Prior Authorization
Imcivree™ (setmelanotide subcutaneous injection)

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Product Identifier(s)
79811

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National Formulary Medical Necessity

Cigna covers setmelanotide (Imcivree™) as medically necessary when the following criteria are met for FDA Indications or Other Uses with Supportive Evidence:

Prior Authorization is recommended for prescription benefit coverage of Imcivree. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of individuals treated with Imcivree as well as the monitoring required for adverse events and long-term efficacy, approval requires Imcivree to be prescribed by or in consultation with a physician who specializes in the condition being treated.

FDA Indication(s)
1. Obesity Due to Proopiomelanocortin (POMC), Proprotein Convertase Subtilisin/Kexin Type 1 (PCSK1), or Leptin Receptor (LEPR) Deficiency. Approve for the duration noted if the individual meets the following criteria (A or B):
   A) Initial Therapy. Approve for 4 months if the individual meets the following criteria (i, ii, iii, and iv):
      i. Individual is ≥ 6 years of age; AND
      ii. Individual meets both of the following criteria (a and b):
         a) Genetic testing demonstrates homozygous or compound heterozygous mutations in one of the following genes: POMC, PCSK1, or LEPR; AND
b) The genetic variant is interpreted as pathogenic, likely pathogenic, or of uncertain significance; AND

iii. Individual meets one of the following criteria (a or b):
   a) Individual is ≥ 18 years of age: Individual currently has a body mass index (BMI) ≥ 30 kg/m²; OR
   b) Individual is 6 to 17 years of age: Individual currently has a BMI ≥ 95th percentile for age and sex; AND

iv. Imcivree is prescribed by or in consultation with an endocrinologist, a geneticist, or a physician who specializes in metabolic disorders.

B) Individual is currently receiving Imcivree. Approve for 1 year if the individual meets the following criteria:
   (Note: For individuals who have not completed at least 4 months of Imcivree therapy, refer to Initial Therapy criteria).
   i. Individual is ≥ 6 years of age; AND
   ii. Individual meets both of the following criteria (a and b):
      a) Genetic testing demonstrates homozygous or compound heterozygous mutations in one of the following genes: POMC, PCSK1, or LEPR; AND
      b) The genetic variant is interpreted as pathogenic, likely pathogenic, or of uncertain significance; AND
   iii. Individual meets one of the following criteria (a or b):
      a) Individual has lost ≥ 5% of baseline body weight since initiating Imcivree therapy; OR
      b) Individual meets both of the following (1 and 2):
         (1) Individual has continued growth potential; AND
         (2) Individual has lost ≥ 5% of baseline BMI since initiating Imcivree therapy; AND
   iv. Imcivree is prescribed by or in consultation with an endocrinologist, a geneticist, or a physician who specializes in metabolic disorders.

**Conditions Not Covered**

Setmelanotide (Imcivree™) is considered experimental, investigational or unproven for ANY other use including the following (this list may not be all inclusive):

1. **Other Genetic Obesity Syndromes.** (Note: Examples of genetic obesity syndromes include Prader-Willi syndrome, Bardet-Biedl syndrome, and Alström syndrome). Imcivree is not indicated for genetic obesity syndromes other than POMC-, PCSK1-, or LEPR-deficient obesity. Studies are currently underway in Bardet-Biedl and Alström syndromes.5

2. **General Obesity.** Imcivree is not indicated in this setting and there are no clinical data to support its use.1

**Background**

**Overview**

Imcivree, a melanocortin 4 receptor agonist, is indicated for chronic weight management in patients ≥ 6 years of age 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.1

As a limitation of use, Imcivree is not indicated for obesity due to suspected POMC, PCSK1, or LEPR deficiency with POMC, PCSK1, or LEPR variants classified as benign or likely benign.1 Imcivree is also not indicated for obesity not related to POMC, PCSK1, or LEPR deficiency, including obesity associated with other genetic syndromes and general (polygenic) obesity.

Weight loss should be evaluated after 12 to 16 weeks of Imcivree treatment.1 If a patient has not lost at least 5% of baseline body weight, or 5% of baseline body mass index for a patient with continued growth potential, Imcivree should be discontinued as it is unlikely that the patient will achieve and sustain clinically meaningful weight loss with continued treatment.
Disease Overview
Monogenic obesity is a rare and severe early-onset form of obesity. Unlike general obesity, environmental factors are much less impactful on obesity development in these patients. Fewer than 50 patients worldwide have been identified with POMC deficiency (POMC or PCSK1 mutations); the prevalence of LEPR deficiency is unknown but is expected to account less than 3% of severe early-onset obesity. The true prevalence of these disorders is unknown and likely underestimated due to lack of provider awareness and genetic testing. Clinical presentation is mainly characterized by major hyperphagia and ravenous hunger. Patients with these disorders experience very rapid and early increase in weight, occurring within the first few days of life to early childhood. Lifestyle interventions may provide initial weight loss but are very difficult to maintain long-term in this population due to constant, insatiable hunger. Isolated case reports of bariatric surgery have demonstrated some efficacy but are generally regarded as disappointing relative to the general population, likely related to the underlying energy imbalance. Caution is urged before considering bariatric surgery in patients with monogenic obesity disorders.

In the pivotal trial for Imcivree, eligible patients were ≥ 6 years of age with obesity due to POMC deficiency (homozygous or compound heterozygous variants in POMC or PCSK1) or LEPR deficiency (homozygous or compound heterozygous variants in LEPR). For patients 6 to < 18 years of age, obesity was defined as bodyweight > 95th percentile for age on growth chart assessment. For patients ≥ 18 years of age, obesity was defined as a BMI ≥ 30 kg/m².

References

Revision History

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<thead>
<tr>
<th>Type of Revision</th>
<th>Summary of Changes</th>
<th>Review Date</th>
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<tbody>
<tr>
<td>New Policy</td>
<td></td>
<td>01/06/2021</td>
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<tr>
<td>Selected Revision</td>
<td>Obesity Due to Proopiomelanocortin (POMC), Proprotein Convertase Subtilisin/Kexin Type 1 (PCSK1), or Leptin Receptor (LEPR) Deficiency: Geneticist was added to the list of prescribing or consulting specialists.</td>
<td>01/20/2021</td>
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