oscar

Clinical Guideline

Guideline Number: CG052, Ver. 1

Preferred Physician-Administered Specialty Drugs

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Oscar may delegate utilization management decisions of certain services to third-party delegates, who may develop and adopt their own clinical criteria.

The clinical guidelines are applicable to all commercial plans. Services are subject to the terms, conditions, limitations of a member's plan contracts, state laws, and federal laws. Please reference the member's plan contracts (e.g., Certificate/Evidence of Coverage, Summary/Schedule of Benefits) or contact Oscar at 855-672-2755 to confirm coverage and benefit conditions.

Summary

Oscar's Preferred Medication List encourages the utilization of clinically appropriate and cost-effective physician-administered specialty drugs. The table below lists both the preferred and non-preferred medications within a therapeutic class.

In most cases, and as long as it's considered safe by your provider, the preferred medications must be used first. Requests for non-preferred medications will be subject to **CVS Exceptions Criteria**, and this criteria is available upon request. Approval for non-preferred medications may require that the member has a contraindication to the preferred medication(s); has tried and failed the preferred medication(s); had an inadequate response to the preferred medication(s); or had an intolerable adverse event with the preferred medication(s). For more information, please call 855-672-2755.

Medical Preferred Drug List

Drug Class	*Preferred Medication(s)*	*Non-Preferred Medication(s)*
Acromegaly	Somatuline Depot Somavert	Sandostatin LAR Depot Signifor LAR
Alpha-1 Antitrypsin Deficiency	Prolastin-C	Aralast Glassia Zemaira

Autoimmune	Remicade Simponi Aria	Actemra Cimzia Entyvio Ilumya Inflectra Orencia Renflexis Stelara
Botulinum Toxins	Botox Dysport	Myobloc Xeomin
Hematologic, Erythropoiesis-Stimulating Agents (ESA)	Retacrit	Aranesp Epogen Mircera Procrit
Hemophilia - Factor VIII	Adynovate Jivi Kogenate FS Kovaltry Novoeight	Eloctate Helixate FS Nuwiq
Hemophilia - Factor IX	Idelvion Rebinyn	Alprolix
Hematologic, Neutropenia Colony Stimulating Factors	Zarxio	Neupogen Granix Leukine
Hereditary Angioedema	Ruconest	Berinert
Lysosomal Storage Disorders - Gaucher Disease	Cerezyme	Elelyso VPRIV
Multiple Sclerosis (Infused)	Tysabri	Lemtrada
Severe Asthma	Nucala	Cinqair Fasenra

Rationale

Acromegaly:

- Sandostatin LAR is a form of long-acting octreotide (octreotide LAR). Somavert is also known as pegmisovant. There have been a number of random controlled trials comparing the two in the treatment of acromegaly. Ghigo et al compared the two in 118 patients randomized to one or the other in a multi-center trial, concluding that "Pegvisomant and octreotide LAR were equally

effective in normalizing IGF-I in the overall population, and pegvisomant was more effective in patients with higher baseline IGF-I levels. Pegvisomant had a more favorable effect on parameters of glycemic control." A separate study by Trainer et al compared Pegvisomant and a combination of Pegvisomant and octreotide LAR and found no differences in toxicity or efficacy. Other studies have largely replicated these findings. Additionally, an UpToDate review on treatment for acromegaly recommends pegmisovant as first-line medical therapy.[1-3]

Alpha-1-antitrypsin deficiency

- These medications are alpha-1-proteinase inhibitors used to treat emphysema as a result of deficiency in this the alpha-1-antitrypsin enzyme. There have been no studies to date demonstrating any clinically significant differences in efficacy or toxicity among the different formulations.

Autoimmune

- There are a number of immunomodulator medications on the market, many of which are FDA-approved biosimilars. There is currently no level 1 evidence in the form of randomized trials that demonstrate greater benefit in efficacy or side effects between the biosimilars.[29-30]

Botulinum toxin

- There are 4 FDA approved and clinically implemented formulations of botulinum toxin. Botox and Dysport have the broadest number of indications and applicability. There is no evidence suggesting the

Hematologic, Erythropoiesis-Stimulating Agents (ESA)

- Retacrit is a biosimilar to the other non-preferred ESA drugs. A biosimilar, per the FDA, is defined as a "biological product that is highly similar to and has no clinically meaningful differences from an existing FDA-approved reference product." A 2018 study by Thadhani et al compared Epogen to Retacrit in a randomized open-label non-inferiority study in 432 patients on hemodialysis. The study found that Retacrit was non-inferior to Epogen at maintaining hemoglobin levels in this population. There have been no clinical studies demonstrating any meaningful difference between these biosimilar agents.[4-5]

Hemophilia - Factor VIII

- Factor VIII treatments for hemophilia A come in several different formulations including recombinant (Helixate, Nuwiq, Jivi, Kogenate, Kovaltry, Novoeight) and plasma derived (Adynovate, Eloctate). The plasma derived factors are considered “long-acting” as they have

longer half-lives than the others. The recent randomized SIPPET trial found that plasma-derived products had lower rates of inhibitor development (e.g. reduced immunogenicity) than the recombinant medications. The most current guidelines from the National Hemophilia Foundation Medical and Scientific Advisory Council addressed this new study but reinforced their recommendation that both recombinant and plasma derived products could be used in new and already treated patients.[6-11]

Hemophilia - Factor IX

- Idelvion and alprolix are both long acting factor IX options. There have been no clinical studies demonstrating a significant difference in efficacy or toxicity between the two, and thus the lower cost option is preferred. Rebinyn has a slightly longer half-life than alprolix and is roughly equivalent to idelvion, again with no studies directly comparing them.[12]

Hematologic, Neutropenia Colony Stimulating Factors

- Zarxio is a biosimilar G-CSF to neupogen. The most recently updated ASCO guidelines recommend that "all preparations of G-CSF, including biosimilars, can be used for the prevention of treatment-related febrile neutropenia and that the choice of agent should be based on convenience, cost, and clinical situation"[18]
- Leukine is a GM-CSF, meaning that in addition to granulocytes it also stimulates macrophages. The data comparing GM-CSF to G-CSF medications is limited. The only randomized data comes from a 1998 study comparing the two in 181 patients, finding comparable efficacy between the two and no clinically meaningful differences. This has been largely reflected in other prospective and retrospective comparisons.[13-16]

Hereditary Angioedema:

- Ruconest is a recombinant medication and berinert is human plasma-derived medication to inhibit C1-esterase. Both are used to treat hereditary angioedema. There have been no clinical studies demonstrating a meaningful difference in efficacy or toxicity between the two options. Ruconest is also more readily accessible as it does not rely on human donors, and thus is the preferred option.[17]

Lysosomal Storage Disorders - Gaucher Disease

- Per an UpToDate review on the different enzyme replacement therapies for Gaucher's disease, "Although there is limited direct and published evidence from head-to-head studies, the available evidence suggests that all the ERTs are approximately equivalent in efficacy". There

have otherwise been no studies demonstrating a clear benefit in any one product over another.[19-22]

Multiple Sclerosis (Infused)

- Data comparing the available treatment options for MS is limited. However, a recent study looked at 41,000 MS patients in a worldwide registry found no differences between the Tysabri and Lemtrada across all outcome measures, except that Tysabri may be superior in providing improvement in function during the first year. Several other studies have found superiority in outcomes using Tysabri or at a minimum, equivalent outcomes across a number of outcome measures and disease stages.[23-26]

Severe Asthma

- Cinqair, Fasenra, and Nucala are anti-IL5 antibodies used to treat severe asthma. There have been no direct treatment comparisons among these options. An indirect comparison (2019) was performed showed that Nucala reduced exacerbations by 34% and 45% compared to the reslizumab and benralizumab, respectively, in patients with severe eosinophilic asthma. As the current literature providing direct, randomized comparisons between these agents is limited, Nucala is the preferred agent.[27-28]

Applicable Billing Codes

*Indicates non-preferred medications subject to CVS Exceptions Criteria

Acromegaly	
J1930	Somatuline Depot Injection, lanreotide, 1 mg
J2353*	SandoSTATIN LAR Depot Injection, octreotide, depot form for intramuscular injection, 1 mg
J2502*	Signifor LAR Injection, pasireotide long acting, 1 mg
J3490	Somavert Unclassified drugs
Alpha-1 Antitrypsin Deficiency	
J0256*	Aralast NP Injection, alpha 1-proteinase inhibitor (human), not otherwise specified, 10 mg
J0256	Prolastin-C

	Injection, alpha 1-proteinase inhibitor (human), not otherwise specified, 10 mg
J0256*	Zemaira Injection, alpha 1-proteinase inhibitor (human), not otherwise specified, 10 mg
J0257*	Glassia Injection, alpha 1 proteinase inhibitor (human), (GLASSIA), 10 mg
Autoimmune	
J0129*	Orencia; Orenica ClickJect Injection, abatacept, 10 mg
J0717*	Cimzia; Cimzia Prefilled; Cimzia Starter Kit Injection, certolizumab pegol, 1 mg
J1602	Simponi Aria Injection, golimumab, 1 mg, for intravenous use
J1745	Remicade Injection, infliximab, excludes biosimilar, 10 mg
J3262*	Actemra Injection, tocilizumab, 1 mg
J3357*	Stelara Ustekinumab, for subcutaneous injection, 1 mg
J3358*	Stelara Ustekinumab, for intravenous injection, 1 mg
J3380*	Entyvio Injection, vedolizumab, 1 mg
J3490*	Entyvio Unclassified drugs
Q5103*	Inflectra Injection, infliximab-dyyb, biosimilar, (Inflectra), 10 mg
Q5104*	Renflexis Injection, infliximab-abda, biosimilar, (Renflexis), 10 mg
J3245	Ilumya Injection, tildrakizumab, 1 mg
J3590	Ilumya Unclassified biologics
Botulinum Toxins	

J0585	Botox Injection, onabotulinumtoxinA, 1 unit
J0586	Dysport Injection, abobotulinumtoxinA, 5 units
J0587*	Myobloc Injection, rimabotulinumtoxinB, 100 units
J0588*	Xeomin Injection, incobotulinumtoxinA, 1 unit
Hematologic, Erythropoiesis-Stimulating Agents (ESA)	
J0881*	Aranesp Injection, darbepoetin alfa, 1 mcg (non-ESRD use)
J0882*	Aranesp Injection, darbepoetin alfa, 1 mcg (for ESRD on dialysis)
J0885*	Epogen Injection, epoetin alfa, (for non-ESRD use), 1000 units
Q4081*	Epogen Injection, epoetin alfa, 100 units (for ESRD on dialysis)
J0885*	Procrit Injection, epoetin alfa, (for non-ESRD use), 1000 units
Q4081*	Procrit Injection, epoetin alfa, 100 units (for ESRD on dialysis)
J0887*	Mircera Injection, epoetin beta, 1 microgram, (for ESRD on dialysis)
J0888*	Mircera Injection, epoetin beta, 1 microgram, (for non-ESRD use)
Q5105	Retacrit Injection, epoetin alfa, biosimilar, (Retacrit) (for ESRD on dialysis), 100 units
Q5106	Retacrit Injection, epoetin alfa, biosimilar, (Retacrit) (for non-ESRD use), 1000 units
Hemophilia - Factor VIII	
J3490	Jivi Unclassified drugs
J7199	Jivi

	Hemophilia clotting factor, not otherwise classified
J7182	Novoeight Injection, Factor VIII, (antihemophilic factor, recombinant), (NovoEight), per IU
J7192*	Helixate FS Factor VIII (antihemophilic factor, recombinant) per IU, not otherwise specified
J7192	Kogenate FS; Kogenate FS Bio-Set Factor VIII (antihemophilic factor, recombinant) per IU, not otherwise specified
J7205*	Eloctate Injection, Factor VIII Fc fusion protein (recombinant), per IU
J7207	Adynovate Injection, Factor VIII, (antihemophilic factor, recombinant), PEGylated, 1 IU
J7209*	Nuwiq Injection, Factor VIII, (antihemophilic factor, recombinant), (Nuwiq), 1 IU
J7211	Kovaltry Injection, Factor VIII, (antihemophilic factor, recombinant), (Kovaltry), 1 IU
Hemophilia - Factor IX	
C9468	Rebinyn Injection, Factor IX (antihemophilic factor, recombinant), glycopegylated, Rebinyn, 1 IU
J7195	Rebinyn Injection, Factor IX (antihemophilic factor, recombinant) per IU, not otherwise specified
J7201*	Alprolix Injection, Factor IX, Fc fusion protein, (recombinant), Alprolix, 1 IU
J7202	Idelvion Injection, Factor IX, albumin fusion protein, (recombinant), Idelvion, 1 IU
Hematologic, Neutropenia Colony Stimulating Factors	
J1442*	Neupogen Injection, filgrastim (G-CSF), excludes biosimilars, 1 microgram
J1447*	Granix Injection, tbo-filgrastim, 1 microgram
J2820*	Leukine Injection, sargramostim (GM-CSF), 50 mcg

Q5101	Zarxio Injection, filgrastim-sndz, biosimilar, (Zarxio), 1 mcg
Hereditary Angioedema	
J0596	Ruconest Injection, C1 esterase inhibitor (recombinant), Ruconest, 10 units
J0597*	Berinert Injection, C-1 esterase inhibitor (human), Berinert, 10 units
Lysosomal Storage Disorders - Gaucher Disease	
J1786	Cerezyme Injection, imiglucerase, 10 units
J3060*	Elelyso Injection, taliglucerase alfa, 10 units
J3385*	VPRIV Injection, velaglucerase alfa, 100 units
Multiple Sclerosis (Infused)	
J0202*	Lemtrada Injection, alemtuzumab, 1 mg
J2323	Tysabri Injection, natalizumab, 1 mg
Severe Asthma	
J2182	Nucala Injection, mepolizumab, 1 mg
J2786*	Cinqair Injection, reslizumab, 1 mg
C9466*	Fasenra Injection, benralizumab, 1 mg
J0517*	Fasenra Injection, benralizumab, 1 mg
J3490*	Fasenra Unclassified drugs

*Indicates non-preferred medications subject to CVS Exceptions Criteria

References

1. Trainer PJ, Ezzat S, D'souza GA, Layton G, Strasburger CJ. A randomized, controlled, multicentre trial comparing pegvisomant alone with combination therapy of pegvisomant and long-acting octreotide in patients with acromegaly. Clin Endocrinol (Oxf). 2009;71(4):549-57.
2. Melmed S. Treatment of acromegaly. Ed. Snyder PJ. UpToDate. Waltham, MA. UpToDate.com)
3. Ghigo E, Biller BM, Colao A, et al. Comparison of pegvisomant and long-acting octreotide in patients with acromegaly naïve to radiation and medical therapy. J Endocrinol Invest. 2009;32(11):924-33.
4. Biosimilar and interchangeable products. US Food and Drug Administration. Updated 10/23/2017. Available at https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapEUticBiologicApplications/Biosimilars/ucm580419.htm.
5. Thadhani R, Guilatco R, Hymes J, Maddux FW, Ahuja A. Switching from Epoetin Alfa (Epogen®) to Epoetin Alfa-Epbx (RetacritTM) Using a Specified Dosing Algorithm: A Randomized, Non-Inferiority Study in Adults on Hemodialysis. Am J Nephrol. 2018;48(3):214-224.
6. Kannicht C, Ramström M, Kohla G, et al. Characterisation of the post-translational modifications of a novel, human cell line-derived recombinant human factor VIII. Thromb Res. 2013;131(1):78-88.
7. Tiede A, Brand B, Fischer R, et al. Enhancing the pharmacokinetic properties of recombinant factor VIII: first-in-human trial of glycoPEGylated recombinant factor VIII in patients with hemophilia A. J Thromb Haemost. 2013;11(4):670-8.
8. Klukowska A, Szczepański T, Vdovin V, Knaub S, Jansen M, Liesner R. Novel, human cell line-derived recombinant factor VIII (Human-cl rhFVIII, Nuwiq) in children with severe haemophilia A: efficacy, safety and pharmacokinetics. Haemophilia. 2016;22(2):232-239.
9. Lieuw K. Many factor VIII products available in the treatment of hemophilia A: an embarrassment of riches? J Blood Med. 2017;8:67-73.
10. MASAC . MASAC Recommendation on SIPPET (Survey of Inhibitors in Plasma-Product-Exposed Toddlers): REsults and Recommendations for Treatment Products for Previously Untreated Patients with Hemophilia A. MASAC; 2016.
11. Peyvandi F, Mannucci PM, Garagiola I, et al. A Randomized Trial of Factor VIII and Neutralizing Antibodies in Hemophilia A. N Engl J Med. 2016;374(21):2054-64.
12. Hoots WK. Hemophilia A and B: Routine management including prophylaxis. Ed. Mahony DH. UpToDate. Waltham, MA. UpToDate.com

13. Beveridge RA, Miller JA, Kales AN, et al. A comparison of efficacy of sargramostim (yeast-derived RhuGM-CSF) and filgrastim (bacteria-derived RhuG-CSF) in the therapeutic setting of chemotherapy-induced myelosuppression. Cancer Invest 1998; 16:366.
14. Stull DM, Bilmes R, Kim H, Fichtl R. Comparison of sargramostim and filgrastim in the treatment of chemotherapy-induced neutropenia. Am J Health Syst Pharm 2005; 62:83.
15. Wong SF, Chan HO. Effects of a formulary change from granulocyte colony-stimulating factor to granulocyte-macrophage colony-stimulating factor on outcomes in patients treated with myelosuppressive chemotherapy. Pharmacotherapy 2005; 25:372.
16. Milkovich G, Moleski RJ, Reitan JF, et al. Comparative safety of filgrastim versus sargramostim in patients receiving myelosuppressive chemotherapy. Pharmacotherapy 2000; 20:1432.
17. Cicardi M. Hereditary angioedema (due to C1 inhibitor deficiency): General care and long-term prophylaxis. Ed. Saini S. UpToDate. Waltham, MA. UpToDate.com
18. Smith TJ, Bohlke K, Lyman GH, et al. Recommendations for the Use of WBC Growth Factors: American Society of Clinical Oncology Clinical Practice Guideline Update. J Clin Oncol. 2015;33(28):3199-212.
19. Weinreb NJ, Charrow J, Andersson HC, et al. Effectiveness of enzyme replacement therapy in 1028 patients with type 1 Gaucher disease after 2 to 5 years of treatment: a report from the Gaucher Registry. Am J Med 2002; 113:112.
20. Anderson LJ, Henley W, Wyatt KM, et al. Long-term effectiveness of enzyme replacement therapy in adults with Gaucher disease: results from the NCS-LSD cohort study. J Inherit Metab Dis 2014; 37:953.
21. Anderson LJ, Henley W, Wyatt KM, et al. Long-term effectiveness of enzyme replacement therapy in children with Gaucher disease: results from the NCS-LSD cohort study. J Inherit Metab Dis 2014; 37:961.
22. Charrow J, Andersson HC, Kaplan P, et al. Enzyme replacement therapy and monitoring for children with type 1 Gaucher disease: consensus recommendations. J Pediatr 2004; 144:112.
23. Kalincik T, Brown JWL, Robertson N, et al. Treatment effectiveness of alemtuzumab compared with natalizumab, fingolimod, and interferon beta in relapsing-remitting multiple sclerosis: a cohort study. Lancet Neurol. 2017;16(4):271-281.
24. Kalincik T, et al "Comparison of 5-year treatment outcomes between alemtuzumab versus natalizumab, fingolimod and interferon **β**-1a" ECTRIMS 2016; Abstract 251.
25. Wang L, Qi CH, Zhong R, Yuan C, Zhong QY. Efficacy of alemtuzumab and natalizumab in the treatment of different stages of multiple sclerosis patients. Medicine (Baltimore). 2018;97(8):e9908.

26. Baroncini D, Ghezzi A, Annovazzi PO, et al. Natalizumab versus fingolimod in patients with relapsing-remitting multiple sclerosis non-responding to first-line injectable therapies. Mult Scler. 2016;22(10):1315-26.
27. Busse W, Chupp G, Nagase H, et al. Anti-IL-5 treatments in patients with severe asthma by blood eosinophil thresholds: Indirect treatment comparison. J Allergy Clin Immunol. 2019;143(1):190-200.e20.
28. Wenzel S. Treatment of severe asthma in adolescents and adults. Ed Bochner BS. UpToDate. Waltham, MA.
29. Chingcuanco F, Segal J, Kim S, Alexander C. Bioequivalence of Biosimilar Tumor Necrosis Factor-α Inhibitors Compared with Their Reference Biologics: A Systematic Review. Ann Intern Med. 2016;165(8):565–74. doi: 10.7326/M16-0428.
30. Bridges, S. Louis et al. "The Science Behind Biosimilars: Entering a New Era of Biologic Therapy." Arthritis & rheumatology 70 3 (2018): 334-344.

Clinical Guideline Revision / History Information

Document History	Approval Signature/Title
Original Date: Reviewed/Revised: Signed:	3/6/2019 Vinod Mitta, MD, Medical Director