Mass General Brigham
Health Plan

Enzyme and Metabolic Disorder Therapies
Aldurazyme (laronidase)
Cerezyme (imiglucerase)
Elaprase (idursulfase)
Elelyso (taliglucerase alfa)
Elfabrio (pegunigalsidase alfa-iwxj)
Fabrazyme (agalsidase beta)
Kanuma (sebelipase alfa)
Lamzede (velmanase alfa-tycv)
Lumizyme (alglucosidase alfa)
Mepsevii (vestronidase alfa-vjbk)
Naglazyme (galsulfase)
Nexviazyme (avalglucosidase alfa-ngpt)
Nulibry (fosdenopterin)
Palynziq (pegvaliase-pqpz)
Revcovi (elapegademase-lvlr)
Ryplazim (plasminogen, human-tvmh)
Vimizim (elosulfase alfa)
Vpriv (velaglucerase alfa)
Xenpozyme (olipudase alfa-rpcp)
Effective 06/01/2025

Plan	☒ MassHealth UPPL ☐Commercial/Exchange	**Program Type**	☒ Prior Authorization ☒ Quantity Limit ☐ Step Therapy
Benefit	☐ Pharmacy Benefit ☒ Medical Benefit		
Specialty Limitations	N/A		
Contact Information	**Medical and Specialty Medications** All Plans | Phone: 877-519-1908 | Fax: 855-540-3693 **Non-Specialty Medications** All Plans | Phone: 800-711-4555 | Fax: 844-403-1029		
Notes	Elfabrio, Fabrazyme, Palynziq, Revcovi, Ryplazim are also available on the pharmacy benefit. Please see the MassHealth Drug List for coverage and criteria. Additional agents from this class are available through the pharmacy benefit. Please see the MassHealth Drug List for coverage and criteria.		

Overview
Lysosomal storage disorders are caused by a deficiency or absence of required enzymes. The consequence is an accumulation of compounds that are normally degraded causing cell and organ dysfunction. Prior to the development of enzyme replacement therapy (ERT), management of these conditions mainly consisted of supportive care and treatment of the complications. Today a number of exogenously supplied enzymes are available for lysosomal storage disorders such as Gaucher Type I disease, Fabry disease, mucopolysaccharidosis Type I, II, and VI and Pompe disease.

Coverage Guidelines
Authorization may be reviewed on a case by case basis for members who are new to the plan currently receiving treatment with requested medication excluding when the product is obtained as samples or via manufacturer's patient assistance programs.
OR
Authorization will be granted when all the following criteria has been met:

Aldurazyme (laronidase)
1. Diagnosis of Mucopolysaccharidosis I (MPS I)
2. Results from genetic testing showing mutations in IDUA gene or an enzyme assay test showing reduced lysosomal alpha-L-iduronidase activity in peripheral blood leukocytes, plasma, or cultured fibroblasts
3. Prescriber is a specialist in genetic or metabolic diseases or consultation notes from a specialist are provided
4. Member's current weight *(use to verify correct dosing)*

Cerezyme (imiglucerase)
Vpriv (velaglucerase alfa*)*
1. Diagnosis of Gaucher disease (Type I)
2. Results from genetic test confirming mutation in GBA gene or an enzyme assay test showing reduced activity of the enzyme glucocerebrosidase
3. Prescriber is a specialist in genetic or metabolic diseases or consultation notes from a specialist are provided
4. Member's current weight *(use to verify correct dosing)*

Elaprase (idursulfase)
1. Diagnosis of Hunter Syndrome (Mucopolysaccharidosis II)
2. Results from genetic testing confirming mutation in IDS gene or iduronate-2-sulfatase assay test showing reduced or absent activity in the serum, white blood cells, or fibroblasts
3. Prescriber is a specialist in genetic or metabolic diseases or consultation notes from a specialist are provided
4. Member's current weight *(use to verify correct dosing)*

Elelyso (taliglucerase alfa)
1. Diagnosis of Gaucher disease (Type I)
2. Results from genetic test confirming mutation in GBA gene or an enzyme assay test showing reduced activity of the enzyme glucocerebrosidase
3. Prescriber is a specialist in genetic or metabolic diseases or consultation notes from a specialist are provided
4. Member is ≥ 4 years of age
5. Member's current weight *(use to verify correct dosing)*

Elfabrio (pegunigalsidase alfa-iwxj)
Fabrazyme (agalsidase beta)
1. Diagnosis of Fabry disease
2. One of the following confirming diagnosis:
    a. Results from an enzyme assay test showing reduced or absent α-GAL enzyme activity in plasma, leukocytes, tears, or biopsied tissue
    b. Genetic testing confirming mutation in GAL gene

    c. Biomarker demonstrating an increase in Gb3 concentration
3. Prescriber is a specialist in genetic or metabolic diseases or consultation notes from a specialist are provided
4. Member's current weight *(use to verify correct dosing)*
5. For Elfabrio (pegunigalsidase alfa-iwxj), inadequate response, adverse reaction, or contraindication to Fabrazyme (agalsidase beta)

Kanuma (sebelipase alfa)
1. Diagnosis of lysosomal acid lipase deficiency
2. **ONE** of the following:
    a. Lab assay documenting low lysosomal acid lipase activity
    b. Genetic testing confirming full or partial loss of LAL gene
3. Prescriber is a specialist in genetic or metabolic diseases or consultation notes from a specialist are provided
4. Member's current weight *(use to verify correct dosing)*

Lamzede (velmanase alfa-tycv)
1. Diagnosis of alpha-mannosidosis
2. Member is ≥ 3 years of age
3. Prescriber is a specialist in genetic or metabolic diseases or consult notes from a specialist are provided
4. Copy of a genetic test confirming diagnosis of alpha-mannosidosis (e.g., mutation of MAN2B1 gene)
5. Baseline measurements for **ALL** of the following tests:
    a. serum oligosaccharides
    b. forced vital capacity
    c. **ONE** of the following motor function tests:
        i. 3-minute stair climb test
        ii. 6-minute walk test
6. Member's current weight *(use to verify correct dosing)*

Lumizyme (alglucosidase alfa)*
1. Diagnosis of Pompe Disease
2. **ONE** of the following confirming diagnosis:
    a. Results from GAA assay test showing reduced or absent activity from cultured skin fibroblasts
    b. lymphocyte testing
    c. blood spot assay
    d. genetic testing confirming mutation in GAA gene
3. Prescriber is a specialist in genetic or metabolic diseases or consultation notes from a specialist are provided
4. Member's current weight *(use to verify correct dosing)*

* Lumizyme and Nexviazyme should not be used concurrently

Mepsevii (vestronidase alfa-vjbk)
1. Diagnosis of Mucopolysaccharidosis VII (MPS VII, Sly syndrome)
2. Results from genetic testing showing mutations in the beta glucuronidase gene
3. Prescriber is a specialist in genetic or metabolic diseases or provides documentation of a consultation notes from a specialist are provided
4. Member's current weight *(use to verify correct dosing)*

Naglazyme (galsulfase)

1. Diagnosis of Mucopolysaccharidosis VI (MPS VI)
2. Results from an enzyme assay test showing reduced arylsulfatase B (ASB) enzyme activity in leukocytes or fibroblasts along with elevated urine glycosaminoglycan (GAG) levels
3. Prescriber is a specialist in genetic or metabolic diseases or provides documentation of a consultation notes from a specialist are provided
4. Member's current weight *(use to verify correct dosing)*

Nexviazyme (avalglucosidase alfa-ngpt) *

1. Diagnosis of late-onset Pompe Disease
2. **ONE** of the following confirming diagnosis:
    a. results from GAA assay test showing reduced or absent activity from cultured skin fibroblasts
    b. lymphocyte testing
    c. blood spot assay
    d. genetic testing confirming mutation in GAA gene
3. Member is ≥ one year of age
4. Prescriber is a specialist in genetic or metabolic diseases or consult notes from a specialist are provided.
5. Member's current weight *(use to verify correct dosing)*
6. **If reviewing under Pharmacy Benefit:** For members weighing < 30 kg, contraindication to Lumizyme

* Lumizyme and Nexviazyme should not be used concurrently

Nulibry (fosdenopterin)

1. Diagnosis of molybdenum cofactor deficiency (MoCD) Type A confirmed by genetic testing
2. Prescriber is a specialist in genetic or metabolic diseases or consultation notes from a specialist are provided
3. Appropriate dosing
4. Member's current weight *(use to verify correct dosing)*

Palynziq (pegvaliase-pqpz)

1. Diagnosis of phenylketonuria
2. Member is ≥ 18 years of age
3. Prescriber is a specialist in genetic or metabolic diseases or consultation notes from a specialist are provided
4. Blood phenylalanine concentrations >600 micromol/L
5. The medication will be used in conjunction with a phenylalanine-restricted diet
6. **If reviewing under Pharmacy Benefit**: Physician attestation of inadequate response, adverse reaction, or contraindication to sapropterin

Revcovi (elapegademase-lvlr)

1. Diagnosis of adenosine deaminase severe combined immunodeficiency (ADA-SCID)
2. Laboratory results documenting **ONE** of the following:
    a. Absent ADA enzymatic activity in lysed erythrocytes
    b. Elevated levels of adenosine and deoxyadenosine in the urine and plasma
    c. A marked increase in deoxyadenosine triphosphate (dATP) levels in erythrocyte lysates
    d. A significant decrease in ATP concentration in red blood cells
    e. Absent or extremely low levels of N adenosylhomocysteine hydrolase in red blood cells

    f. Severe T cell deficiency manifested by lymphopenia and poor T cell responses to mitogens and antigens
    g. Absent thymic shadow on chest radiograph
3. Prescriber is a specialist in genetic or metabolic diseases or consultation notes from a specialist are provided
4. Member's current weight *(use to verify correct dosing)*

Ryplazim (plasminogen, human-tvmh)
1. Diagnosis of PLGD type 1
2. History of lesions (external and/or internal) and symptoms consistent with a diagnosis of PLGD type 1 (e.g., ligneous conjunctivitis, ligneous gingivitis or gingival overgrowth, vision abnormalities, respiratory distress and/or obstruction, abnormal wound healing)
3. Baseline plasminogen activity level ≤45%
4. ONE of the following:
    a. Results from genetic testing showing mutations in PLG gene
    b. Member has plasminogen antigen levels ≤9 mg/dL
5. Requested dose is ≤ 6.6 mg/kg every two to four days

Vimizim (elosulfase alfa)
1. Diagnosis of Mucopolysaccharidosis IVA (Morquio A syndrome)
2. Member is ≥ 5 years of age
3. Results from an enzyme assay test showing reduced N-acetylgalactosamine-6-sulfatase activity in blood and/or skin cells
4. Prescriber is a specialist in genetic or metabolic diseases or consultation notes from a specialist are provided
5. Member's current weight *(use to verify correct dosing)*

Xenpozyme (olipudase alfa-rpcp)
1. Diagnosis of non-central nervous system manifestations of acid sphingomyelinase deficiency (ASMD) type B, or ASMD type A/B
2. Prescriber is a specialist (e.g., medical geneticist or a specialist familiar with lysosomal storage disorders) or consultation notes from a specialist are provided
3. ONE of the following:
    a. For members ≥ 18 years of age, **BOTH** of the following:
        i. DLco ≤ 70% of predicted normal value
        ii. Spleen volume ≥ 6 MN
    b. For members < 18 years of age, spleen volume ≥ 5 MN
4. Member does **NOT** have acute or rapidly progressive neurologic abnormalities
5. BOTH of the following:
    a. Member does **NOT** require invasive ventilatory support
    b. Member does **NOT** require noninvasive ventilatory support while awake for > 12 hours a day
6. Member's current weight *(use to verify correct dosing)*
7. Appropriate dosing

<u>Continuation of Therapy</u>
Lamzede:
Prescriber provides documentation of **ONE** of the following:

1. Current tests (within the past 3 months) documenting positive response to therapy for **ALL** of the following tests:
    a. serum oligosaccharides
    b. forced vital capacity
    c. **ONE** of the following motor function tests:
        i. 3-minute stair climb test
        ii. 6-minute walk test
2. Medical necessity for continuing therapy (e.g., disease stabilization or a reduction in normal motor decline)

Ryplazim and **Nulibry**: Reauthorization will require physician documentation of a positive response to therapy or clinical rationale for continued use if dosing is appropriate based on updated member's weight where applicable.

Xenpozyme: Prescriber provides documentation of **BOTH** of the following:
1. Improvement from baseline in DLco and spleen volume
2. Updated member weight

All other drugs: Resubmission by prescriber will infer a positive response to therapy.

Limitations
1. Initial approvals will be granted for the following:
    a. Lamzede, Nulibry, Palynziq, Xenpozyme: 6 months
    b. Ryplazim: 24 weeks
    c. All other agents: 1 year
2. Reauthorizations will be granted for the following:
    a. Xenpozyme – improvement in DLco and spleen volume: 6 months
    b. All other agents: 1 year
3. Members who are stable on Nulibry (fosdenopterin) must meet both the initial and reauthorization criteria for approval.

References

1. Gieselmann V. Lysosomal storage diseases. Biochim Biophys Acta. 1995 Apr 24;1270(2-3):103-36. PMID: 7727535.
2. Bruni S, Loschi L, Incerti C, Gabrielli O, Coppa GV. Update on treatment of lysosomal storage diseases. Acta Myol. 2007 Jul;26(1):87-92. PMID: 17915580.
3. Wilcox WR. Lysosomal storage disorders: the need for better pediatric recognition and comprehensive care. J Pediatr. 2004 May;144(5 Suppl):S3-14. PMID: 15126978.
4. Lachmann R. Treatments for lysosomal storage disorders. Biochem Soc Trans. 2010 Dec;38(6):1465-8. PMID: 21118108.
5. Beck M. Therapy for lysosomal storage disorders. IUBMB Life. 2010; 62(1):33-40.
6. Aldurazyme [package insert on the internet]. Cambridge (MA): Genzyme Corporation; 2019 July [cited 2021 Jun 29]. Available from: http://www.aldurazyme.com.
7. Han S. Mucopolysaccharidoses: clinical features and diagnosis. UpToDate [database on the internet]. Waltham (MA): UpToDate; 2021 [cited 2022 Jan 26]. Available from http://www.utdol.com/utd/index.do.

8. Wraith JE, Clarke LA, Beck M, Kolodny EH, Pastores GM, Muenzer J, et al. Enzyme replacement therapy for mucopolysaccharidosis I: A randomized, double-blinded, placebo-controlled, multinational study of recombinant human alpha-L-iduronidase (laronidase). J Pediatr 2004 May; 144(5):581-8.
9. National Organization for Rare Diseases. Mucopolysaccharidosis Type I [webpage on the internet]. Danbury (CT): National Organization for Rare Diseases; 2019 [cited 2021 Jun 29]. Available from: https://rarediseases.org/rare-diseases/mucopolysaccharidosis-type-i/.
10. Cerezyme [package insert on the internet]. Cambridge (MA): Genzyme Corporation; 2018 Apr [cited 2022 Jan 26]. Available from: https://www.cerezyme.com/.
11. Hughes D. Gaucher disease: Pathogenesis, clinical manifestations, and diagnosis. UpToDate [database on the internet]. Waltham (MA): UpToDate; 2021 [cited 2022 Jan 26]. Available from:
12. National Organization for Rare Diseases. Gaucher Disease [webpage on the internet]. Danbury (CT): National Organization for Rare Diseases; 2019 [cited 2021 Jun 29]. Available from: https://rarediseases.org/rare-diseases/gaucher-disease/.
13. Merritt II JL, Vockley J. Overview of fatty acid oxidation disorders. In: Hahn S (Ed). UpToDate [database on the internet]. Waltham (MA): UpToDate; 2021 [cited 2022 Jan 26]. Available from: https://www-uptodate-com.umassmed.idm.oclc.org/contents/overview-of-fatty-acid-oxidation-disorders.
14. Elelyso [package insert on the internet]. New York (NY): Pfizer Labs; 2021 Jul [cited 2022 Jan 26]. Available from: http://www.elelyso.com.
15. Elaprase [package insert on the internet]. Cambridge (MA): Shire Human Genetic Therapies, Inc.; 2021 Sep [cited 2022 Jan 26]. Available from: http://www.elaprase.com.
16. National Organization for Rare Diseases. Mucopolysaccharidosis Type II [webpage on the internet]. Danbury (CT): National Organization for Rare Diseases; 2019 [cited 2021 Jun 29]. Available from: https://rarediseases.org/rare-diseases/mucopolysaccharidosis-type-ii-2/.
17. Fabrazyme [package insert on the internet]. Cambridge (MA): Genzyme Corporation; 2021 May [cited 2022 Jan 26]. Available from: http://www.fabrazyme.com.
18. Eng CM, Guffon N, Wilcox WR, Germain DP, Lee P, Waldek S et al. Safety and efficacy of recombinant human alpha-galactosidase. A replacement therapy in Fabry's disease. N Engl J Med. 2001; 345(1):9-16.
19. IDORSIA. Fabry Disease [webpage on the internet]. Allschwil (Switzerland): IDORSIA; ; 2022 [cited 2022 Jan 26]. Available from: https://www.idorsia.com/about-idorsia/target-diseases/fabry-ebook.
20. Amicus Therapeutics Launches Galafold™ (Migalastat) for Treatment of Fabry Disease in Italy. Amicus Therapeutics: 2018 Aug 10 [cited 2017 Mar 8] Available from: http://ir.amicusrx.com/news-releases/news-release-details/amicus-therapeutics-launches-galafoldtm-migalastat-treatment-0
21. Hughes D.A, Nicholls K, Shankar S.P, et al., Oral pharmacological chaperone migalastat compared with enzyme replacement therapy in Fabry disease: 18- month results from the randomized phase III ATTRACT study, J. Med. Genet. 54 (2017) 288–296.
22. Kanuma [package insert on the internet]. Cheshire (CT): Alexion; 2015 Dec [cited 2021 Jun 29]. Available from: http://www.kanuma.com.
23. Bernstein DL, Hülkova H, Bialer MG, Desnick RJ. Cholesteryl ester storage disease: Review of the findings in 135 reported patients with an underdiagnosed disease. J Hepatol [Internet]. European Association for the Study of the Liver; 2013;58(6):1230–43. Available from: http://dx.doi.org/10.1016/j.jhep.2013.02.014.
24. National Center for Advancing Translational Sciences. Lysosomal acid lipase deficiency [webpage on the internet]. Gaithersburg (MD): National Center for Advancing Translational Sciences; 2021 [cited 2021 Apr 27]. Available from: https://rarediseases.info.nih.gov/diseases/12097/lysosomal-acid-lipase-deficiency.
25. National Center for Biotechnology Information. Wolman Disease [webpage on the internet]. Bethesda (MD): National Center for Biotechnology; 2020 [cited 2021 Apr 27]. Available from: https://www.ncbi.nlm.nih.gov/gtr/conditions/C0043208/.

26. National Organization for Rare Diseases. Phenylketonuria [webpage on the internet]. Danbury (CT): National Organization for Rare Diseases; 2019 [cited 2021 Jun 29]. Available from: https://rarediseases.org/rare-diseases/phenylketonuria/.
27. Bodamer OA. Overview of phenylketonuria. In: Hanh S (Ed). UpToDate [database on the internet]. Waltham (MA): UpToDate; 2021 [cited 2022 Jan 26]. Available from: http://www.utdol.com/utd/index.do.
28. Lumizyme [package insert]. Cambridge (MA): Genzyme Corporation; 2020 Feb.
29. Merritt JL. Lysosomal acid alpha-glucosidase deficiency (Pompe disease, glycogen storage disease II, acid maltase deficiency). UpToDate [database on the internet]. Waltham (MA): UpToDate2021 [cited 2022 Jan 26]. Available from http://www.utdol.com/utd/index.do.
30. Nexviazyme [package insert]. Cambridge (MA): Genzyme Corporation; 2021 Aug.
31. Mepsevii [package insert] Novato (CA): Ultragenyx Pharmaceuticals; 2022 Dec.
32. Naglazyme [package insert on the internet]. Novato (CA): BioMarin Pharmaceutical Inc.; 2019 Dec [cited 2022 Jan 26]. Available from: http://www.naglazyme.com.
33. Palynziq [package insert on the internet]. Novato (CA): BioMarin Pharmaceutical; 2020 Nov [cited 2022 Jan 26]. Available from: https://www.palynziq.com.
34. Revcovi [package insert] Gaithersburg (MD): Leadiant Biosciences Inc; 2020 Dec [cited 2022 Jan 26]. Available from: https://revcovi.com/.
35. National Organization for Rare Diseases. Hypophosphatasia [webpage on the internet]. Danbury (CT): National Organization for Rare Diseases; 2021 [cited 2022 Jan 26]. Available from: https://rarediseases.org/rare-diseases/hypophosphatasia/.
36. Treem WR, McAdams L, Stanford L, Kastoff G, Justinich C, Hyams J. Sacrosidase therapy for congenital sucrase-isomaltase deficiency. J Pediatr Gastroenterol Nutr. 1999 Feb;28(2):137-42.
37. Robayo-Torres CC, Opekun AR, Quezada-Calvillo R, et al. 13C-breath tests for sucrose digestion in congenital sucrase isomaltase-deficient and sacrosidase-supplemented patients. J Pediatr Gastroenterol Nutr. 2009;48(4):412-418. PMID:19330928.
38. Metabolic Solutions. Sucrose Breath Test [webpage on the internet]. Nashua (NH): Metabolic Solutions; 2014 [cited 2021 Apr 15]. Available from: https://www.metsol.com/wp-content/uploads/2014/04/Sucrose-Breath-Test.pdf.
39. Vimizim [package insert]. Novato (CA): BioMarin Pharmaceutical, Inc.; 2019 Dec [cited 2022 Jan 26]. Available from: http://www.vimizim.com.
40. Hanh S. Mucopolysaccharidoses: Treatment. UpToDate [database on the internet]. Waltham (MA): UpToDate; 2021 [cited 2022 Jan 26]. Available from http://www.utdol.com/utd/index.do.
41. Balasubramaniam S, Duley JA, Christodoulou J. Inborn errors of pyrimidine metabolism: clinical update and therapy. J Inherit Metab Dis. 2014 Sep; 37(5):687-98.
42. Vpriv [package insert on the internet]. Cambridge (MA): Shire Human Genetic Therapies, Inc.; 2021 Nov [cited 2022 Jan 26]. Available from: http://www.vpriv.com.
43. Shire announces FDA approval of Vpriv (velaglucerase alfa for injection for the treatment of type 1 Gaucher disease [press release on the internet]. Cambridge (MA): Shire plc: 2010 Feb 26 [cited 2018 Mar 26]. Available from: https://www.shire.com/newsroom/2010/february/shire-announces-fda.
44. National Organization for Rare Diseases. Hereditary Orotic Aciduria [webpage on the internet]. Danbury (CT): National Organization for Rare Diseases; 2019 [cited 2021 Apr 20]. Available from: https://rarediseases.org/rare-diseases/hereditary-orotic-aciduria/.
45. Pancreatic Enzyme Replacement Products containing Lipase, Protease, and Amylase. American Society of Health-System Pharmacists [webpage on the Internet]. Atlanta (GA): American Society of Health-System Pharmacists; Nov 2012 [cited 2018 Mar 26]. Available from: http://www.ashp.org/menu/DrugShortages/ResolvedShortages/Bulletin.aspx?id=619.

46. FDA Approves First Treatment for Molybdenum cofactor Deficiency Type A. [press release on the Internet]. Food and Drug Administration (US); 2021 Feb 26 [cited 2021 Jun 30]. Available from: https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-molybdenum-cofactor-deficiency-type.
47. Shellhaas R. Etiology and prognosis of neonatal seizures. In Trobe J (Ed). UpToDate [database on the internet]. Waltham (MA): UpToDate; 2021 [cited 2022 Jan 26]. Available from: http://www.utdol.com/utd/index.do.
48. National Institutes of Health. Molybdenum cofactor deficiency. Last updated 2021 Feb [cited 2022 Jan 26]. Available from: https://medlineplus.gov/genetics/condition/molybdenum-cofactor-deficiency/#frequency.
49. Nulibry [package insert]. Boston (MA): Origin Biosciences, Inc.; 2021 Feb.
50. Hughes D. Gaucher disease: Treatment. In: Hanh S (Ed). UpToDate [database on the internet]. Waltham (MA): UpToDate; 2021 [cited 2022 Jan 26]. Available from: http://www.utdol.com/utd/index.do
51. Lee B. Urea cycle disorders: Clinical features and diagnosis. In: Hahn S. (Ed). UpToDate [database on the internet]. Waltham (MA): UpToDate; 2022 [cited 2022 May 11]. Available from: http://www.utdol.com/utd/index.do.
52. Bodamer OA. Organic acidemias: An overview and specific defects. In: Hahn S. and Patterson MC (Ed). UpToDate [database on the internet]. Waltham (MA): UpToDate; 2022 [cited 2022 Mau 11]. Available from: http://www.utdol.com/utd/index.do.
53. Diaz GA, Krivitzky LS, Mokhtarani M, Rhead W, Bartley J, Feigenbaum A, et al. Ammonia control and neurocognitive outcome among urea cycle disorder patients treated with glycerol phenylbutyrate. Hepatology. 2013 Jun;57(6):2171-9.
54. FDA approves treatment for anemia in adults with rare inherited disorder [press release on the Internet]. FDA; 2022 Feb 17 [cited 2022 May 17]. Available from: https://www.fda.gov/drugs/news-events-human-drugs/fda-approves-treatment-anemia-adults-rare-inherited-disorder.
55. Agios Announces FDA Approval of PYRUKYND (mitapivat) as First Disease-Modifying Therapy for Hemolytic Anemia in Adults with Pyruvate Kinase Deficiency [press release on the Internet]. Agios Pharmaceuticals, Inc.; 2022 Feb 17 [cited 2022 May 17]. Available from: https://investor.agios.com/news-releases/news-release-details/agios-announces-fda-approval-pyrukyndr-mitapivat-first-disease.
56. National Organization for Rare Disorders: PIK3CA-Related Overgrowth Spectrum. Danbury (CT): NORD; 2022 [citied 2022 May 25]. Available from: https://rarediseases.org/rare-diseases/pik3ca-related-overgrowth-spectrum/.
57. Balwania M, Burrowb TA, Charrowc J, Goker-Alpand O, Kaplane P, Kishnani PS, et al. Recommendations for the use of eliglustat in the treatment of adults with Gaucher disease type 1 in the United States. Molecular Genetics and Metabolism; 117(2):95-103.
58. Schiffmann R, Fitzgibbon EJ, Harris C, DeVile C, Davies EH, Abel L, et al. Randomized, controlled trial of miglustat in Gaucher's disease type 3. Ann Neurol. 2008; 64(5):514-522.
59. Lee B. Urea cycle disorders: Management. In: Hahn S. (Ed). UpToDate [database on the internet]. Waltham (MA): UpToDate; ; 2022 [cited 2022 Mar 22]. Available from: http://www.utdol.com/utd/index.do.
60. Caruthers RL, Johnson CE. Stability of extemporaneously prepared sodium phenylbutyrate oral suspensions. Am J Health Syst Pharm. 2007 Jul 15;64(14):1513-5.
61. Valayannopoulos V, Baruteau J, Delgado MB, Cano A, Couce ML, Del Toro M, et al. Carglumic acid enhances rapid ammonia detoxification in classical organic acidurias with a favourable risk-benefit profile: a retrospective observational study. Orphanet J Rare Dis. 2016 Mar 31;11:32.
62. Xenpozyme TM [package insert]. Cambridge (MA): Genzyme Corporation.; 2022 Aug.

63. FDA Approves First Treatment for Acid Sphingomyelinase Deficiency, a Rare Genetic Disease [press release on the Internet]. Rockville (MD): Food and Drug Administration (US); 2022 Aug 31 [cited 2022 Dec 9]. Available from: http://www.fda.gov/bbs/topics/NEWS/2007/NEW01587.html.
64. Genzyme Corporation. XenpozymeTM (Olipudase alfa-rpcp) [webpage on the internet]. Cambridge (MA): Genzyme Corporation 2022 [cited 2022 November 20]. Available from: https://www.xenpozyme.com/
65. Wasserstein MP, Schuchman EH, Adam MP, Everman DP, Mirzaa GM, Pagon RA, et al. Acid Sphingomyelinase Deficiency. GeneReviews 2006 December 7. PMID: 20301544
66. McGovern MM, Avetisyan R, Sanson BJ, Lidove O. Disease manifestations and burden of illness in patients with acid sphingomyelinase deficiency (ASMD). Orphanet J Rare Dis. 2017 Feb 23;12(1):41.
67. National Organization for Rare Disorders (NORD). Acid Sphingomyelinase Deficiency [webpage on the internet]. Fort Atkinson (WI): NORD: 2021 [cited 2022 November 20]. Available from: https://rarediseases.org/rare-diseases/acid-sphingomyelinase-deficiency/
68. Patterson M. Overview of Niemann-Pick Disease. In: Basow DS (Ed). UpToDate [database on the internet]. Waltham (MA): UpToDate; 2022 [cited 2022 November 20]. Available from: http://www.utdol.com/utd/index.do.
69. Wasserstein M, Lachmann R, Hollak C, Arash-Kaps L, Barbato A, Gallagher RC, et al. A randomized, placebo-controlled clinical trial evaluating olipudase alfa enzyme replacement therapy for chronic acid sphingomyelinase deficiency (ASMD) in adults: One-year results. Genet Med. 2022 Jul;24(7):1425-1436.
70. Diaz GA, Jones SA, Scarpa M, Mengel KE, Giugliani R, Guffon Net al. One-year results of a clinical trial of olipudase alfa enzyme replacement therapy in pediatric patients with acid sphingomyelinase deficiency. Genet Med. 2021 Aug;23(8):1543-1550.
71. Xenpozyme TM (olipudase alfa) approved by European Commission as first and only treatment for ASMD [press release on the internet]. Paris (France): Sanofi; 2022 June 28. [cited 2022 November 28] Available from: https://www.sanofi.com/en/media-room/press-releases/2022/2022-06-28-05-30-00-2469974
72. Genzyme Corporation. XenpozymeTM (Olipudase alfa-rpcp) Billing and Coding Guide [webpage on the internet]. Cambridge (MA): Genzyme Corporation 2022 [cited 2022 November 20]. Available from: https://www.xenpozyme.com/
73. Lamzede [package insert]. Cary (NC): Chiesi USA, Inc.; 2023 Feb.
74. Genetic and Rare Disease Information Center. Alpha-mannosidosis – About the Disease [webpage on the internet]. Gaithersburg (MD): GARD; 2023 [cited 2023 Apr 26]. Available from: https://rarediseases.info.nih.gov/diseases/6968/alpha-mannosidosis.
75. Boston Children's Hospital. Alpha-mannosidosis [webpage on the internet]. Boston (MA): Boston Children's Hospital; [cited 2023 Apr 26]. Available from: https://www.childrenshospital.org/conditions/alpha-mannosidosis.
76. MedlinePlus. Alpha-mannosidsis [webpage on the internet]. Bethesda (MD): National Library of Medicine (US); 2014 [cited 2023 Apr 26]. Available from: https://medlineplus.gov/genetics/condition/alpha-mannosidosis/.
77. Elfabrio [package insert on the internet]. Cary (NC): Chiesi USA, Inc.; 2023 May [cited 2023 Sep 25]. Available from: https://elfabrio.com/.
78. Elfabrio Approved for the Treatment of Fabry Disease [database on the internet]. Aventura (FL): IPD Analytic, LLC; 2023 Jun [cited 2023 Sep 22]. Available from: https://www.ipdanalytics.com/.
79. FDA approves first treatment for activated phosphoinositide 3-kinase delta syndrome [press release on the Internet]. Rockville (MD): Food and Drug Administration (US); 2023 Mar 24 [cited 2023 Sep 18]. Available from: https://www.fda.gov/drugs/news-events-human-drugs/fda-approves-first-treatment-activatedphosphoinositide-3-kinase-delta-syndrome

80. Lougaris V, Cancrini C, Rivalta B, Castagnoli R, Giardino G, Volpi S, et al. Activated phosphoinositide 3-dinase delta syndrome (APDS): An update. Pediatr Allergy Immunol. 2022 Jan;33 Suppl 27(Suppl 27):69-72.

Review History

02/08/2023 - Reviewed and created for Feb P&T; matched MH UPPL. Created criteria to be in compliance with Masshealth unified formulary requirements (Effective 4/1/23).
05/10/23 – Reviewed and updated for P&T. Added new drug, Ryplazim (plasminogen, human-tvmh), to policy. Added initial and reauthorization criteria for Xenpozyme for the treatment of non-central nervous system manifestations of acid sphingomyelinase deficiency (ASMD) in adult and pediatric patients. A noted was added for Fabrazyme to clarify that Gb3 may be referred to as GL-3. References updated. Effective 6/5/23
06/14/23 – Reviewed and updated for P&T. Removed preferred product requirement from Palynziq and Nexviazyme for requests through MB. Effective 6/30/23
07/12/23 – Reviewed and updated for P&T. Added new drug, Lamzede, to policy requiring PA under MB. Brand preferred and mandatory generic language was added under Limitations. Effective 7/31/23
11/15/23 – Reviewed and updated for P&T. Policy update to restrict Nexviazyme to medical billing. Genetic testing requirement was removed from criteria for Kuvan and Palynziq. Effective 12/4/23
12/13/23 – Reviewed and updated for P&T. Elfabrio, Joenja, and Olpruva added to criteria requiring PA. Effective 1/2/24
05/15/25 – Reviewed and updated for P&T. Updated formatting and references. Removed drugs that are managed through pharmacy benefit as it is available on MHDL. Medical benefit drugs remain. Effective 6/1/25