PRIOR AUTHORIZATION POLICY

POLICY: Metabolic Disorders – Imcivree Prior Authorization Policy
- Imcivree™ (setmelanotide subcutaneous injection – Rhythm Pharmaceuticals)

REVIEW DATE: 01/06/2021; selected revision 01/20/2021

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.[2] 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.[3] Clinical presentation is mainly characterized by major hyperphagia and ravenous hunger.[2] 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.[4] 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*).[3] 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/m^2.

POLICY STATEMENT

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 patients 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.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Imcivree is recommended in those who meet the following criteria:

FDA-Approved Indications

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 patient meets the following criteria (A or B):
   - **A)** Initial Therapy. Approve for 4 months if the patient meets the following criteria (i, ii, iii, and iv):
     - **i.** Patient is ≥ 6 years of age; AND
     - **ii.** Patient 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.** Patient meets one of the following criteria (a or b):
       - **a)** Patient is ≥ 18 years of age: Patient currently has a body mass index (BMI) ≥ 30 kg/m^2; OR
       - **b)** Patient is 6 to 17 years of age: Patient 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)** Patient is currently receiving Imcivree. Approve for 1 year if the patient meets the following criteria:
     (Note: For patients who have not completed at least 4 months of Imcivree therapy, refer to Initial Therapy criteria).
     - **i.** Patient is ≥ 6 years of age; AND
     - **ii.** Patient 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.** Patient meets one of the following criteria (a or b):
       - **a)** Patient has lost ≥ 5% of baseline body weight since initiating Imcivree therapy; OR
       - **b)** Patient meets both of the following (1 and 2):
         - **(1)** Patient has continued growth potential; AND
         - **(2)** Patient 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 RECOMMENDED FOR APPROVAL

Coverage of Imcivree is not recommended in the following situations:

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]

3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Imcivree™ subcutaneous injection [prescribing information]. Boston, MA: Rhythm Pharmaceuticals; November 2020.
2. Huvenne H, Dubern B, Clément K, Poitou C. Rare genetic forms of obesity: clinical approach and current treatments in 2016. *Obes Facts*. 2016;9(3):158-73.
3. Clément K, van den Akker E, Argente J, et al; setmelanotide POMC and LEPR Phase 3 Trial Investigators. Efficacy and safety of setmelanotide, an MC4R agonist, in individuals with severe obesity due to LEPR or POMC deficiency: single-arm, open-label, multicentre, phase 3 trials. *Lancet Diabetes Endocrinol*. 2020 Dec;8(12):960-970.
4. Poitou C, Mosbah H, Clément K. Mechanisms in endocrinology: update on treatments for patients with genetic obesity. *Eur J Endocrinol*. 2020 Nov;183(5):R149-R166.
5. Rhythm Pharmaceuticals. Our Pipeline. Available at: https://www.rhythmtx.com/our-pipeline/. Accessed on January 4, 2021.