Vimizim (elosulfase alfa)
Policy Number: C7068-A

CRITERIA EFFECTIVE DATES:

<table>
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<tr>
<th>ORIGINAL EFFECTIVE DATE</th>
<th>LAST REVIEWED DATE</th>
<th>NEXT REVIEW DATE</th>
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<tr>
<td>04/2015</td>
<td>6/17/2020</td>
<td>6/17/2021</td>
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J CODE: J1322- Injection, elosulfase alfa, 1 mg
TYPE OF CRITERIA: RxPA
LAST P&T APPROVAL/VERSION: Q3 2020 20200722C67068-A

PRODUCTS AFFECTED:
Vimizim (elosulfase alfa)

DRUG CLASS:
Mucopolysaccharidosis IV (MPS IV) - Agents

ROUTE OF ADMINISTRATION:
Intravenous

PLACE OF SERVICE:
Specialty Pharmacy or Buy and Bill
The recommendation is that medications in this policy will be for medical benefit coverage and the IV infusion products administered in a place of service that is a non-hospital facility-based location (i.e., home infusion provider, provider’s office, free-standing ambulatory infusion center) unless the therapy/member meets the Site of Care exceptions. (See appendix for excerpt from Specialty Medication Administration Site of Care Policy) and the Pre- Filled Syringe product for self-administered

AVAILABLE DOSAGE FORMS:
Vimizim SOLN 5MG/5ML (5ml vial)

FDA-APPROVED USES:
Mucopolysaccharidosis type IVA (MPS IVA; Morquio A syndrome) Treatment of mucopolysaccharidosis type IVA (MPS IVA; Morquio A syndrome) in adults and children 5 years of age and older E76.210 Morquio A mucopolysaccharidoses

COMPENDIAL APPROVED OFF-LABELED USES:
None

COVERAGE CRITERIA: INITIAL AUTHORIZATION

DIAGNOSIS:
Diagnosis of mucopolysaccharidosis IVA (MP IVA, Morquio A syndrome)

REQUIRED MEDICAL INFORMATION:
A. MUCOPOLYSACCHARIDOSIS IVA (MORQUIO A SYNDROME)
   1. Diagnosis of mucopolysaccharidosis IVA (MP IVA, Morquio A syndrome) confirmed by: Documented reduced fibroblast or leukocyte GALNS enzyme activity OR Molecular genetic testing of GALNS
AND

2. Prescriber attests to the member reporting or having documented at least ONE (1) of the following symptoms of the disease: kyphoscoliosis, genu valgum, pectus carinatum, gait disturbance, growth deficiency, short stature, spinal abnormalities, chest abnormalities, joint abnormalities, respiratory compromise, cardiac valve abnormalities, muscular weakness, visual impairment, hearing loss, or dental abnormalities and oral health challenges

AND

3. Documentation member’s weight dated within 1 month of the prior authorization request

NOTE: Member’s weight must be provided at time of prior authorization request and for any subsequent dose increases. Requests for amounts above initially authorized limits will require documentation of an updated member weight for review and authorization.

AND

4. Baseline 6-minute walk test (6-MWT) indicating the member walked at least 30 meters in six (6) minutes is provided

DURATION OF APPROVAL:
Initial authorization: 6 months, Continuation of treatment: 12 months

QUANTITY:
ADULTS: 2 mg/kg IV once weekly, PEDIATRICS (5 years and older): 2 mg/kg IV once weekly

PRESCRIBER REQUIREMENTS:
Prescribed by, or in consultation with, a board-certified geneticist, metabolic specialist, or physician experienced in the management of members with mucopolysaccharidoses. Submit consultation notes if applicable

AGE RESTRICTIONS:
5 years of age and older

CONTINUATION OF THERAPY:
A. MUCOPOLYSACCHARIDOSIS IVA (MORQUIO A SYNDROME)
   1. If Prescriber is not a board-certified geneticist, metabolic specialist, or physician experienced in the management of members with mucopolysaccharidoses recent consultation notes must be submitted for continuation of treatment requests.
   AND
   2. Adherence to therapy at least 85% of the time as verified by Prescriber and member’s medication fill history (review Rx history for compliance)
   AND
   3. Prescriber attests to stabilization or improvement to Vimizim (elosulfase alfa) therapy as evaluated by the Prescriber: Based on the submission of medical records documenting tolerance and effectiveness of therapy based on the results of the comparison of baseline and current 6-minute walk test (6-MWT)
   AND
   4. Documentation member’s weight dated within 1 month of the prior authorization request

NOTE: Member’s weight must be provided at time of prior authorization request and for any subsequent dose increases. Requests for amounts above initially authorized limits will require documentation of an updated member weight for review and authorization.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Vimizim (elosulfase alfa) that are not an FDA-approved indication or not included in this policy are considered
experimental/investigational or not a covered benefit of this policy. This subject to change based on research and medical literature, or at the discretion of Molina Healthcare.

OTHER SPECIAL CONSIDERATIONS:
None

BACKGROUND:
MPS IVA is a rare and debilitating genetic disorder which is caused by a deficiency of the enzyme, N-acetylgalactosamine-6 sulfatase, which results in excessive lysosomal storage of keratan sulfate in many tissues and organs. Accumulation of keratan sulfate causes systemic skeletal dysplasia, short stature, and joint abnormalities, which limit mobility and endurance. Malformation of thorax impairs respiratory function and malformation of neck vertebrae and ligament weakness causes cervical spinal instability and, potentially, cord compression. Other symptoms include hearing loss, corneal clouding, and heart valve disease.

Vimizim (elosulfase alfa) is the first pharmacotherapy available for mucopolysaccharidosis type IVA (MPS IVA; Morquio A Syndrome) syndrome and the first enzyme replacement therapy (ERT) designed to target the underlying cause of MPS IVA syndrome, a rare, progressive, debilitating disorder caused by a deficiency in the enzyme N-acetylgalactosamine-6 sulfatase (GALNS). Elosulfase alfa is indicated for the treatment of MPS IVA in adults and pediatric members 5 years and older. Elosulfase alfa is intended to replace GALNS in the metabolic pathway.

Elosulfase alfa is a recombinant form of human GALNS and is identical to the naturally occurring human lysosomal enzyme in terms of the amino acid sequence and N-linked glycosylation. Elosulfase alfa provides exogenous GALNS that is taken up into the lysosomes and catabolizes the GAGs keratan sulfate and chondroitin-6-sulfate. Elosulfase alfa uptake by cells into lysosomes is most likely mediated by the binding of mannose-6-phosphate-terminated oligosaccharide chains of elosulfase alfa to the cation-independent mannose-6-phosphate receptor (CI-M6PR).

The FDA approval of elosulfase alfa was based on a randomized trial of 176 members with MPS IVA. Weekly elosulfase alfa treatment improved distance walked in a 24-week randomized, placebo-controlled trial. Members who continued to receive weekly elosulfase alfa for an additional 48 weeks had no further improvement in walking ability beyond the first 24 weeks. No further improvement in walking ability was seen in a 48-week extension trial.

In this pivotal phase 3 study of elosulfase alfa (MOR-004) members treated with 2.0 milligrams per kilogram per week (mg/kg/week) of elosulfase alfa had a statistically significant increase from baseline in mean distance walked during the 6MWT at 24 weeks compared with placebo or members treated with 2.0 mg/kg every other week.

The results showed that elosulfase alfa improved performance on the 6MWT (primary outcome) but not the 3MSCT (secondary outcome). Elosulfase therapy was also associated with a greater reduction in urinary keratan sulphate levels compared with placebo; however, the clinical significance of this finding has not been established. As with other ERT products, members may develop neutralizing antibodies (NAbs) to elosulfase alfa. All members treated with Vimizim 2 mg/kg once per week tested positive for NAbs. The relationship between the presence of NAbs and long-
term therapeutic response cannot be assessed. Although the presence of NAbs did not appear to have a significant effect on the efficacy or safety of elosulfase alfa, the long-term effect of the immunogenicity of the product is unknown. Prior to the approval of this ERT for the treatment for MPS IVA, the only alternatives were palliative or supportive care, which does not treat the underlying cause of the disease, so it continues to progress. In consideration of the unmet need for treatment of MPS IVA, the benefits of elosulfase alfa therapy for members with MPS IVA outweigh the known risks since there are no clinical alternatives to elosulfase alfa for ERT in members with MPS IVA. Elosulfase alfa has a reasonable safety profile with consideration of the seriousness of the disorder though this therapy is associated with development of NAbs and infusion reactions.

The single phase 3 pivotal supports the efficacy of the recombinant enzyme; however, efficacy was established based primarily on subjective tests of endurance (the 6MWT and 3MSCT are subjective tests depend on the effort and motivation of the individual member, which may be difficult to control in younger children) and long-term outcomes have not been published. The American Journal of Medical Genetics recommends initiating treatment as soon as the diagnosis has been confirmed by an enzyme activity test

APPENDIX:
None

Molina Healthcare, Inc. covers injectable/infused treatment in a hospital outpatient setting or at a hospital-affiliated infusion suite* when the level of care is determined to be medically necessary. Considerations used to determine if an alternative level of care is not suitable may include the following findings:

1. The member is clinically unstable based on documented medical history and susceptible to complication with drug administration (e.g., cardiopulmonary or renal dysfunction, risk for fluid overload)
2. The requested medication is administered as part of a chemotherapy regimen (e.g., anti-neoplastic agent, colony stimulating factor, erythropoiesis-stimulating agent, anti-emetic) for treatment of cancer or with dialysis
3. The member exhibits physical or cognitive impairment and a capable caregiver is not available to assist with safe administration of prescribed medication in the home
4. It is the member’s first dose of the medication or it is being re-initiated after at least 12 months*
5. The member has experienced adverse events with past administration of the drug and cannot be managed by premedication or resources available at a non-hospital facility based location (NHFBL)
6. Documented history of difficulty establishing and maintaining patent vascular access, or is not a candidate for a mode of long-term vascular access during the duration of prescribed treatment

Note: a hospital outpatient setting, or a hospital-affiliated infusion suite is expected to have immediate access to specific services of a medical center/hospital setting, including having emergency resuscitation equipment and personnel (ACLS protocol), emergency services, and inpatient admission or intensive care, if necessary
Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, member records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

REFERENCES: