 was covered under Part B apparently because it is an injectable.)

b. The Defendants' decisions are based on errors of law in that the decisions were made without legal basis and their interpretation of "medically accepted indication" is unlawfully restrictive and has no rational basis.

B. Violation of the Due Process Clause of the Fifth Amendment to the United States Constitution Against DHHS, Envision and Blue Shield.

36. Plaintiff refers to, and incorporates herein by reference, all the preceding paragraphs as though fully set forth herein.

37. The DHHS, in upholding both the of the decisions of ALJ Myles and ALJ Gulin, violated Plaintiff's due process rights under the Fifth Amendment to the United States Constitution.

38. Neither ALJ Myles nor ALJ Gulin made a finding that it was HIV, as opposed to antiviral medications used to treat HIV, which caused wasting disease or lipodystrophy in HIV-positive individuals.

39. Although more research is needed, studies have shown that some antiviral medications have been the cause of lipodystrophy in HIV-positive population as opposed to the HIV itself.

40. The DHHS did not find that lipodystrophy or wasting/cachexia is caused by HIV. In Plaintiff's case, the cause of lipodystrophy/life-threatening weight loss is likewise unknown, linked to an unidentified virus. The DHHS/AC states in its decision that it makes a *de novo* review, and only reviews what is in Beneficiary's Appeals Council's brief if Beneficiary is represented. Beneficiary (Plaintiff Steven Bruce) was not represented.

41. Defendants Envision and Blue Shield violated Plaintiff's due process rights under the Fifth Amendment to the United States Constitution by refusing to provide coverage for life-saving medication to Plaintiff for the same reasons as DHHS (See ¶¶ 38-40)

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C. Violation of Section 504 of the Rehabilitation Act of 1973, 29 U.S.C. § 794, Against Defendant DHHS, Envision and Blue Shield.

42. Plaintiff refers to, and incorporates herein by reference, all the preceding paragraphs as though fully set forth herein.

43. Section 504 of the Rehabilitation Act of 1973, 29 U.S.C. § 794 ("Section 504") provides that no otherwise qualified individual with a disability in the United States shall, solely by reason of his or her disability, be excluded from the participation in, be denied the benefits of, or be subjected to discrimination under any program or activity receiving Federal financial assistance or activity conducted by any federal agency.

44. Plaintiff is entitled to Section 504 protection as an individual with a disability - wasting disease and lipodystrophy.

45. Defendant DHHS is a federal agency and is bound by the regulations it has promulgated under Section 504 of the Rehabilitation Act, 45 C.F.R. Part 85.

46. As alleged herein, the DHHS has and continues to discriminate against Plaintiff by denying coverage for Serostim under Medicare Part D – a drug without which Plaintiff can die.

47. Defendants Envision and Blue Shield are federal contractors administering Medicare Part D, and are bound by both Section 504 and ADA laws and regulations.

48. By providing coverage for Serostim only to individuals who have HIV, the DHHS denied Plaintiff, as an individual with a disability, the opportunity to participate in, or benefit from, DHHS's aids, benefits, or services afforded to those with HIV.

49. By providing coverage for Serostim only to individuals who have HIV, Envision and Blue Shield denied Plaintiff, as an individual with a disability (Lipodystrophy), the opportunity to participate in, or benefit from, Envision's and Blue Shield's aids, benefits, or services afforded to those with HIV.

50. There is no rational basis for providing Serostim to treat cachexia, wasting syndrome or lipodystrophy only to individuals who have been also diagnosed with HIV, as

Plaintiff's condition is auto-immune in nature, not genetically based, and is most likely a product of a virus. Defendants provided no evidence to the contrary.

51. Plaintiff has exhausted his administrative remedies by alleging Section 504 violations before the ALJ and again before the AC subject to the Medicare AC not considering his ALJ arguments under a DHHS false assertion that Plaintiff was represented in the administrative proceedings.

D. Violation of Title III of the Americans with Disabilities Act (ADA) Against Defendants Envision Insurance Company and Blue Shield of California.

52. Plaintiff refers to, and incorporates herein by reference, all the preceding paragraphs as though fully set forth herein.

53. The ADA prohibits discrimination based on disability.

54. Defendants Envision Insurance and Blue Shield have, and continue to, discriminate against Plaintiff based on his disability – wasting syndrome/lipodystrophy, by denying him life-saving medication, Serostim, without which he can die.

55. This discrimination is based in part on the fact that, although Plaintiff's lipodystrophy is not caused by HIV or antiretroviral medications used to treat it, his disability is essentially the same as lipodystrophy caused by either HIV or the medications used to treat it. Essentially, Defendants are penalizing Plaintiff for his HIV-negative status.

VII. JURY DEMAND

56. Plaintiff demands that this case be tried to a jury.

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VIII. PRAYER FOR RELIEF

WHEREFORE, Plaintiff requests this Court to:

1. Reverse and set aside the decision of the DHHS and award such benefits as to which Plaintiff is entitled;
2. Award Plaintiff all out of pocked moneys spent through the end of this case,
3. Award Plaintiff reasonable attorney's fees and costs; and
4. Grant Plaintiff such additional and alternative relief as equity and justice may require.

Dated: 9/20/2018

PEOPLE WITH DISABILITIES FOUNDATION

By: /s/ Zoya Yarnykh
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UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

STEVEN BRUCE,

Plaintiff,

vs.

ALEX M. AZAR II, Secretary of the Department of Health and Human Services, ENVISION INSURANCE COMPANY, BLUE SHIELD OF CALIFORNIA, and DOES 1-50,

Defendants.

Case No. 4:18-cv-05022 HSG

PLAINTIFF'S OPPOSITION TO DEFENDANT ALEX M. AZAR, II'S MOTION TO DISMISS FIRST AMENDED COMPLAINT

Date: March 7, 2019
Time: 2:00 PM
Judge: Hon. Haywood S. Gilliam, Jr., Ctrm 2
Location: 1301 Clay St., Floor 4, Oakland, California 94612

I. INTRODUCTION

Defendant Alex M. Azar, II (hereinafter "DHHS") brought this motion seeking dismissal of Plaintiff's causes of action for Due Process Violation under the Fifth Amendment to the United States Constitution and violation of Section 504 of the Rehabilitation Act of 1973. Defendant's motion should be denied. Contrary to Defendant's assertion, Plaintiff is not seeking Medicare benefits *per se*. Plaintiff's claims are collateral to his current benefit status. The issue here is whether DHHS can exclude prescription coverage on a solely irrational basis by requiring that a beneficiary should also have HIV. The complaint was filed pursuant to the final Medicare Appeals

Council (MAC) decision which states "[i]f a civil action is commenced, the complaint should name the Secretary of Health and Human Services as the defendant..." At the time that this opposition is written, the DHHS did not file Administrative Record (AR) including the specific compendium it relied on in its Motion to Dismiss, and which, in part, is the basis for Plaintiff's Motion to either produce the AR or have Defendant's Motion to Dismiss be stricken. In that the Court did not grant Plaintiff's request to shorten time on this matter, Plaintiff will cite the AR, (unknown page numbers) and herby represents to this Court that Plaintiff is unduly prejudiced in responding to this Motion to Dismiss as stated in Plaintiff's Motion to Supplement the Administrative Record (Doc. 24).

II. ARGUMENT

A. Legal Standard for Motions Under FRCP 12(b)(6) and 12(b)(1)

A court should dismiss a complaint only when its allegations fail to state a claim upon which relief can be granted. Fed. R. Civ. P. 12(b)(6). Iqbal Fed. R. Civ. P. 8(a)(2). "'[D]detailed factual allegations' are not required." *Ashcroft v. Iqbal*, 556 U.S. 662, 129 S. Ct. 1937, 1949, 173 L. Ed. 2d 868 (2009) (quoting *Bell Atl. Corp. v. Twombly*, 550 U.S. 544, 555, 127 S. Ct. 1955, 167 L. Ed. 2d 929 (2007)) (emphasis added.) The court must accept as true all factual allegations in the complaint and must draw all reasonable inferences from those allegations, construing the complaint in the light most favorable to the plaintiff. *Pollard v. Geo Group, Inc.*, 607 F.3d 583, 585 n.3 (9th Cir. 2010); *Westlands Water Dist. v. Firebaugh Canal*, 10 F.3d 667, 670 (9th Cir. 1993). Here, Plaintiff has sufficiently alleged facts compliant with the heightened pleading standard of *Iqbal* and *Twombly* in his causes of action against DHHS. In *Iqbal*, mere conclusions were pleaded with no supporting facts as opposed to this case, which has a lot of facts. Defendant's motion should be denied.

In *Bowen v. New York*, 476 U.S. 467, 473, 106 S. Ct. 2022 (1986) the Court stated "...[t]he gravamen of respondents' complaint was that petitioners had adopted an unlawful, unpublished policy under which countless deserving claimants were denied benefits..." Although that case involved exhaustion of administrative remedies, the concept of DHHS having no policy or a secret

policy (See ALJ Myles decision stating there is no policy and AR as a whole), DHHS cannot legally challenge subject matter under for the same or similar reasons as in *Bowen*. Both ALJs Myles and Gulin in their respective decisions refer to a National Coverage Determination ('NCD") which, if existing, would be binding on an ALJ. 42 CFR 405.1060(a)(4). There are no NCDs. If an ALJ does not follow a policy s/he must explain why. See ALJ Myles Dec. at 5. If not FDA approved it can be supported by "the literature or the plain language of the policy guidance...." *Id.* or by citations in the compendia. DHHS refused to provide the compendia which is the subject of a Motion to Supplement the AR (Doc 24.) What is telling in this case is that DHHS relies on a compendium in its motion but states it will not provide it, in part, because Plaintiff in the administrative proceedings was represented. He was not. This misrepresentation is calculated to deprive Plaintiff of due process and again is the subject of a motion, Doc 24.

B. Plaintiff Has Exhausted All Administrative Remedies Over A Three-Year Period After Which DHHS Told Him in Its MAC Decision That He Had 60 Days to File a Complaint in Federal District Court. The Court Does Have Subject Matter Jurisdiction Over the Section 504 Claim and the Due Process Claim

Plaintiff is a current beneficiary of Medicare, and has been for over three years. Defendant does not contend otherwise. Defendant acknowledges that Serostim is the only medication that can benefit Plaintiff in light of his life-threatening disease, Lipodystrophy. The only "benefit" at issue here is coverage for Serostim, the retail price of which is approximately $14,500, less about $2,000.00 covered by Medicare Part B, not his eligibility for Medicare. Part B was before the ALs in that Medicare covered $2,000 of the cost, and, therefore, Part B is also before this Court. A plaintiff's claim is collateral if it is not essentially a claim for benefits. Here Plaintiff's claim is sufficiently distinct in that he alleges that:

DHHS discriminated against Plaintiff solely by reason of disability (Lipodystrophy) in violation of Section 504 of the Rehabilitation Act of 1973. Plaintiff's allegation is simple – there is no rational basis to deny coverage for Plaintiff's wasting syndrome/cachexia because it is not also accompanied by HIV. It is unclear whether wasting/cachexia and the underlying disorder,

Lipodystrophy, a rare auto immune disorder, is caused by HIV or by the anti-viral medications used to manage HIV. NIH studies show that some such medications used to treat HIV have been associated with Lipodystrophy.[1] Plaintiff challenges the arbitrary classification requiring HIV as it does not provide meaningful access to individuals with disabilities such as Plaintiff, who has the underlying condition that Serostim was envisioned to treat. This fact is not contested by any Defendant. (See AR generally.) This is the crux of the discrimination claim, i.e. Plaintiff was denied meaningful access.

Mr. Bruce's claim is related to plan design, not to a precise level of care. The plan was designed to save money, as was the implicit testimony of the insurance companies' witness before the ALJ. So-called "off-label" drugs, such as Neurontin and Lyrica, for example, can be covered at the discretion of the carriers. The fact that Defendant Blue Shield markets the compound in question which, according Plaintiff's testimony, led him to switch to this carrier, means it intentionally violated Section 504 of the Rehabilitation Act of 1973. There is no safe harbor provision for a federal contractor under Section 504. If the Agency cannot withhold this compound for people who need it, neither can federal contractors. The ADA does not apply to DHHS, but Section 504 does apply as does it federal contractors. *DiCrescenzo v. UnitedHealth Grp. Inc.*, No. 15-00021 DKW-RLP, 2015 U.S. Dist. LEXIS 123852 (D. Haw. Sep. 16, 2015)

C. Plaintiff Has Sufficiently Alleged that Defendant Violated Plaintiff's Rights Under the Due Process Clause of the Fifth Amendment.

The Fifth Amendment applies to actions of the federal government. *Schweiker v. Wilson*, 450 U.S. 221, 227, 101 S. Ct. 1074, 67 L. Ed. 2d 186 (1981); *see also Lee v. City of L.A.*, 250 F.3d 668, 687 (9th Cir. 2001). Social Security benefits are property within the meaning of the Due Process clause of the Fifth Amendment. *Mathews v. Eldridge,* 424 U.S. 319 (1976).

As stated above under statutory interpretation, Plaintiff has a claim for substantive due process violation because there is no rational basis for the decision to deny coverage for Serostim

[1] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4297925/; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2095035/ (as of 11/19/2018)

to Plaintiff because he does not have HIV. Centers for Medicare and Medicaid Services (CMS) have adopted a regulation that interprets the Medicare statute to exclude from Part D's coverage all indications that are not "medically accepted." *See* 42 C.F.R. § 423.100. Under *Chevron, U.S.A., Inc. v. Natural Resources Defense Council, Inc.*, 467 U.S. 837, 104 S. Ct. 2778, (1984), the courts defer to this interpretation unless it is (1) contrary to "the unambiguously expressed intent of Congress" or (2) unreasonable. *Id.* at 842-43. *United States v. Celgene Corp.*, 226 F. Supp. 3d 1032, 1045 (C.D. Cal. 2016). Furthermore, the agency's interpretation is not even entitled to the *Chevron* deference pursuant to 42 C.F.R. §§ 405.1048, 405.1130 because it is non-precedential. *See Tangney v. Burwell*, 186 F.Supp.3d 45, 51-52 (D.Mass. 2016); *Layzer v. Leavitt*, 770 F.Supp.2d 579 (S.D.N.Y. 2011).

Under *Skidmore v. Swift & Co.*, 323 U.S. 134 (1994), one of the more salient factors to be considered is whether the agency has consulted appropriate sources, employed sensible heuristic tools, and adequately substantiated its ultimate conclusion. Here, the agency failed to do so by discounting, for no stated reason, NIH studies that showed that wasting/cachexia was not caused by the HIV, but by the drugs used to treat it (ft. 1, *supra*). This is in direct contradiction to the statement by ALJ Myles that AIDS is the underlying basis for cachexia (AR unknown).

Medicare offered no objectives it sought to achieve by denying coverage of Serostim to Plaintiff. DHHS does not contest the fact that it has no policy, otherwise it might have articulated it during and after the three years of administrative review. There exists no rational basis for the non-coverage policy because the medication is "off-label" (AR, unknown) if the policy is, as a cost-saving measure, drastically under inclusive, let alone founded upon a prohibited or arbitrary ground. *Lazy Y Ranch Ltd. v. Behrens*, 546 F.3d 580, 590 (9th Cir. 2008). Although *Lazy Ranch* was about the equal protection clause of the Fourteenth Amendment, by analogy that case centered on there being a rational basis for the sufficiency of a "Proffered Rational Basis" and applies here to the Rule 12(b)(6) motion under the Due Process Clause of the Fifth Amendment. Whether someone has HIV or not is not a rational basis for denying life-saving medication, if the underlying condition, cachexia/wasting syndrome, is the same. There is no rational relationship

between someone's HIV status and the government's desire to limit medication coverage; the government could save far more money using other measures, such as by eliminating coverage completely. Indeed, Dr. Dennis Watson testified at the second hearing before ALJ Myles that it is true that coverage is discretionary for FDA "off-label" uses. One such medication, for example, was Neurontin, which has had an off-label use for many years for pain relief. Dr. Watson pointed out that Lyrica is similarly covered for off-label use. When asked if the reason to deny coverage was because Serostim retail price was approximately $14, 500 per month, the implication from this witness was in the affirmative. Specifically, by his silence he acquiesced.

A separate but related due process violation came to light in the MAC final decision wherein the MAC judge stated that all issues before the ALJs are analyzed if the Beneficiary (now Plaintiff) is unrepresented. The MAC Judge did not do this, even though Plaintiff was not represented at any time during the administrative proceedings. Had the MAC followed this regulation/rule, the DHHS would have clearly articulated material facts; e.g., that there is no policy under these facts and why Judge Myles found, did Serostim, the medication for Lipodystrophy (severe wasting syndrome), would not be covered. Had he MAC followed its own rule of doing analysis, it would have likely narrowed issues in the court case. In Sum, so long as there is a colorable claim under the Due Process Clause this Court has jurisdiction. A colorable Due Process claim exits to seek reconsideration of an adverse benefits determination. *See Udd v. Massanari,* 245 F.3d 1096, 1099 (9th Cir. 2001). There are a lot of facts alleged in support of the due process cause of action.

Process issues relating to the unknown policy that was the basis to conclude the "off-label" assertion led to the conclusion that the NIH studies had to effect the finding of no coverage based on the ALJ limited jurisdiction to engage is statutory interpretation as was done in *Tangnet v. Burwell,* 186 F. Supp.3d45 (2016.)

D. Plaintiff Properly Alleged Section 504 Violation by DHHS.

Section 504 of the Rehabilitation Act broadly prohibits discrimination in programs conducted by the federal government or receiving federal financial assistance. *Doe v. Attorney*

Gen. of United States, 941 F.2d 780, 786 n.6 (9th Cir. 1991).

The Ninth Circuit has recognized that the focus of the prohibition in § 504 is "whether disabled persons were denied 'meaningful access' to state-provided services." *Crowder v. Kitagawa*, 81 F.3d 1480, 1484 (9th Cir. 1996) (quoting *Alexander v. Choate*, 469 U.S. 287, 302 (1985)); *Bird v. Lewis & Clark College*, 303 F.3d 1015, 1020 (9th Cir. 2002) ("[T]he College must provide Bird with 'meaningful access' to its programs.") (internal quotations omitted). Clearly here, Plaintiff has been denied "meaningful access" to prescription medication that has been afforded to individuals who have HIV, despite having the same resulting disability. Evidence that appropriate services were provided to *some* disabled individuals does not demonstrate that others were not denied meaningful access "solely on the basis of their disability." *See Lovell v. Chandler*, 303 F.3d 1039, 1054 (9th Cir. 2002) ("The State's appropriate treatment of some disabled persons does not permit it to discriminate against other disabled people under any definition of 'meaningful access.'". (internal citations omitted)

Generally, in balancing accommodations versus undue hardships to include individuals with a disability, total federal agency program cost must be considered. In *US Airways, Inc. v. Barnett*, 535 U.S. 391, 402, 122 S. Ct. 1516 (2002) the Court surmised that "undue hardship inquiry focuses on the hardships imposed . . . in the context of the particular agency's operations"). *See also Am. Council of the Blind v. Astrue*, No. C 05-04696 WHA, 2009 U.S. Dist. LEXIS 97599, at *44 (N.D. Cal. Oct. 20, 2009).

In a 1992 decision, the Ninth Circuit held that claims predicated on Section 504 of the Rehabilitation Act do not "arise under" the Social Security Act. *J.L. v. Soc. Sec. Admin.*, 971 F.2d 260, 263 (9th Cir. 1992), overruled in part on other grounds, *Lane v. Pena*, 518 U.S. 187, 116 S. Ct. 2092, 135 L. Ed. 2d 486 (1996). *See aso Am. Council of the Blind v. Astrue*, No. C 05-04696 WHA, 2008 U.S. Dist. LEXIS 86524, at *13-14 (N.D. Cal. Apr. 23, 2008). "The Rehabilitation Act, not the Social Security Act, establishes the basis for plaintiffs' discrimination claims because the Rehabilitation Act creates the duty on the part of the agency to provide meaningful access to participants..." *Id.* at 16. In *Bowen v. Michigan Academy of Family Physicians*, 476 U.S. 667,

681, 106 S. Ct. 2133, 90 L. Ed. 2d 623 (1986), the Supreme Court declined to extend the Section 405(h) judicial bar to claims concerning Medicare Part B because to do so would mean the claims would receive no judicial review at all. "This is an extreme position, and one we would be most reluctant to adopt without a showing of 'clear and convincing evidence' to overcome the strong presumption that Congress did not mean to prohibit all judicial review of executive action." *Id.* at 680-681.

III. CONCLUSION

Based on the above, Defendant's motion to dismiss should be denied. In the alternative, Plaintiff asks that the Court grant leave to amend the complaint to cure any deficiencies.

Dated: November 27, 2018

PEOPLE WITH DISABILITIES FOUNDATION

By: /s/ Zoya Yarnykh
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ALEX M. AZAR II

UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

OAKLAND DIVISION

STEVEN BRUCE, Plaintiff, v. ALEX M. AZAR II ET AL., Defendants.	Case No. 4:18-cv-05022-HSG **DECLARATION OF KIMBERLY A. ROBINSON RE: 2016 AHFS-DI COMPENDIUM**

I, Kimberly Robinson, declare as follows:

1. I am employed as an Assistant United States Attorney for the Northern District of California. I represent Federal Defendant Alex M. Azar II in the above-captioned action. I have personal knowledge of the matters set forth below, except those matters that are based on information and belief, which I believe to be true, and could and would testify competently to them if called to do so.

2. Attached hereto as Exhibit A is a true and correct copy of an excerpt from the 2016 AHFS-DI compendium. The excerpt, which consists of the 2016 version of the compendium's cover

Exhibit A1

page and relevant part of the table of contents, was given to me by a librarian at National Institutes of Health library in Washington, DC. I personally examined the table of contents of the compendium to determine whether it contained an entry for the drug Serostim or Somatropin, which I understand to be the drug's generic name. I determined that Somatropin was the generic name of the drug based on the FDA label, which also refers to Serostim as Somatropin. After reviewing the table of contents, I determined that the compendium did not contain Serostim or Somatropin because the drug names did not appear in the table of contents.

I declare under penalty of perjury that the foregoing is true and correct and that this declaration was executed under the laws of the United States on this 6th day of March, 2019, in San Francisco, California.

/s/ *Kimberly Robinson*
KIMBERLY ROBINSON

DATED: March 6, 2019

STEVEN BRUCE, SBN 70300
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UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

OAKLAND DIVISION

STEVEN BRUCE Plaintiff, vs. ALEX M. AZAR II, ET AL., Defendant(s).	Case Number: 4:18-cv-05022-HSG DECLARATION OF ANNE-MARIE CHANDLER RE: REQUESTING THE 2016-2019 AHFS COMPENDIUM IN SUPPORT OF PLAINTIFF'S REPLY TO HHS MOTION FOR SUMMARY JUDGEMENT

I, Anne-Marie Chandler, declare as follows:

1. I am employed as a legal assistant for People With Disabilities Foundation.

2. I have personal knowledge of all facts stated in this declaration, and if called to testify, I could and would testify competently thereto.

3. On September 5, 2019, I called the National Institutes of Health (NIH) library to request from the librarian parts of the Medicare compendia for Serostim (generic is Somatropin) to see information on if and why it was used from 2015 through 2019, how long it takes for Plaintiff to get the info and, if there is a charge, how much.

Exhibit A2

4. On Friday September 6, 2019 I attempted to reach the National Institute of Health Library at (301) 496-1080, in Bethesda, Maryland based on the Internet website. I was instructed to leave a message; I left my name and telephone (415) 931-3070 with the information I needed: Medicare Compendium for Serostim/Somatropin.

5. Not receiving a return call, I called Monday morning, September 9, 2019. I spoke to a librarian, Patrick Hanrahan, requesting a copy of the Compendium. He asked me if I was an NIH employee because only employees can access these compendia. He stated that I should contact the National Library of Medicine in the hospital at Bethesda, Maryland as his library only serves the NIH employees.

6. About ten minutes later, I placed a call to the National Library of Medicine. I asked for a librarian and the woman told me she was a librarian and would assist me; she did not provide her name when I asked for my reference. I told her my call today was to request the Compendia for a Medicare case. She asked me if I had read the article about requesting that information; I told her I did not read nor know about the article. She said that there were two ways to get the information: on site in Bethesda or to request it from my local library. She stated she would send me an email with the link to read the article with the instructions for use in requesting this information. I gave her my email.

7. I did not receive the link.

I declare under penalty of perjury under the laws of the United States that the foregoing is true and correct and that this declaration was executed in San Francisco, California.

DATED: 10/14/19

/s/ *Anne-Marie Chandler*

Anne-Marie Chandler
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UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

STEVEN BRUCE, Plaintiff, vs. ALEX M. AZAR II, Secretary of the Department of Health and Human Services, ENVISION INSURANCE COMPANY, BLUE SHIELD OF CALIFORNIA, and DOES 1-50, Defendants.	Case No. 4:18-cv-05022 HSG **PLAINTIFF'S ADMINISTRATIVE MOTION RE: ADDITIONAL FILING OF ONE OF DEFENDANT'S DOCUMENTS IN RESOLUTION OF A DISPUTED MATERIAL FACT IN BOTH PARTIES' MOTIONS FOR SUMMARY JUDGEMENT [Rule 7-11]** **DATE OF HEARING: DECEMBER 5, 2010, 2 P.M.** Judge: Hon. Haywood S. Gilliam, Jr.

TO ALL PARTIES AND THEIR ATTORNEYS OF RECORD:

Plaintiff Steven Bruce respectfully moves pursuant to Local Rule 7-11 for an Order allowing him to file a Health & Human Services' (HHS) 3 page internet post dated September 19, 2019.

In both parties' Motions for Summary Judgement, a major issue is that Serostim is used to treat lipodystrophy with or without HIV. The government argues that one must also have an unrelated autoimmune disease, HIV. Our position is that causation is irrelevant to this case

because the virus that causes acquired generalized Lipodystrophy (without HIV) has never been discovered. The purpose of Serostim, in both cases, is for Lipodystrophy. This internet HHS post is factual evidence to resolve this conflict. It explains that the HIV population no longer needs Serostim but the population with Lipodystrophy without HIV does need it.

Opposing counsel has declined to stipulate to this motion.

Respectfully submitted,

Dated: November 18, 2019

PEOPLE WITH DISABILITIES FOUNDATION

By: /s/ Steven Bruce
STEVEN BRUCE
Attorneys for Plaintiff

AIDSinfo

Side Effects of HIV Medicines

HIV and Lipodystrophy

Last Reviewed: September 19, 2019

Key Points

- Lipodystrophy refers to the changes in body fat that can affect some people with HIV.
- Lipodystrophy can include buildup of body fat, loss of body fat, or both.
- Lipodystrophy may be due to HIV infection or medicines used to treat HIV. Newer HIV medicines are less likely to cause lipodystrophy than HIV medicines developed in the past.
- Lipodystrophy will not be a concern for most people who start HIV treatment now.

What is lipodystrophy?

Lipodystrophy refers to the changes in body fat that can affect some people with HIV. Lipodystrophy can include buildup of body fat, loss of body fat, or both.

Fat buildup (also called lipohypertrophy) can occur:

- Around the organs in the abdomen
- On the back of the neck between the shoulders (called a buffalo hump)
- In the breasts

Fat loss (also called lipoatrophy) tends to occur:

- In the arms and legs
- In the buttocks
- In the face

What causes lipodystrophy?

Lipodystrophy may be due to HIV infection or medicines used to treat HIV. Newer HIV medicines are less likely to cause lipodystrophy than HIV medicines developed in the past.

Lipodystrophy will not be a concern for most people who start HIV treatment now.

How is lipodystrophy treated?

If you have lipodystrophy, talk to your health care provider about treatment options. Your health care provider may recommend that you switch to another HIV medicine.

There are ways to manage lipodystrophy. Making dietary changes and getting regular exercise may help to build muscle and reduce abdominal fat.

Liposuction (surgical removal of fat) and injectable facial fillers are sometimes used to treat lipodystrophy. There are also medicines that may help lessen the effects of lipodystrophy.

This fact sheet is based on information from the following sources:

- From the Department of Health and Human Services: Guidelines for the Use of Antiretroviral

Agents in Adults and Adolescents with HIV: Adverse Effects of Antiretroviral Agents

- From the Department of Veterans Affairs: FAQ: Will HIV medicines cause changes to your fat and stomach?
- From the Health Resources and Services Administration: Guide for HIV/AIDS Clinical Care: Abnormalities of Body-Fat Distribution

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UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

STEVEN BRUCE, Plaintiff, vs. ALEX M. AZAR II, Secretary of the Department of Health and Human Services, ENVISION INSURANCE COMPANY, BLUE SHIELD OF CALIFORNIA, and DOES 1-50, Defendants.	Case No. 4:18-cv-05022 HSG **PLAINTIFF'S SECOND ADMINISTRATIVE MOTION RE: ADDITIONAL FILING OF FOUR OF DEFENDANT'S DOCUMENTS IN RESOLUTION OF A DISPUTED MATERIAL FACT IN BOTH PARTIES' MOTIONS FOR SUMMARY JUDGMENT [Rule 7-11]** **DATE OF HEARING: DECEMBER 5, 2010, 2 P.M.** Judge: Hon. Haywood S. Gilliam, Jr.

TO ALL PARTIES AND THEIR ATTORNEYS OF RECORD:

Plaintiff Steven Bruce respectfully moves pursuant to Local Rule 7-11 for an Order allowing him to file four abstracts available from the HHS National Institutes of Health, PubMed website.

The reasons for filing this administrative motion are the same as the reasons for our first administrative motion: they are to a relevant to a resolution of a disputed material fact and consistent with and corroborative of the documents filed on November 18, 2019 These documents

were discovered by Plaintiff on November 26, 2019, and are evidence that Defendant HHS has had knowledge of research on non HIV-associated lipodystrophy going back approximately 20 years.

We asked opposing counsel today if they would stipulate to this motion. She responded, "I will ask my client and get back to you. Have a nice holiday." Due to the upcoming Thanksgiving holiday and the proximity to oral argument on December 5, 2019, we are filing this motion today.

Respectfully submitted,

Dated: November 27, 2019

PEOPLE WITH DISABILITIES FOUNDATION

By: /s/ Steven Bruce
STEVEN BRUCE
Attorneys for Plaintiff

Endocr Pract. 2010 Mar-Apr;16(2):310-23. doi: 10.4158/EP09154.RA.

Clinical classification and treatment of congenital and acquired lipodystrophy.

Chan JL[1], Oral EA.

Author information

1 Amylin Pharmaceuticals, Inc., San Diego, California, USA.

Abstract

OBJECTIVE: To review the initial clinical manifestations of congenital and acquired lipodystrophy syndromes, discuss novel classifications associated with genetic mutations, and assess currently available therapeutic options for patients with lipodystrophy.

METHODS: This review is the result of the authors' collective clinical experience and a comprehensive MEDLINE literature search on the English-language literature published between January 1966 and October 2009 on "lipodystrophy." This review focuses primarily on severe dystrophy not related to human immunodeficiency virus (HIV) infection, in light of the additional scope required to cover HIV-related lipodystrophy.

RESULTS: Congenital lipodystrophy syndromes are characterized by a paucity of adipose tissue and classified on the basis of the extent of fat loss and heritability Paradoxically, they are associated with metabolic abnormalities often found in obese patients, including insulin resistance, diabetes, and severe hypertriglyceridemia. Patients with severe forms of lipodystrophy are also deficient in adipokines such as leptin, which may contribute to metabolic abnormalities. The search for molecular defects has revealed a role for genes that affect adipocyte differentiation (for example, peroxisome proliferator-activated receptor gamma), lipid droplet morphology (seipin, caveolin-1), or lipid metabolism (AGPAT2). Others (lamin A/C) are known to be associated with completely different diseases. There are also acquired forms of lipodystrophy that are thought to occur primarily attributable to autoimmune mechanisms. Recently, recombinant leptin has emerged as a useful therapy.

CONCLUSION: Lipodystrophy syndromes have advanced our understanding of the physiologic role of adipose tissue and allowed identification of key molecular mechanisms involved in adipocyte differentiation. Novel therapeutic strategies are being developed on the basis of the pathophysiologic aspects of these syndromes.

Comment in

W(h)ither metreleptin for lipodystrophy and the metabolic syndrome? [Endocr Pract. 2010]

PMID: 20061300 DOI: 10.4158/EP09154.RA

[Indexed for MEDLINE]

Publication types, MeSH terms +

LinkOut - more resources +

J Clin Endocrinol Metab. 2019 Nov 1;104(11):5120-5135. doi: 10.1210/jc.2018-02730.

Comorbidities and Survival in Patients With Lipodystrophy: An International Chart Review Study.

Akinci B[1], Oral EA[2], Neidert A[2], Rus D[2], Cheng WY[3], Thompson-Leduc P[3], Cheung HC[3], Bradt P[4], Foss de Freitas MC[5], Montenegro RM[6], Fernandes VO[6], Cochran E[7], Brown RJ[7].

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Abstract

CONTEXT: Limited natural history data are available in patients with non-HIV-related lipodystrophy syndromes who never received disease-specific therapies, making interpretation of benefits of therapies in lipodystrophy syndromes challenging.

OBJECTIVE: We assessed the natural history of non-HIV-related generalized lipodystrophy (GL) and partial lipodystrophy (PL) in patients who have never received leptin or other lipodystrophy-specific therapies.

DESIGN/SETTING/PATIENTS: We conducted an international chart review of 230 patients with confirmed GL or PL at five treatment centers who never received leptin or other lipodystrophy-specific therapies. Patients were observed from birth to loss to follow-up, death, or date of chart abstraction.

OUTCOME MEASURES: Lifetime prevalence of diabetes/insulin resistance and select organ abnormalities, time to diabetes/insulin resistance, first organ abnormality, disease progression, and mortality were described.

RESULTS: Diabetes/insulin resistance was identified in 58.3% of patients. Liver abnormalities were the most common organ abnormality (71.7%), followed by kidney (40.4%), heart (30.4%), and pancreatitis (13.0%). Kaplan-Meier estimates of mean (SE) time to first organ abnormality were 7.7 years (0.9) in GL and 16.1 years (1.5) in PL ($P < 0.001$). Mean time to diabetes/insulin resistance was 12.7 years (1.2) in GL and 19.1 years (1.7) in PL ($P = 0.131$). Mean time to disease progression was 7.6 years (0.8) and comparable between GL and PL subgroups ($P = 0.393$). Mean time to death was 51.2 years (3.5) in GL and 66.6 years (1.0) in PL ($P < 0.001$).

CONCLUSIONS: This large-scale study provides comprehensive, long-term data across multiple countries on the natural history of non-HIV-related lipodystrophy.

PMID: 31314093 PMCID: PMC6760298 [Available on 2020-07-17] DOI: 10.1210/jc.2018-02730

LinkOut - more resources

Published in final edited form as:
Dermatol Clin. 2008 October ; 26(4): 569–ix. doi:10.1016/j.det.2008.05.004.

LIPODYSTROPHY SYNDROMES

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SYNOPSIS

Lipodystrophies are a group of heterogeneous disorders characterized by varying degrees of body fat loss and predisposition to insulin resistance and its metabolic complications. They are subclassified depending on the degree of fat loss and whether the disorder is genetic or acquired. The two most common genetic varieties include congenital generalized lipodystrophy and familial partial lipodystrophy; and the two most common acquired varieties include acquired generalized lipodystrophy and acquired partial lipodystrophy. Highly active antiretroviral therapy-induced lipodystrophy in HIV-infected patients and drug-induced localized lipodystrophy are other common subtypes. The metabolic abnormalities associated with lipodystrophy include insulin resistance, often leading to diabetes mellitus and its complications, hypertriglyceridemia that may be severe enough to cause acute pancreatitis, and hepatic steatosis that may lead to cirrhosis. The severity of the metabolic abnormalities is usually proportional to the extent of fat loss, with patients with congenital and acquired generalized lipodystrophies developing complications at early ages. Localized lipodystrophy does not have associated metabolic derangements and it is mostly a cosmetic problem. Management of lipodystrophies focuses on preventing and treating metabolic complications. Diet and exercise are an integral part of management. Conventional therapies, including metformin and insulin, are used to treat diabetes mellitus and lipid-lowering drugs are used to treat dyslipidemia. Patients with generalized lipodystrophy have markedly reduced serum leptin levels and metreleptin replacement therapy has been used successfully in such patients to improve metabolic profile.

Keywords

Lipodystrophy; congenital generalized lipodystrophy; familial partial lipodystrophy; acquired generalized lipodystrophy; acquired partial lipodystrophy; metreleptin

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Disclosure Statement: Dr. Hussain has no disclosures.

INTRODUCTION

Lipodystrophies are a group of rare disorders of diverse etiology which are characterized by variable loss of body fat. The loss of body fat may affect nearly the entire body (generalized), only certain body regions (partial) or small areas under the skin (localized). Depending upon the severity and extent of body fat loss, patients may be predisposed to metabolic complications associated with insulin resistance[1,2]. These metabolic complications include early onset of diabetes mellitus, hypertriglyceridemia and hepatic steatosis[1–3]. In some patients, these metabolic complications are challenging to manage and can lead to complications including diabetic nephropathy and retinopathy, acute pancreatitis (from extreme hypertriglyceridemia and chylomicronemia), hepatic cirrhosis and premature cardiovascular disease. Other common clinical manifestations include polycystic ovarian syndrome (PCOS), acanthosis nigricans as a result of severe insulin resistance, and eruptive xanthomas due to extreme hypertriglyceridemia[1–3].

The loss of body fat can result from underlying genetic defects (genetic lipodystrophies including autosomal recessive or dominant subtypes) or from autoimmune mechanisms (acquired lipodystrophies including generalized or partial subtypes) or drugs (e.g. highly active antiretroviral therapy (HAART)-induced partial lipodystrophy in human immunodeficiency virus (HIV)-infected patients or localized lipodystrophies from insulin and other injected drugs)[1–3]. The localized lipodystrophies and lipodystrophy in HIV-infected patients are the most prevalent subtype of lipodystrophies while the other genetic and acquired lipodystrophies are quite rare[2]. Localized lipodystrophies do not predispose to metabolic complications as the loss of fat is trivial; however, other partial or generalized lipodystrophies cause variable predisposition to metabolic complications (Figure 1).

The major subtypes of lipodystrophy have been described in Table 1. However, it is important to note that given the heterogeneity of manifestations, variable patterns of fat loss and genetic bases that have yet to be identified, all lipodystrophy syndromes cannot be classified into these categories[4]. Regardless of the etiology, patients with generalized lipodystrophy have extremely low serum levels of adipocytokines, such as leptin and adiponectin[5,6], whereas serum leptin and adiponectin levels in those with partial lipodystrophies can range from low to high. Marked hypoleptinemia may induce excessive appetite and can exacerbate metabolic complications of insulin resistance[3]. This review will cover the major types of lipodystrophy syndromes.

GENETIC LIPODYSTROPHIES

The two main types of genetic lipodystrophies are congenital generalized lipodystrophy (CGL), an autosomal recessive syndrome (Table 2 and 3) and familial partial lipodystrophy (FPLD), mostly an autosomal dominant syndrome (Table 4). There are other extremely rare types which have been reported in approximately 30 patients or less (Table 5). These extremely rare types of genetic lipodystrophies are not discussed further in details in this review.

Congenital Generalized Lipodystrophy

Congenital generalized lipodystrophy (CGL), or Berardinelli-Seip syndrome, is an autosomal recessive disorder characterized by generalized lack of adipose tissue either at birth or within the first year of life. Patients have prominent musculature and subcutaneous (sc) veins[1,7,8]. Most cases are diagnosed at birth or early in childhood because of the striking fat loss, but a few patients without access to regular medical care may be identified later in life.

Patients with CGL can develop hyperphagia as a result of profound leptin deficiency in early childhood, and may have accelerated linear growth, advanced bone age and features suggestive of acromegaly such as enlarged hands, feet and jaw[5,6]. Severe metabolic complications, along with hepatomegaly and splenomegaly, develop at an early age. Hyperinsulinemia leads to development of widespread acanthosis nigricans, followed by onset of diabetes mellitus during adolescence[7,8]. Diabetes is generally ketosis-resistant. Some patients develop extreme hypertriglyceridemia especially after the onset of insulin-resistant diabetes mellitus and are prone to recurrent attacks of acute pancreatitis[7,8]

Hepatic steatosis is common and severe, and can progress to steato-hepatitis, cirrhosis and liver failure[4]. Female CGL patients have additional clinical features including hirsutism, clitoromegaly, irregular menstrual periods, polycystic ovaries, and/or infertility[1]. There are four genetically distinct subtypes of CGL[9,10,7,8,11,12] and besides common clinical features listed above, each one has some peculiar clinical features (Tables 2, 3).

Familial Partial Lipodystrophy

Familial partial lipodystrophy (FPLD) is mostly inherited as an autosomal dominant disorder and is characterized by sc fat loss from both the upper and lower extremities and variable fat loss from the trunk[13,14]. These patients have normal fat distribution during childhood, followed by onset around late childhood or puberty of progressive and variable sc fat loss typically from the extremities (causing the musculature to appear prominent), but variably from the anterior abdomen and chest[13,14]. Some patients may have small size of the breasts due to reduced or lack of overlying sc fat. At the same time, there is often fat accumulation in the face, neck, perineal and intra-abdominal areas, especially in women. Excess fat accumulation in the dorso-cervical (causing a buffalo-hump), supraclavicular and submental regions gives these patients a "Cushingoid appearance" and many of these patients may be confused with having "Cushing's syndrome". These patients may be clinically hard to detect if the fat loss is subtle, and particularly males since many normal men are also quite muscular[13].

FPLD in women may present with masculinization and menstrual irregularity as well as metabolic complications. Women with FPLD have a high prevalence of polycystic ovarian syndrome (PCOS) compared to the 6–8% prevalence observed in the general population, however infertility is not common[13]. This increased prevalence of PCOS and metabolic complications occurs more frequently in those women who have excess fat accumulation in non-lipodystrophic regions.

As compared to patients with generalized lipodystrophies, hepatic steatosis and acanthosis nigricans is less pronounced, however, hypertriglyceridemia is common and severe, with high risk of acute pancreatitis. In addition, these patients may also develop myopathy, cardiomyopathy and/or conduction system abnormalities[15]. There are several genetically distinct varieties of FPLD[16–26], however, the clinical differences between these various subtypes have not been very clear so far (Table 4).

ACQUIRED LIPODYSTROPHIES

Acquired Generalized Lipodystrophy

Acquired generalized lipodystrophy (AGL), or Lawrence syndrome, is characterized by generalized loss of sc fat that occurs gradually in individuals who are born with a normal fat distribution. The fat loss typically begins in childhood or adolescence, but can rarely begin after 30 years of age[27]. It can occur over a variable time period, ranging from a few weeks to months or years, and affects all sc areas of the body especially the face and extremities and may include the palms and soles. Orbital and bone marrow fat depots appear to be preserved, while intra-abdominal fat loss is variable. AGL is more frequent in the females than males (3:1)[27]. AGL patients are predisposed to the same metabolic complications as other patients with lipodystrophies such as insulin resistance associated with diabetes mellitus and hypertriglyceridemia, with hypoleptinemia thought to be contributing to the pathogenesis. Usually these complications are quite severe in these patients. Most of the patients have associated autoimmune diseases, especially juvenile dermatomyositis, or panniculitis (pathologically infiltration of adipose tissue with inflammatory cells of various types resulting in loss of sc fat) (Table 6). In some patients, the underlying mechanism of fat loss is not clear (Idiopathic variety). Usually the metabolic complications are less severe in patients with panniculitis-associated AGL as compared to the other two subtypes.

Acquired Partial Lipodystrophy (Barraquer-Simons Syndrome)

Acquired partial lipodystrophy (APL) is characterized by gradual loss of subcutaneous fat from the upper body, i.e., the face, neck, upper extremities and upper trunk[28]. Usually the lower abdomen, hips and lower extremities are spared and in fact, after puberty, especially female patients may accumulate excess fat there. APL is more frequent in the females than males (4:1). It is frequently associated with autoimmune diseases. Most patients have a circulating auto-antibody called complement 3 nephritic factor, and have low circulating levels of serum complement 3[28]. Approximately 20% of the patients develop membrano-proliferative glomerulonephritis and some of these patients develop end stage renal disease requiring renal transplantation. Rare patients have drusen on fundus examination. Metabolic complications are not seen as frequently as in other types of lipodystrophy[28].

Highly Active Anti-Retroviral Therapy-induced Lipodystrophy in HIV-infected patients

Lipodystrophy in HIV-infected patients usually occurs after approximately 2 – 4 years of highly active anti-retroviral therapy (HAART) consisting of HIV-1 protease inhibitors (PIs) or nucleoside reverse transcriptase inhibitors (NRTIs) (Table 7)[29,30]. It is characterized by the loss of subcutaneous fat from the upper and lower extremities as well as from the face, with increased fat accumulation in the neck, anteriorly and posteriorly, as well as in the

upper trunk and intra-abdominal region[29,30]. Many PIs have been shown to inhibit zinc metalloprotease, the key enzyme involved in post-translation processing of prelamin A to mature lamin A[31]. Thus, PI-based HAART may result in accumulation of toxic prelamin A. NRTIs may induce lipodystrophy by causing mitochondrial dysfunction[32].

Localized Lipodystrophies

Localized lipodystrophies are characterized by loss of fat from small areas, either single or multiple. Sometimes it can affect portions of the limbs or large contiguous areas on the trunk. Patients with localized lipodystrophies do not develop any metabolic abnormalities. There are several etiologies of localized lipodystrophies (Table 8)[33].

MANAGEMENT

The treatment of lipodystrophy is focused on managing the metabolic abnormalities to prevent complications, and cosmetic appearance. Although there is no cure for lipodystrophy, morbidity and mortality can be improved through early intervention. Diet and exercise form an integral part of the treatment plan, although clinical trial data are not available.

A diet with a well-balanced macronutrient composition of about 50 – 60% carbohydrates, 20 – 30% fat and about 10 – 20% protein is appropriate for most patients. Over-feeding should be avoided, especially in infants and children (despite their lack of weight gain), as this can accelerate hepatic steatosis and worsen diabetes and hyperlipidemia. Energy restricted diets are more appropriate in adults, as children with growth and developmental needs may otherwise develop deficiencies.

Exercise, in the absence of contraindications, can help improve metabolic parameters, so patients should be encouraged to be physically active. Those who are predisposed to cardiomyopathy, such as patients with CGL, FPLD2, and progeroid syndromes should undergo a cardiac evaluation before engaging in an exercise program, and should avoid strenuous exercise. To avoid traumatic injuries, patients with severe hepatosplenomegaly and CGL patients with lytic lesions in the bones should avoid contact sports.

Strategies to reduce hypertriglyceridemia include medium chain triglyceride-based formulas in infants[34], and very low fat diets in older individuals. Any fat intake should be in the form of *cis*-mono-unsaturated fats and long chain omega-3 fatty acids. Patients who have developed acute pancreatitis secondary to hypertriglyceridemia, parental nutrition should be administered until they recover and they should subsequently be on an extremely low fat (total dietary fat less than 20 grams/day) diet. In patients who have not reached lipid-lowering goals after diet and lifestyle intervention, lipid-lowering drugs may be used.

Patients with insulin resistance and diabetes mellitus should be treated with conventional therapies, including both oral (metformin is the first-line drug) and insulin. Insulin therapy often provides the mainstay of treatment, and many patients require concentrated forms (such as U-500 regular insulin) because of severe insulin resistance. Whether thiazolidinediones are particularly efficacious in FPLD patients with *PPARG* mutations

remains unclear. Simple sugars should be avoided in favor of high-fiber complex carbohydrates consumed throughout the day in combination with protein and/or fat, to avoid blood glucose spikes. The treatment goals are similar to diabetic patients without lipodystrophy.

Hypertension, if uncontrolled, may be treated with angiotensin converting enzyme inhibitors or angiotensin receptor blockers, as these medications also have favorable effects on proteinuria. No specific treatments have been shown to be particularly effective for hepatic steatosis or steato-hepatitis associated with lipodystrophy.

Generalized lipodystrophies are characterized by extremely low serum leptin levels[5], which led to research into recombinant human leptin (metreleptin) as a treatment option[35], and since then several long term studies have shown beneficial effects[36–39].

Metreleptin therapy has been shown to improve metabolic abnormalities in generalized lipodystrophy patients, including decreased serum triglyceride levels, increased insulin sensitivity and reduced hepatic steatosis (Table 9)[3]. It is currently the only drug specifically approved for treatment of lipodystrophy[3]. It is administered as a daily sc injection[40], and dose adjustments are made every 3 – 6 months based on metabolic parameters and weight change. The most common side effects include hypoglycemia and injection site reactions such as erythema and/or urticaria. The other side effects include development of neutralizing antibodies to metreleptin, and development of cutaneous T cell lymphomas especially in patients with AGL[41]. The precise significance of neutralizing antibodies to leptin remains unclear at this time and some patients with AGL who have never received metreleptin therapy have also been reported to develop lymphomas. Because of paucity of data, approval of metreleptin for different types of lipodystrophy varies by country, depending on their regulatory boards.

Change in body shape caused by lipodystrophy can often lead to psychological distress, and sometimes even physical discomfort, such as from absent fat pads on the feet and buttocks. Patients should be referred to appropriate mental health providers for emotional distress. Plastic surgery may improve appearance in some people, though data are limited. Possible interventions include autologous fat transfer, dermal fillers or muscle grafts to treat facial lipoatrophy; surgical reduction or liposuction of areas with excessive fat; and breast implants for improved cosmetics in women.

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KEY POINTS

- Lipodystrophies are a group of heterogeneous disorders characterized by varying degrees of body fat loss and predisposition to insulin resistance related metabolic complications.
- The two main subtypes of lipodystrophies are genetic and acquired lipodystrophies.
- Highly active antiretroviral therapy-induced lipodystrophy in HIV-infected patients and drug-induced localized lipodystrophy are common subtypes followed by genetic and acquired autoimmune lipodystrophies.
- Common metabolic abnormalities and complications associated with lipodystrophies include insulin resistance and diabetes mellitus, hypertriglyceridemia and hepatic steatosis.
- Management options include diet and exercise, conventional anti-hyperglycemic agents and lipid-lowering therapy, and metreleptin therapy, which is the only drug approved specifically for generalized lipodystrophy.

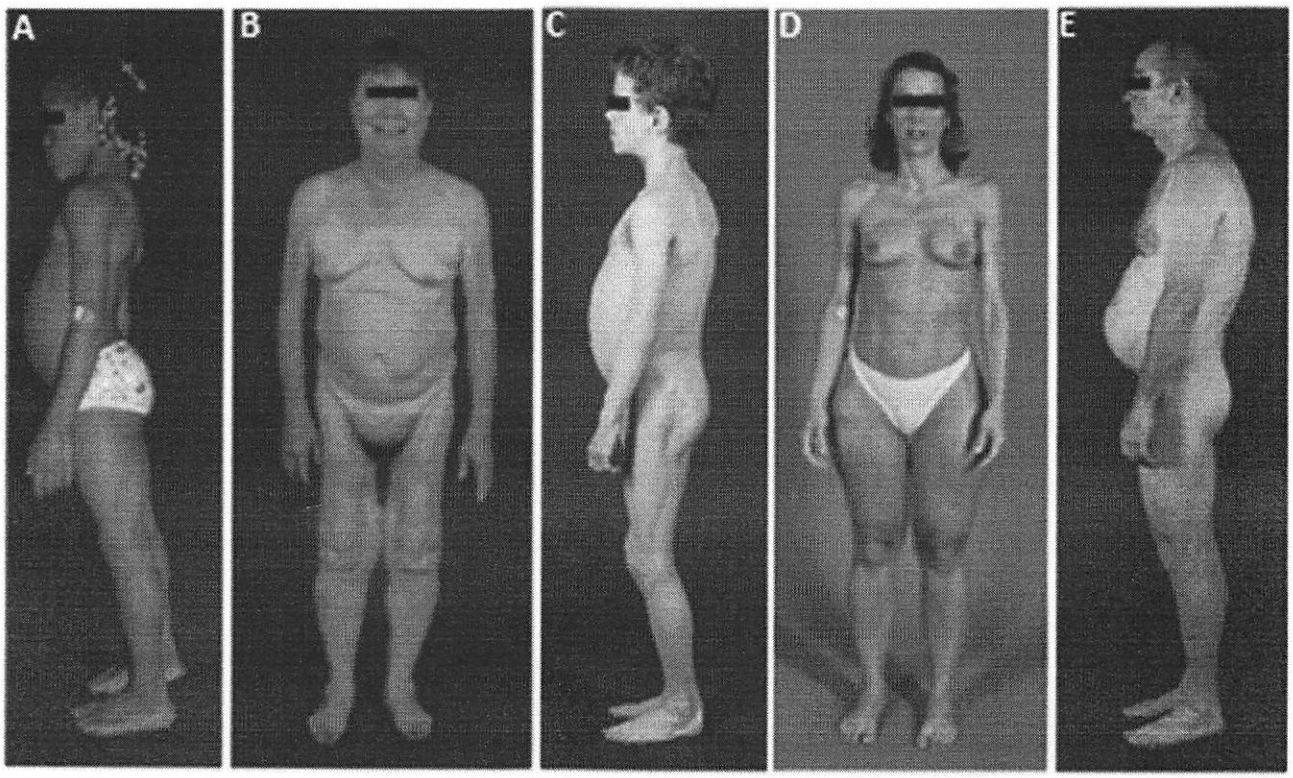

Fig. 1.

Clinical features of patients with various types of lipodystrophies. A. Lateral view of an 8-year-old African-American female with congenital generalized lipodystrophy (also known as Berardinelli-Seip congenital lipodystrophy), type 1 due to homozygous c.377insT (p.Leu126fs*146) mutation in *AGPAT2*. The patient had generalized loss of sc fat at birth and developed mild acanthosis nigricans in the axillae and neck later during childhood. She had umbilical prominence and acromegaloid features (enlarged mandible, hands and feet). B. Anterior view of a 65-year-old Caucasian female with familial partial lipodystrophy of the Dunnigan variety due to heterozygous p.Arg482Gln mutation in *LMNA*. She noticed loss of sc fat from the limbs at the time of puberty and later lost sc fat from the anterior truncal region. The breasts were atrophic. She had increased sc fat deposits in the face, anterior neck, suprapubic and vulvar region, and medial parts of the knees. C. Lateral view of an 8-year-old German boy with acquired generalized lipodystrophy. He started experiencing generalized loss of sc fat at age 3 with marked acanthosis nigricans in the neck, axillae and groin. He developed Crohn's disease at age 11 requiring hemicolectomy at age 13. D. Anterior view of a 39-year-old Caucasian female with acquired partial lipodystrophy (Barraquer-Simons syndrome). She noticed marked loss of sc fat from the face, neck, upper extremities, chest and abdomen at the age of 12 years but later developed increased sc fat deposition in the lower extremities. E. Lateral view of a 39-year-old Caucasian male infected with human immunodeficiency (HIV) virus with protease inhibitor containing highly active antiretroviral therapy induced lipodystrophy. He had marked loss of sc fat from the face and limbs but had increased sc fat deposition in the neck region anteriorly and posteriorly

showing buffalo hump. Abdomen was protuberant due to excess intra-abdominal fat. He had been on protease inhibitor containing antiretroviral therapy for more than 7 years.
From Garg A. Lipodystrophies: genetic and acquired body fat disorders. J Clin Endocrinol Metab 96:3313–25, 2011, with permission.

Table 1

General Classification of Major Lipodystrophy Subtypes

Lipodystrophy Subtype	Main Characteristics
Congenital generalized lipodystrophy (CGL)	Presents with near total loss of body fat at birth or during infancy. Autosomal recessive inheritance.
Familial Partial lipodystrophy (FPL)	Presents with variable loss of sc fat from the upper and lower extremities and the truncal region at puberty or later. Autosomal dominant inheritance.
Acquired generalized lipodystrophy (AGL)	Characterized by gradual loss of sc fat from nearly all over the body. Associated with auto-immune diseases.
Acquired partial lipodystrophy (APL)	Characterized by gradual loss of fat from the upper body, including head, neck, upper extremities and truncal region during childhood. Associated with autoantibodies called complement 3 nephritic factor and in ~20% of patients with membranoproliferative glomerulonephritis.
HAART-induced lipodystrophy in HIV patients	Associated with therapy including HIV-protease inhibitors or nucleoside analogues.
Localized lipodystrophy	Usually due to insulin injections or other injectables such as steroids

Abbreviations: HIV, human immunodeficiency virus; HAART, highly active antiretroviral therapy; sc, subcutaneous

Table 2

Subtypes of congenital generalized lipodystrophy (CGL) on the basis of genetic mutations

Subtype	Gene	Molecular Basis	Prevalence
CGL1	*AGPAT2*	AGPAT enzymes play a key role in biosynthesis of triglycerides and phospholipids in various organs. AGPAT isoform 2 is highly expressed in the adipose tissue.	Most common subtype[7,8,10]
CGL2	*BSCL2*	Seipin, encoded by *BSCL2*, plays a key role in fusion of small lipid droplets in the adipocytes and in adipocyte differentiation.	Second most common subtype [7–9]
CGL3	*CAV1*	Caveolin 1, is an integral component of caveolae, which are present on adipocyte membranes. Caveolae translocate fatty acids and other lipids to lipid droplets.	Only one patient reported[11]
CGL4	*PTRF*	PTRF (also known as cavin-1) is involved in biogenesis of caveolae and regulates expression of caveolins 1 and 3.	About 20 patients reported[12,42,43]

Abbreviations: CGL, congenital generalized lipodystrophy; *AGPAT2*, 1-acylglycerol-3-phosphate O-acyltransferase 2; *BSCL2*, Berardinelli-Seip congenital lipodystrophy 2; *CAV1*, caveolin 1; *PTRF*, polymerase I and transcript release factor.

Table 3

Unique clinical features in CGL subtypes

Affected feature	CGL type 1 (*AGPAT2*)	CGL type 2 (*BSCL2*)	CGL type 3 (*CAV1*)	CGL type 4 (*PTRF*)
Body fat loss	Only metabolically active adipose tissue is lost. Mechanical adipose tissue preserved.	Both metabolically active and mechanical adipose tissues are lost.	Absent metabolically active adipose tissue. Preserved mechanical and bone marrow adipose tissue.	Absent metabolically active adipose tissue. Preserved mechanical and bone marrow adipose tissue.
Cardiovascular complications	N/A	Cardiomyopathy	N/A	Cardiomyopathy, Catecholaminergic polymorphic ventricular tachycardia, prolonged QT, and sudden death.
Lytic bone lesions in long bones	Most frequent	Occasional	Not reported	Not reported
Gastrointestinal complications	N/A	N/A	Functional mega-esophagus	Congenital pyloric stenosis requiring surgery
Skeletal muscle	N/A	N/A	N/A	Congenital myopathy Developmental delay. Muscle weakness, Percussion-induced myotonia
Other features	N/A	Terato-zoospermia	Short stature, Hypocalcemia, Vitamin D resistance	Low bone density for age, distal metaphyseal deformation with joint stiffness, atlanto-axial instability. Late onset of lipodystrophy in infancy

Abbreviations: CGL, congenital generalized lipodystrophy; N/A, not applicable.

Table 4

Subtypes of familial partial lipodystrophy (FPLD)

Subtypez	Genetic Mutation	Prevalence
FPLD 1 (Kobberling-type)	Molecular basis unknown	Rare[16]
FPLD2 (Dunnigan-type)	Missense mutations in *LMNA*	Most common subtype. More than 500 patients reported[17–19]
FPLD3	Heterozygous mutations in *PPARG*	Second most common subtype. About 30–50 patients reported[20,21].
FPLD4	Heterozygous mutations in *PLIN1*	Reported in three families[22].
FPLD5	Homozygous nonsense mutation in *CIDEC* (Autosomal recessive)	One patient reported[23]
FPLD6	Homozygous mutation in *LIPE* (Autosomal recessive)	Six patients reported[24,25].
***AKT2*-linked lipodystrophy**	Heterozygous mutation in *AKT2*	Reported in one family[26].

Abbreviations: *FPLD*, familial partial lipodystrophy; *LMNA*, lamin A/C; *PPARG*, peroxisome proliferator-activated receptor gamma; *PLIN1*, perilipin 1; *CIDEC*, cell death-inducing DFFA-like effector c; *LIPE*, hormone sensitive lipase; *AKT2*, v-akt murine thymoma viral oncogene homolog 2.

Table 5

Extremely rare genetic lipodystrophy syndromes

Lipodystrophy Type	Gene	Molecular Basis	Clinical features
MAD type A	*LMNA*	Mutations may disrupt nuclear function resulting in premature cell death in many tissues.	Mandibular and clavicular hypoplasia, acro-osteolysis,. Partial lipodystrophy affecting the extremities and trunk[44,45].
MAD type B	*ZMPSTE24*	Mutations result in accumulation of farnesylated prelamin A that can disrupt nuclear function in several tissues.	Mandibular and clavicular hypoplasia, acro-osteolysis,. More generalized loss of fat, premature renal failure, progeroid features[46].
JMP/CANDLE	*PSMB8*	PSMB8 encodes subunit of immunoproteasomes that degrade abnormal/excess proteins in cells.	Joint contractures, muscle atrophy, microcytic anemia and panniculitis-induced lipodystrophy. Recurrent fevers, annular erythematous skin lesions, violaceous eyelid swelling, partial lipodystrophy [47,48]
SHORT syndrome	*PIK3R1*	PIK3R1 plays a role in metabolic actions of insulin, mutations associated with insulin resistance.	Variable loss of sc fat, short stature, hyper-extensibility, ocular depression, teething delay[49].
MDP syndrome	*POLD1*	Critical for DNA replication and repair.	Mandibular hypoplasia, deafness, and progeroid features[50,51].
Neonatal progeroid syndrome, type A	*FBN1*	Fibrillin 1	Generalized loss of body fat and muscle mass, and progeroid appearance at birth. Marfanoid habitus[52,53].
Neonatal progeroid syndrome, type B	*CAV1*	Caveolin 1, present on adipocyte membranes, binds fatty acids and translocates them to lipid droplets.	Generalized loss of body fat and muscle mass, and progeroid appearance at birth [54].
Atypical Progeroid Syndrome	*LMNA*	Different heterozygous, mostly *de novo* mutations cause nuclear dysfunction.	Partial or generalized loss of sc fat, progeroid features[55].
Hutchinson-Gilford progeria	*LMNA*	Specific *de novo* mutations induce abnormal splicing and accumulation of truncated farnesylated prelamin A.	Generalized loss of sc fat, progeroid features[56].

Abbreviations: MAD, mandibuloacral dysplasia; *LMNA*, lamin A/C; *ZMPSTE24*, zinc metalloprotease STE24; CANDLE, chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperature; *PSMB8*, proteasome subunit beta 8; JMP, Joint contractures, Muscle atrophy, Microcytic anemia and Panniculitis-induced lipodystrophy; SHORT, Short stature, Hyper-extensibility or inguinal hernia, Ocular depression, Rieger anomaly and Teething delay; *PIK3R1*, phosphoinositide-3-kinase regulatory subunit 1; MDP, Mandibular hypoplasia, Deafness, Progeroid features; *POLD1*, *polymerase* (DNA) delta 1, catalytic subunit; *CAV1*, caveolin 1

Table 6

Classification of AGL

Subtype	Prevalence	Clinical Features
Panniculitis-associated AGL	~25%	Initial development of panniculitis (sc inflammatory nodules) followed by localized fat loss when these lesions heal. Ongoing panniculitis later on results in generalized loss of sc [27].
Auto-immune AGL	~25%	Gradual generalized fat loss associated with auto-immune diseases, especially juvenile dermatomyositis. Some patients have low levels of serum complement 4[27,57].
Idiopathic AGL	~50%	Gradual generalized sc fat loss of unclear etiology[27].

Abbreviations: AGL, acquired generalized lipodystrophy

Table 7

Etiology of Drug-induced Lipodystrophy in HIV-infected patients

Type/Etiology	Pathogenesis and molecular basis
PI-induced	PIs inhibit ZMPSTE24, which is important for the correct maturation and processing of prelamin A. Thus, PIs result in accumulation of toxic farnesylated prelamin A[31]. May also cause dysregulation of transcription factors involved in adipogenesis. They may also inhibit glucose transporter 4 expression leading to insulin resistance.
NRTI-induced	NRTIs (especially stavudine and zidovudine) inhibit mitochondrial polymerase-γ and subsequently cause mitochondrial toxicity[32].

Abbreviations: PI, protease inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; ZMPSTE24, zinc metallatoproteinase STE24; polymerase-γ, polymerase gamma.

Table 8

Characteristics of different types of localized lipodystrophies

Type	Etiology	Clinical Features
Drug-induced localized lipodystrophy	Insulin therapy (more common before purified/human insulin was available), steroids and antibiotics. High local production of TNF-α may cause dedifferentiation of adipocytes. Other mechanisms include presence of lipases, repeated trauma and/or auto-immune processes.	More common in patients with high titers of anti-insulin antibodies. May have deposition of IgA and C3 locally. Sometimes responds to local corticosteroids.
Pressure-induced localized lipodystrophy	Trauma and decreased perfusion caused by repeated pressure to the same area over a long period of time.	Fat atrophy localized to the area exposed to repeated pressure. This tends to improve when the pressure is avoided.
Panniculitis-associated localized lipodystrophy	Associated with serum ANA or anti dsDNA antibodies; may also have auto-immune diseases such as SLE.	Initial development of panniculitis (sc inflammatory nodules in several areas) followed by localized fat loss when these lesions heal.
Centrifugal lipodystrophy (lipodystrophia centrifugalis abdominalis infantalis)	Cause is unknown and most patients recover spontaneously with no intervention.	More common in Asians. Fat loss spreads in a centrifugal pattern from abdomen and groin area and is associated with peripheral panniculitis. It begins in infancy, stops spreading between the ages of 3 and 8 and then in most cases, resolves by itself.
Idiopathic localized lipodystrophy	Undetermined etiology.	

Abbreviations: TNF-α, tumor necrosis factor alpha; IgA, immunoglobulin A; C3, complement 3; ANA, anti-nuclear antibodies; anti dsDNA Ab, anti-double stranded deoxyribonucleic acid antibodies; SLE, systemic lupus erythematous; AGL, acquired generalized lipodystrophy.

Data from Garg A. Lipodystrophies. Am J Med. 2000;108(2):143–152.

Table 9

Approval and indications of metreleptin therapy.

Type of Lipodystrophy	Approvals	Indications	Clinical considerations
Generalized lipodystrophy (both CGL and AGL)	USA: approved as adjunct to diet for treatment of metabolic complications. Japan: approved Europe: available through compassionate care programs.	First line drug treatment (after diet /exercise intervention) for metabolic and endocrine abnormalities. May prevent comorbidities and metabolic complications in young children.	Decreases hyperphagia, leading to weight loss. May need to be discontinued if excessive weight loss occurs.
Partial lipodystrophy (both FPLD and APL)	USA: not approved. Japan: approved as an adjunct to diet Europe: through compassionate care programs.	May be considered for hypoleptinemic (leptin < 4 ng/mL) patients who have severe metabolic abnormalities such as HbA1c > 8% and/or triglycerides > 500 mg/dL.	Clinical response not as good as in generalized lipodystrophy. Patients with lower leptin levels show the most benefit.

Abbreviations: CGL, congenital generalized lipodystrophy; AGL, acquired generalized lipodystrophy; FPLD, familial partial lipodystrophy; APL, acquired partial lipodystrophy; USA, United States of America; HbA1c, glycated hemoglobin.

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New advances in the treatment of generalized lipodystrophy: role of metreleptin.

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Abstract

Recombinant methionyl human leptin or metreleptin is a synthetic leptin analog that has been trialed in patients with leptin-deficient conditions, such as leptin deficiency due to mutations in the leptin gene, hypothalamic amenorrhea, and lipodystrophy syndromes. These syndromes are characterized by partial or complete absence of adipose tissue and hormones derived from adipose tissue, most importantly leptin. Patients deficient in leptin exhibit a number of severe metabolic abnormalities such as hyperglycemia, hypertriglyceridemia, and hepatic steatosis, which can progress to diabetes mellitus, acute pancreatitis, and hepatic cirrhosis, respectively. For the management of these abnormalities, multiple therapies are usually required, and advanced stages may be progressively difficult to treat. Following many successful trials, the US Food and Drug Administration approved metreleptin for the treatment of non-HIV-related forms of generalized lipodystrophy. Leptin replacement therapy with metreleptin has, in many cases, reversed these metabolic complications, with improvements in glucose-insulin-lipid homeostasis, and regression of fatty liver disease. Besides being effective, a daily subcutaneous administration of metreleptin is generally safe, but the causal association between metreleptin and immune complications (such as lymphoma) is still unclear. Moreover, further investigation is needed to elucidate mechanisms by which metreleptin leads to the development of anti-leptin antibodies. Herein, we review clinical aspects of generalized lipodystrophy and the pharmacological profile of metreleptin. Further, we examine studies that assessed the safety and efficacy of metreleptin, and outline some clinical perspectives on the drug.

KEYWORDS: adipose tissue; leptin; lipodystrophy; metreleptin; pharmacology

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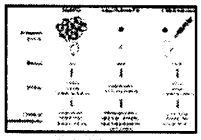

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