Executive Summary

**Purpose:** Ensure appropriate utilization and control of agents for Sickle Cell Disease

**Why Issue Selected:** Sickle cell disease (SCD) is a genetic disorder that results in the formation of sickled red blood cells. SCD acutely presents with vascular occlusion, resulting in recurrent pain episodes, severe infections as a result of splenic infarction, acute chest syndrome, pulmonary hypertension, stroke, and cumulative multiorgan damage. These episodes are categorized as vaso-occlusive crises (VOC). Recurrent VOC cause an inflammatory response in the endothelium which ultimately leads to reduced blood flow, obstruction, and pain crises. SCD affects roughly 100,000 Americans and is one of the most common inherited blood disorders. Until recently, the only FDA approved therapies for SCD were hydroxyurea (Siklos® and Droxia®) and L-glutamine (Endari™). Hydroxyurea, a first-line therapy, reduces the incidence of acute painful episodes and hospitalization rates and prolongs survival. Hydrea® (hydroxyurea 500mg capsules) are not FDA approved for SCD and are not included in this edit. Endari was approved in 2017 to reduce acute complications in patients > 5 years of age with SCD; the mechanism is unknown but is thought to involve an antioxidant effect. In November 2019, the FDA approved two new therapies for SCD, Adakveo® (crizanlizumab-tcma) and Oxbryta™ (voxelotor). Adakveo, a humanized IgG2 kappa monoclonal antibody, is approved to reduce the frequency of VOC in patients 16 years and older. Oxbryta, a hemoglobin S polymerization inhibitor, is approved for the treatment of SCD in patients 12 years and older. Oxbryta was approved under accelerated approval based on an increase in hemoglobin; continued approval may be contingent upon verification and description of clinical benefit in confirmatory trials.

### Program-Specific Information:

<p>| Date Range FFS 1-1-2019 to 12-31-2019 |
|-------------------------------|---------------------|---------------------|---------------------|
| Drug                          | Claims | Spend    | Cost per unit     |
| Adakveo® 100mg/10ml vial      | 0      | -        | $234.77 per ml MAC |
| Droxia® 200mg capsule         | 13     | $623.25  | $0.75 per cap WAC |
| Droxia® 300mg capsule         | 61     | $3,469.65| $0.73 per cap NADAC |
| Droxia® 400mg capsule         | 93     | $5,974.34| $0.80 per cap WAC |
| Endari™ 5g powder packet      | 68     | $180,594.35| $19.15 per packet MAC |
| Oxbryta™ 500mg tablet         | 0      | -        | $115.28 per tab MAC |
| Siklos® 100mg tablet          | 0      | -        | $5.25 per tab WAC  |
| Siklos® 1,000mg tablet        | 0      | -        | $52.50 per tab WAC |</p>
<table>
<thead>
<tr>
<th>Drug</th>
<th>Cost per month</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adakveo®</td>
<td>$9,390.80</td>
<td>(4 vials for maintenance dosing every 4 weeks)</td>
</tr>
<tr>
<td>Droxia®</td>
<td>$166.50</td>
<td>(6 of 400mg &amp; 1 of 200mg caps once a day)</td>
</tr>
<tr>
<td>Endari™</td>
<td>$3,447.00</td>
<td>(3 packets 2 times a day)</td>
</tr>
<tr>
<td>Oxbryta™</td>
<td>$10,368.00</td>
<td>(3 tablets once a day)</td>
</tr>
<tr>
<td>Siklos®</td>
<td>$3,937.50</td>
<td>(2 &amp; 1/2 of 1,000mg tablet daily)</td>
</tr>
</tbody>
</table>

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

**Data Sources:**
- ☐ Only Administrative Databases
- ☒ Databases + Prescriber-Supplied

**Setting & Population**
- Drug class for review: Agents for Sickle Cell Disease
- Age range: All appropriate MO HealthNet participants aged 2 years or older

**Approval Criteria**
- Participant is aged ≥ 2 years **AND**
- Documented diagnosis of sickle cell disease in the past 2 years **AND**
- Prescribed by or in consultation with a hematologist or other appropriate specialist for the treated disease state **AND**
- Participant is not currently pregnant **AND**
- For Siklos (hydroxyurea tablets):
  - Documentation of inability to swallow oral capsule formulations of hydroxyurea due to participant age or clinical condition - approval based on Clinical Consultant Review
- For Endari (L-glutamine oral powder):
  - Participant is aged ≥ 5 years **AND**
  - For initial therapy:
    - Documentation of at least 2 sickle cell-related VOCs in the past year **AND**
    - Documentation of previous therapeutic trial (at least 3 months of therapy) or concurrent treatment, intolerance, insufficient response or contraindication with hydroxyurea
  - For renewal of prior authorization: Documentation of reduction in the number of sickle cell-related VOCs
- For Adakveo (crizanlizumab-tmca):
  - Participant is aged ≥ 16 years **AND**
  - For initial therapy:
    - Documentation of at least 2 sickle cell-related VOCs in the past year **AND**
    - Documentation of previous therapeutic trial (at least 3 months of therapy) or concurrent treatment, intolerance, insufficient response or contraindication with hydroxyurea
    - Initial approval of prior authorization is 12 months
  - For renewal of prior authorization: Documentation of reduction in the number of sickle cell-related VOCs
- For Oxbryta (voxelotor):
  - Participant is aged ≥ 12 years **AND**
  - For initial therapy:
    - Documentation of abnormal hemoglobin level > 5.5 to < 10.5 g/dL **AND**
    - Documentation of baseline indirect bilirubin **AND**
    - Documentation of baseline reticulocytes **AND**
    - Documentation of previous therapeutic trial (at least 3 months of therapy) or concurrent treatment, intolerance, insufficient response or contraindication with hydroxyurea
• Initial approval of prior authorization is 6 months
  o Renewal of prior authorization may be up to 12 months following documentation of the following:
    ▪ Documentation of increase in hemoglobin by > 1 g/dL from baseline to 24 weeks of therapy AND
    ▪ Documentation of reduction in indirect bilirubin from baseline AND
    ▪ Documentation of reduction in reticulocytes from baseline

**Denial Criteria**

• Therapy will be denied if no approval criteria are met

**Required Documentation**

<table>
<thead>
<tr>
<th>Laboratory Results:</th>
<th>X</th>
</tr>
</thead>
<tbody>
<tr>
<td>MedWatch Form:</td>
<td></td>
</tr>
<tr>
<td>Progress Notes:</td>
<td>X</td>
</tr>
<tr>
<td>Other:</td>
<td>X</td>
</tr>
</tbody>
</table>

**Disposition of Edit**

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

**Default Approval Period**

6 months

**References**

• SIKLOS (hydroxyurea) tablets. [package insert]. Bryn Mawr, PA: Medunik USA, Inc; May 2018.