MEDICAL POLICY STATEMENT

Original Effective Date	Next Annual Review Date	Last Review / Revision Date
06/15/2011	12/05/2015	02/27/2015
Policy Name		**Policy Number**
Enzyme Replacement Therapy and Agents		**SRx-0019**

Medical Policy Statements prepared by CSMG Co. and its affiliates (including CareSource) are derived from literature based on and supported by clinical guidelines, nationally recognized utilization and technology assessment guidelines, other medical management industry standards, and published MCO clinical policy guidelines. Medically necessary services include, but are not limited to, those health care services or supplies that are proper and necessary for the diagnosis or treatment of disease, illness, or injury and without which the patient can be expected to suffer prolonged, increased or new morbidity, impairment of function, dysfunction of a body organ or part, or significant pain and discomfort. These services meet the standards of good medical practice in the local area, are the lowest cost alternative, and are not provided mainly for the convenience of the member or provider. Medically necessary services also include those services defined in any Evidence of Coverage documents, Medical Policy Statements, Provider Manuals, Member Handbooks, and/or other policies and procedures.

Medical Policy Statements prepared by CSMG Co. and its affiliates (including CareSource) do not ensure an authorization or payment of services. Please refer to the plan contract (often referred to as the Evidence of Coverage) for the service(s) referenced in the Medical Policy Statement. If there is a conflict between the Medical Policy Statement and the plan contract (i.e., Evidence of Coverage), then the plan contract (i.e., Evidence of Coverage) will be the controlling document used to make the determination.

For Medicare plans please reference the below link to search for Applicable National Coverage Descriptions (NCD) and Local Coverage Descriptions (LCD):

A. SUBJECT

Enzyme Replacement Therapy and Agents

- laronidase (Aldurazyme)
- imiglucerase (Cerezyme)
- idursulfase (Elaprase)
- velaglucerase alfa (Vpriv)
- agalsidase beta (Fabrazyme)
- alglucosidase alfa (Lumizyme, Myozyme)
- galsulfase (Naglazyme)
- taliglucerase alfa (Elelyso) ***New addition***
- miglustat (Zavesca)
- eliglustat (Cerdelga) ***New addition***
- elosulfase alfa (Vimizim) ***New addition***

B. BACKGROUND

CareSource medication policies are therapy class policies that are used as a guide when determining health care coverage for our members with benefit plans covering prescription drugs requiring prior authorization or Step-Therapy. The medication policy is used as a tool to be interpreted in conjunction with the member's specific benefit plan.

The intent of the enzyme replacement agents medication (PA) program is to encourage appropriate selection of patients for therapy according to product labeling and/or clinical guidelines and/or clinical studies, and also to encourage use of preferred agents.

C. DEFINITIONS

N/A

D. POLICY

CareSource will approve the use of **laronidase (Aldurazyme)** and consider its use medically necessary when **ALL** of the following criteria have been met:

- Prescribed by an endocrinologist or under the recommendation of an endocrinologist diagnosis of mucopolysaccharidosis I, as indicated by **1 or more** of the following:
  - Hurler variant (severe mucopolysaccharidosis I; also MPS IH)
  - Hurler-Scheie variant (attenuated mucopolysaccharidosis I; also MPS IHS)
  - Scheie variant (attenuated mucopolysaccharidosis I; also MPS IS)
- Signs or symptoms of mucopolysaccharidosis I, as indicated by **1 or more** of the following:
  - Cardiac abnormalities (e.g., arrhythmia, cardiomyopathy, congestive heart failure, valvular disease)
  - Dysostosis multiplex (i.e., defective ossification of bones)
  - Hepatosplenomegaly
  - Hurler variant (severe) phenotype
  - Joint restriction
  - Obstructive sleep apnea
  - Restrictive lung disease (i.e., forced vital capacity 80% or less than predicted)
  - Skeletal abnormalities (e.g., claw hand, genu valgus or varus, gibbus deformity, kyphosis, scoliosis, trigger finger)

CareSource will approve the use of **imiglucerase (Cerezyme), velaglucerase (Vpriv) or taliglucerase alfa (Elelyso) , eliglustat (Cerdelga)or miglustat (Zavesca)** and consider its use as medically necessary when the **ALL** of the following criteria have been met:

- Diagnosis of type 1 Gaucher disease
- Prescribed by an endocrinologist or under the recommendation of an endocrinologist or under care of physician with expertise in Gaucher disease.
- Patient has non-neurologic clinical manifestations of Gaucher disease, as indicated by **1 or more** of the following:
  - Abdominal pain
  - Cachexia
  - Cardiopulmonary disease (e.g., pulmonary hypertension)
  - Exertional limitations
  - Fatigue
  - Growth failure
- Hematologic abnormalities, as indicated by **1 or more** of the following:
  - Documented abnormal bleeding episodes
  - Hemoglobin less than or equal to 2 g/dL (20 g/L) below lower limit of normal range for age and gender
  - Symptomatic anemia
  - Thrombocytopenia, with platelet count less than 120,000/mm^3 (120 x10^9/L)
  - Transfusion dependent
  - Impaired quality of life secondary to Gaucher disease
- Liver or spleen disease, as indicated by **1 or more** of the following:
  - Hepatic or splenic infarcts
  - Hepatitis
  - Hepatomegaly
  - Portal hypertension
  - Splenomegaly
- Skeletal involvement, as indicated by **1 or more** of the following:
  - Bone pain
  - Erlenmeyer flask deformity on x-ray

- History of bone infarcts or painful crises
- Lytic lesions
- Osteonecrosis
- Osteopenia
- Osteosclerosis
- Pathologic fracture
- Subchondral collapse
- Weakness
- Weight loss

CareSource will approve the use of **idursulfase (Elaprase)** and consider its use as medically necessary when the **ALL** of the following criteria have been met:

- Diagnosis of mucopolysaccharidosis II (Hunter syndrome)
- Prescribed by an endocrinologist or under the recommendation of an endocrinologist
- Signs or symptoms of mucopolysaccharidosis II, as indicated by **1 or more** of the following:
  - Cardiac abnormalities (e.g., cardiomyopathy, valvular dysfunction)
  - Dysostosis multiplex (e.g., defective ossification of bones)
  - Hepatosplenomegaly
  - Joint restriction
  - Restrictive lung disease
  - Skeletal abnormalities
  - Upper airway obstruction

CareSource will approve the use of **agalsidase (Fabrazyme)** and consider its use as medically necessary when the **ALL** of the following criteria have been met:

- Diagnosis of Fabry disease
- Prescribed by an endocrinologist or under the recommendation of an endocrinologist
- Enzyme replacement needed, as indicated by **1 or more** of the following:
  - Cardiac involvement that is clinically significant (e.g., left ventricular hypertrophy, conduction abnormalities)
  - Chronic severe abdominal pain or diarrhea, not due to other etiology
  - Glomerular filtration rate less than 80 mL/min/1.73m^2 (1.34 mL/sec/1.73m^2)
  - History of cerebrovascular accident
  - History of transient ischemic attacks
  - Ischemia on brain MRI
  - Male with complete lack of endogenous alpha-galactosidase A enzyme
  - Neuropathic pain in hands or feet
  - Proteinuria greater than 300 mg/day (0.3 g/day)

CareSource will approve the use of **alglucosidase alfa (Lumizyme, Myozyme)** and consider its use as medically necessary when 1 of the following criteria have been met:

- Infantile-onset form of Pompe disease
- Late (non-infantile)-onset Pompe disease, as indicated by **ALL** of the following:
  - Age 8 years or older
  - Enzyme replacement needed, as indicated by **1 or more** of the following:
    - Proximal muscle weakness
    - Reduced forced vital capacity in upright or supine position
    - No evidence of cardiac hypertrophy

CareSource will approve the use of **galsulfase (Naglazyme)** and consider its use as medically necessary when **1 or more** of the following criteria have been met:

- Documented diagnosis of mucopolysaccharidosis VI (Maroteaux-Lamy Syndrome)
- Prescribed by an endocrinologist or under the recommendation of an endocrinologist
- Clinical manifiestations are present as indicated by **1 or more** of the following:
  - Growth failure with bone deformities (Dysotosis Multiplex)
  - Corneal clouding of the eye(s)
  - Hydrocephalus
  - Spinal cord compression
  - Carpal tunnel syndrome
  - Malfunctioning heart valves, thickening and stiffening of heart wall, narrowing of blood vessels
  - Hearing loss
  - Narrowed trachea with diagnosis of Sleep Apnea

CareSource considers **galsulfase (Naglazyme)** experimental and investigational for all other indications because its effectiveness for indications other than the one listed has not been established.

CareSource will approve the use of **elosulfase alfa (Vimizim)** and consider its use as medically necessary when **ALL** of the following criteria have been met:

- Documented diagnosis of mucopolysaccharidosis IV (Morquio A Syndrome: Type A)
- Prescribed by an endocrinologist or under the recommendation of an endocrinologist or under care of physician with expertise in mucopolysaccharidosis;
- Clinical manifestations are present as indicated by **1 or more** of the following:
  - Abnormal development of spine and bones
  - Bell-shaped chest with ribs flared out at bottom
  - Coarse facial features
  - Hypermobile joints
  - Knock-knees
  - Macrocephaly
  - Short stature with a particularly short trunk
  - Widely spaced teeth

CareSource considers **elosulfase alfa (Vimizim)** experimental and investigational for all other indications because its effectiveness for indications other than the one listed has not been established.

All other uses of laronidase, imigluceragse, agalsidase beta, galsulfase, idursufase, alglucosidase alfa or taliglucerase alfa are considered experimental/investigational and therefore, will follow CareSources' Off-Label policy.

Note: Documented diagnosis must be confirmed by portions of the individual's medical record which will confirm the presence of disease and will need to be supplied with prior authorization request. These medical records may include, but not limited to test reports, chart notes from provider's office or hospital admission notes.

Refer to the product package insert for dosing, administration and safety guidelines.
For Medicare Plan members, reference the below link to search for Applicable National Coverage Descriptions (NCD) and Local Coverage Descriptions (LCD):

If there is no NCD or LCD present, reference the CareSource Policy for coverage.

CONDITIONS OF COVERAGE

HCPCS	J1931	Aldurazyme (laronidase)
	J1786	Cerezyme (imiglucerase)
	J1743	Elaprase (idursulfase)
	J3060	Eleyso (taliglucerasde alfa)
	J0180	Fabrazyme (agalsidase beta)
	J0220	Myozyme, Lumizyme (alglucosidase alfa)
	J1458	Naglazyme (galsulfase)
	J3385	Vpriv (velaglucerase alfa)
	J3490	Zavesca (miglustat)
	J8499	Cerdelga (eliglustat)
	C9022	Vimizim (elosulfase alfa)

CPT

PLACE OF SERVICE
Office, Outpatient, Home
Preferred place of service is in the home.
This medication can be self-administered and can be billed through the pharmacy benefit.
Note: CareSource supports administering inject able medications in various setting, as long as those services are furnished in the most appropriate and cost effective setting that are supportive of the patient's medical condition and unique needs and condition. The decision on the most appropriate setting for administration is based on the member's current medical condition and any required monitoring or additional services that may coincide with the delivery of the specific medication.

AUTHORIZATION PERIOD
Approved initial authorizations are valid for 3 months. Continued treatment may be considered when the member has shown biological response to treatment. A reauthorization after successful initiation period will be placed for 1 year. ALL authorizations are subject to continued eligibility.

E. REVIEW/REVISION HISTORY

Date Issued:	06/15/2011
Date Reviewed:	06/15/2011, 12/05/2014
Date Revised:	12/05/2014 – removed Ceredase & added Elelyso
	02/27/2015 – placed into new template

F. REFERENCES

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2. Milliman's Guidelines 18th edition, 2014.
3. UpToDate, Kakkis, E. et. al. Mucopolysaccharidoses: Clinical features and diagnosis; Mucopolysaccharidoses: Complications and management; Accessed September 26, 2014.
4. Sidransky, E., Steiner, R., Windle, M., Youssoufian, H., Descartes, M., & Petry, P. (2014, October 6). Gaucher Disease Treatment & Management. Retrieved October 23, 2014, from http://emedicine.medscape.com/article/944157-treatment
5. Harmatz, P., Garcia, P., Guffon, N., Randolph, L., Shediac, R., Braunlin, E., ... Decker, C. (2013, October 10). Galsufase (Naglazyme) Therapy in Infants with Mucopolysaccharidosis VI. Retrieved October 23, 2014, from http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3976509/.

6. VPRIV (Velaglucerase Alfa for Injection; Shire Human Genetic Therapies Inc.) for Type 1. (2013, January 1). Retrieved January 1, 2014, from https://www.hayesinc.com/subscribers/subscriberArticlePDF.pdf?articleId=15158.
7. Morquio Syndrome. (2014, January 1). Retrieved November 5, 2014, from http://www.nlm.nih.gov/medlineplus/ency/article/001206.htm

"This guideline contains custom content that has been modified from the standard care guidelines and has not been reviewed or approved by MCG Health, LLC."

The medical Policy Statement detailed above has received due consideration as defined in the Medical Policy Statement Policy and is approved.