Clinical Policy: Setmelanotide (Imcivree)
Reference Number: ERX.SPA.404
Effective Date: 11.25.20
Last Review Date: 02.21
Line of Business: Commercial, Medicaid

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Setmelanotide (Imcivree™) is melanocortin-4 receptor pathway activator.

FDA Approved Indication(s)
Imcivree is indicated for chronic weight management in adult and pediatric patients 6 years of age and older with obesity due to proopiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (LEPR) deficiency confirmed by genetic testing demonstrating variants in POMC, PCSK1, or LEPR genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance (VUS).

Limitation(s) of use: Imcivree is not indicated for the treatment of patients with the following conditions as Imcivree would not be expected to be effective:
- Obesity due to suspected POMC-, PCSK1-, or LEPR-deficiency with POMC, PCSK1, or LEPR variants classified as benign or likely benign
- Other types of obesity not related to POMC, PCSK1 or LEPR deficiency, including obesity associated with other genetic syndromes and general (polygenic) obesity

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Imcivree is medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Genetic Obesity Disorders (must meet all):
      1. Diagnosis of POMC-, PCSK1-, or LEPR-deficiency obesity;
      2. Prescribed by or in consultation an endocrinologist or expert in rare genetic disorders of obesity;
      3. Member meets one of the following (a or b):
         a. Age ≥ 6 and < 18 years with weight > 95th percentile for age on growth chart assessment (see Appendix D);
         b. Age ≥ 18 years of age and body mass index (BMI) ≥ 30 kg/m²;
      4. Genetic testing confirms that variants in the following genes are interpreted as pathogenic, likely pathogenic, or of uncertain significance (a, b, or c):
         a. POMC;
         b. PCSK1;
         c. LEPR;
      5. Documentation of baseline weight (in past 60 days) in kilograms;
      6. Documentation of creatinine clearance ≥ 60 mL/min/1.73 m²;
      7. If member has had prior gastric bypass surgery, member meets one of the following (a or b):
         a. Member has not had > 10% weight loss from baseline pre-operative weight;
         b. Member has regained weight after an initial response to surgery;
8. Documentation that member is actively enrolled in a weight loss program that involves a reduced calorie diet and increased physical activity adjunct to therapy;
9. Dose does not exceed the following (a and b):
   a. First 2 weeks (i or ii):
      i. Age ≥ 6 and < 18 years: 1 mg per day;
      ii. Age ≥ 18 years: 2 mg per day;
   b. Maintenance: 3 mg per day.

Approval duration:
New starts: 4 months
Maintenance: 6 months

B. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy
A. Genetic Obesity Disorders (must meet all):
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy as evidenced by one of the following (a, b, or c):
   a. After 12 weeks of treatment: reduction in weight compared with baseline;
   b. After 1 year: ≥ 10% reduction in weight compared with baseline;
   c. After > 1 year: maintenance of ≥ 10% reduction in weight compared with baseline;
3. If request is for a dose increase, new dose does not exceed 3 mg per day.

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2):
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.

Approval duration: Duration of request or 6 months (whichever is less);
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:
A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents;
B. Obesity disorders not caused by POMC-, PCSK1-, or LEPR-deficiency obesity;
C. Obesity disorder in patients with POMC, PCSK1, or LEPR genes variants that are interpreted as benign or likely benign.

IV. Appendices/General Information
Appendix A: Abbreviation/Acronym Key
BMI: body mass index
FDA: Food and Drug Administration
LEPR: leptin receptor
PCSK1: proprotein convertase subtilisin/kexin type 1
POMC: pro-opiomelanocortin

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: General Information
• Body mass index calculator: https://globalrph.com/medcalcs/body-mass-index-bmi/
CLINICAL POLICY
Setmelanotide

- CDC Clinical Growth Charts from 3rd to 97th percentiles:
  - 2 to 20 years: Boys Stature-for-age and Weight-for-age percentiles [https://www.cdc.gov/growthcharts/data/set2clinical/cj41c071.pdf]
  - 2 to 20 years: Girls Stature-for-age and Weight-for-age percentiles [https://www.cdc.gov/growthcharts/data/set2clinical/cj41c072.pdf]

V. Dosage and Administration

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<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
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<tr>
<td>POMC, PCSK1, LEPR deficiency obesity</td>
<td>≥ 12 years and older: 2 mg SC once daily for 2 weeks; if tolerated, titrate up to 3 mg SC once daily</td>
<td>3 mg/day</td>
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<tr>
<td>Age 6 to 12 years: 1 mg SC once daily for 2 weeks; if tolerated, titrate up to 3 mg SC once daily</td>
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VI. Product Availability

Vial: 10 mg/mL (1 mL multi-dose)

VII. References

Reviews, Revisions, and Approvals

<table>
<thead>
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<th>Policy created pre-emptively</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
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<tr>
<td>Drug is now FDA approved - criteria updated per FDA labeling: added PCSK1-deficiency obesity, revised lower age limit from 12 years to 6 years old; revised percentile for age on growth chart assessment from 97th to 95th percentile; clarified that genetic variants in POMC, PCSK1, and LEPR should be interpreted as pathogenic, likely pathogenic, or of uncertain significance; clarified that baseline documentation of weight be in kg; revised specialist requirement from bariatric physician to experts in rare genetic disorders of obesity; added creatinine clearance requirement for normal renal function or mild renal impairment; added criteria requiring documentation of weight loss program to align with other weight-loss agent policies; expanded initial approval duration from 12 weeks to 4 months; added in Section III that coverage will be excluded for obesity disorder in patients with POMC, PCSK1, or LEPR genes variants that are interpreted as benign or likely benign; references reviewed and updated.</td>
<td>01.05.21</td>
<td>02.21</td>
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Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.
This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.

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