Executive Summary

**Purpose:** Ensure appropriate utilization and control of Enzyme Deficiency, Select Agents.

**Why Issue Selected:** Enzymes play an important role in the human body by carrying out various chemical functions such as digesting food, healing wounds, and breaking down toxins. Certain disease states result in deficiencies in enzymes and potentially lead to life-changing or life-threatening symptoms. Agents used to treat these disease states are sometimes classified as enzyme replacement therapies, which supplement the deficient enzyme, or have other mechanisms of action that result in increased enzyme levels in the body. By increasing levels of the deficient enzyme, these therapies treat the symptoms of the disease.

Due to the high cost and specific approved indications, MO HealthNet will impose clinical criteria to ensure appropriate utilization of Enzyme Deficiency, Select Agents.

### Program-Specific Information:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Date Range FFS 1/1/21 to 12/31/21</th>
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<tbody>
<tr>
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<td>Claims</td>
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<tr>
<td>ALDURAZYME 2.9 MG/5 ML VIAL</td>
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<td>BRINUERA 150 MG/5 ML VIAL</td>
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<td>BUPHENYL 500 MG TAB</td>
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<td>CERDELGA 84 MG CAP</td>
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<td>ELAPRASE 6 MG/3 ML VIAL</td>
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<td>KANUMA 20 MG/10 ML VIAL</td>
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<td>NITISINONE 10 MG CAP</td>
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### Approval Criteria

**Initial Therapy:**
- Prescribed by or in consultation with an appropriate specialist in the treated disease state **AND**
- Documented diagnosis of adenosine deaminase severe combined immune deficiency (ADA-SCID): **Claim is for Revcovi **AND**

**Type of Criteria:**
- ☒ Increased risk of ADE
- ☐ Preferred Drug List
- ☒ Appropriate Indications
- ☐ Clinical Edit
- ☒ Databases + Prescriber-Supplied

### Setting & Population

- Drug class for review: Enzyme Deficiency, Select Agents
- Age range: All appropriate MO HealthNet participants

### Data Sources:
- ☒ Only Administrative Databases
- ☐ Clinical Edit

### Data Table

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<th>Item Description</th>
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- **Documented diagnosis of Gaucher disease:**
  - Claim is for Cerdelga, Cerezyme, Elelyso, Vpriv, or Zavesca **AND**
  - For Cerdelga and Zavesca: participant is aged at least 18 years
  - For generic Zavesca: documentation of reason why participant cannot utilize brand Zavesca
  - Initial approval for 6 months
- **Documented diagnosis of hereditary tyrosinemia type 1:**
  - Claim is for Orfadin or Nityr **AND**
  - Initial approval for 12 months
  - For Orfadin 20 mg capsule: documentation of reason why participant cannot utilize lower strength capsules
  - For Nityr: documentation of reason why participant cannot utilize Orfadin
- **Documented diagnosis of perinatal/infantile- and juvenile-onset hypophosphatasia (HPP):**
  - Diagnosis confirmed by:
    - Presence of a known pathogenic variant in the ALPL gene as detected by ALPL molecular genetic testing **OR**
    - Diagnosis supported by all of the following:
      - Radiographic imaging demonstrating skeletal abnormalities **AND**
      - Serum alkaline phosphatase (ALP) level below the gender- and age-specific reference range **AND**
      - Elevated tissue-nonspecific alkaline phosphatase substrate level **AND**
  - Disease onset prior to age 18 years **AND**
  - Participant has clinical manifestations of hypophosphatasia (i.e. skeletal abnormalities, respiratory problems, failure to thrive, rickets, etc.) **AND**
  - Claim is for Strensiq **AND**
  - Initial approval for 6 months
- **Documented diagnosis of late-infantile neuronal ceroid lipofuscinosis type 2 (CLN2), tripeptidyl peptidase 1 (TPP1) deficiency:**
  - Diagnosis confirmed by:
    - Deficient TPP1 enzyme activity in leukocytes, fibroblasts, or dried blood spots **OR**
    - Genetic testing confirming two pathogenic variants in the TPP1 or CLN2 genes **AND**
  - Claim is for Brineura **AND**
  - Participant has mild to moderate disease documented by a two-domain score of 3 to 6 on motor and language domains in the Hamburg CLN2 Clinical Rating Scale, with a score of at least 1 in each of these two domains **AND**
  - Participant is aged at least 3 years **AND**
  - Participant is ambulatory **AND**
  - Documentation of baseline Hamburg CLN2 Clinical Rating Scale score
  - Initial approval for 12 months
- **Documented diagnosis of lysosomal acid lipase deficiency:**
  - Claim is for Kanuma **AND**
  - Initial approval for 12 months
- **Documented diagnosis of mucopolysaccharidosis I (MPS I):**
  - Claim is for Aldurazyme **AND**
  - Initial approval for 12 months
- **Documented diagnosis of mucopolysaccharidosis II (MPS II):**
  - Claim is for Elaprase **AND**
  - Initial approval for 12 months
- **Documented diagnosis of mucopolysaccharidosis IVA (MPS IVA):**
  - Claim is for Vimzim **AND**
  - Participant is aged at least 5 years **AND**
  - Initial approval for 12 months
- **Documented diagnosis of mucopolysaccharidosis VI (MPS VI):**
  - Claim is for Naglazyme **AND**
Participant is aged at least 5 years AND
Initial approval for 12 months

Documented diagnosis of mucopolysaccharidosis VII (MPS VII):
• Claim is for Mepsevii AND
Initial approval for 12 months

Documented diagnosis of phenylketonuria:
• Claim is for Kuvan AND
Initial approval for 12 months

Documented diagnosis of plasminogen deficiency type 1:
• Diagnosis confirmed by:
  ▪ Baseline plasminogen activity level ≤ 45% AND
  ▪ Documented history of lesions (external and/or internal) and symptoms consistent with a diagnosis of plasminogen deficiency type 1 AND
  ▪ Genetic testing confirming pathogenic variant in PLG gene AND
• Claim is for Ryplazim AND
Initial approval for 12 months

Documented diagnosis of symptomatic pyruvate kinase deficiency:
• Diagnosis confirmed by:
  ▪ Documentation of genetic testing confirming presence of at least 2 variant alleles in the PKLR gene, of which at least 1 is a missense variant AND
• Documentation of previous red blood cell transfusions for hemolytic anemia in the past year AND
• Baseline hemoglobin level of ≤ 10 g/dL AND
• Claim is for Pyrukynd AND
Initial approval for 3 months

Documented diagnosis of urea cycle disorder:
• Diagnosis confirmed by enzymatic, biochemical, or genetic testing AND
• Claim is for Buphenyl or Ravicti AND
Initial approval for 3 months
• For Ravicti:
  ▪ Failure to achieve therapeutic response after minimum of 90 days of therapy with Buphenyl OR
  ▪ Documented ADE/ADR to Buphenyl

Continuation of Therapy:
• Compliance to prescribed drug therapy AND

For Brineura:
• Documentation of benefit of therapy demonstrated by stabilization or lack of decline in motor function based on the Motor domain of the Hamburg CLN2 Clinical Rating Scale (decline is defined as having an unreversed (sustained) 2-category decline or an unreversed score of 0 in the Motor domain of the CLN2 Clinical Rating Scale)
• Continued approval for 12 months

For Pyrukynd:
• Documentation of increase in hemoglobin of at least 1.5 g/dL from baseline OR
• Documentation of reduction in transfusion burden from baseline
• Continued approval for 12 months

For Strensiq:
• Documented benefit from therapy including one of the following:
  ▪ Improved respiratory status
  ▪ Improved growth from baseline
  ▪ Improvement of skeletal manifestations from baseline
  ▪ Lack of evidence of disease progression
• Continued approval for 12 months
### Denial Criteria

- Therapy will be denied if all approval criteria are not met
- For Brineura:
  - Participant has acute intraventricular access device-related complication
  - Participant has ventriculoperitoneal shunts
- For Buphenyl/Ravicti: medication is being used for the treatment of acute hyperammonemia
- For Pyrukynd:
  - Participant is currently pregnant
  - Documentation of moderate to severe hepatic disease
  - Claim exceeds 2 tablets per day
- For Ravicti: documentation of N-acetylglutamate synthase (NAGS) deficiency
- For Ryplazim: participant is currently pregnant

### Required Documentation

<table>
<thead>
<tr>
<th>Laboratory Results:</th>
<th>Progress Notes:</th>
<th>Other:</th>
</tr>
</thead>
<tbody>
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### Disposition of Edit

- Denial: Exception code “0682” (Clinical Edit)
- Rule Type: CE

### Default Approval Period

- 1 year

### References

- Ravicti® (glycerol phenylbutyrate) [package insert]. Lake Forest, IL: Horizon Therapeutics USA, Inc.; September, 2021.