IMCIVREE (SETMELANOTIDE) (REQUIRES PREAUTHORIZATION)

X.171

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DESCRIPTION

The intent of the setmelanotide prior authorization is to encourage appropriate use according to clinical trial data and FDA approved labeling.

IMCIVREE is a melanocortin 4 (MC4) receptor agonist 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).

Dates

Original Effective
05-26-2021
Last Review
11-06-2024
Next Review
11-10-2025

POLICY

Target Agent(s) will be approved when ALL of the following are met:

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OR

b. The prescriber has provided information in support of using the requested agent for the patient's age

AND

2. The patient has a diagnosis of obesity and ONE of the following:
   a. BOTH of the following:
      i. The patient has proopiomelanocortin (POMC) deficiency

      AND

      ii. Genetic testing has confirmed a mutation in the POMC gene (medical records required)

      OR

   b. BOTH of the following:
      i. The patient has proprotein convertase subtilisin/kexin type 1 (PCSK1) deficiency

      AND

      ii. Genetic testing has confirmed a mutation in the PCSK1 gene (medical records required)

      OR

   c. BOTH of the following:
      i. The patient has leptin receptor (LEPR) deficiency

      AND

      ii. Genetic testing has confirmed a mutation in the LEPR gene (medical records required)

      AND

3. ALL of the following:
   a. The patient's genetic status is bi-allelic, homozygous, or compound heterozygous (NOT double heterozygous)

   AND

   b. The patient's genetic variant is interpreted as pathogenic or likely pathogenic

   AND

   c. The patient's genetic variant is NOT classified as benign or likely benign or of uncertain significance (VUS)

   AND

4. ONE of the following:
   a. For adult patients, the body mass index (BMI) is ≥30 kg/m^2

   OR

   b. For pediatric patients, weight is ≥95^{th} percentile using growth chart assessments

   AND

5. ONE of the following:
   a. The patient is newly starting therapy

   OR

   b. The patient is currently being treated and has received less than 16 weeks (4 months) of therapy

   OR

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initiation of the requested agent)

OR

ii. For patients with continued growth potential, weight loss of ≥5% of baseline BMI (prior to the initiation of the requested agent)

AND

6. The prescriber is a specialist in the area of the patient's diagnosis (e.g., geneticist, metabolic disorders) or the prescriber has consulted with a specialist in the area of the patient's diagnosis

AND

7. The patient does NOT have any FDA labeled contraindications to the requested agent

AND

8. ONE of the following:

a. The requested quantity (dose) does NOT exceed the program quantity limit

OR

b. ALL of the following:

i. The requested quantity (dose) is greater than the program quantity limit

AND

i. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication

AND

ii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit

Length of Approval: 4 months

Renewal Evaluation

Target Agent(s) will be approved when ALL of the following are met:

1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process

AND

requested agent)

OR

b. For patients with continued growth potential, weight loss of ≥5% of baseline BMI (prior to the initiation of the requested agent)

AND

3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., geneticist, metabolic disorders) or the prescriber has consulted with a specialist in the area of the patient's diagnosis

AND

4. ONE of the following:

a. The requested quantity (dose) does NOT exceed the program quantity limit

OR

b. ALL of the following:

i. The requested quantity (dose) is greater than the program quantity limit

AND

i. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication

AND

ii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit

Length of Approval: 12 months

CLINICAL RATIONALE

There is a strong genetic component to human obesity. Most genes that influence an individual's predisposition to gain weight are not yet known. However, a glimpse into the long-term regulation of body weight has come from studying extreme human obesity caused by single gene defects. These monogenic (single-gene) obesity disorders have confirmed that the hypothalamic leptin-melanocortin system is critical for energy balance in humans because disruption of these pathways causes the most severe obesity phenotypes. Approximately

obesity can be divided into three broad categories; the category further discussed in this program is that which is caused by mutations in genes that have a physiologic role in the hypothalamic Leptin-Melanocortin system of energy balance. Obesity due to leptin receptor mutations, proopiomelanocortin mutations, and proprotein convertase mutations will be

addressed further here.[2,3]

Congenital leptin (LEP) and leptin receptor (LEPR) deficiency are rare, autosomal recessive disorders associated with severe obesity from a very young age (before 2 years). The clinical phenotypes associated with congenital leptin and leptin receptor deficiencies are similar. Patients are born of normal birth weight but exhibit rapid weight gain in the first few months of life resulting in severe obesity. Affected subjects are characterized by intense hyperphagia with food seeking behavior and aggression when food is denied.[4]

Leptin suppresses food intake in part by acting on hypothalamic neurons expressing POMC. People who are homozygous or compound heterozygous for loss of function mutations in the pro-opiomelanocortin gene, POMC, are hyperphagic and develop early-onset obesity due to loss of melanocortin signaling at the MC4R in the hypothalamus. In the pituitary, POMC is the precursor for adrenocorticotrophin (ACTH). As such, POMC deficiency presents in neonatal life with findings of secondary adrenal insufficiency: hypoglycemia, cholestatic jaundice, or other features of adrenal crisis requiring long-term corticosteroid replacement therapy.[2,4,5,6] Such children have pale skin, and white Caucasians have red hair, due to the lack of melanocortin function at melanocortin 1 receptors in the skin.[2,4,6] The prevalence of POMC is believed to be fewer than 10 patients worldwide.[2,3,5]

Prohormone convertase-1 (PCSK1, also known as PC1/3) is an enzyme that acts upon a range of substrates including proinsulin, proglucagon, and POMC. Compound heterozygous or homozygous mutations in

processing of proinsulin to insulin as well as severe, early onset obesity.[4] The prevalence of PCSK1 deficiency is believed to be fewer than 20 patients worldwide.[3]

Rhythm Pharmaceuticals has started a registry for patients with certain rare genetic disorders of obesity, and their “Uncovering Rare Obesity Program” offers free genetic testing in the United States for patients of all ages.

Setmelanotide is an MC4 receptor agonist with 20-fold less activity at the melanocortin 3 (MC3) and melanocortin 1 (MC1) receptors. MC4 receptors in the brain are involved in regulation of hunger, satiety, and energy expenditure.[1,5] In patients with obesity due to POMC, PCSK1, and LEPR deficiency associated with insufficient activation of the MC4 receptor, setmelanotide may re-establish MC4 receptor pathway activity to reduce hunger and promote weight loss through decreased caloric intake and increased energy expenditure.[1,6]

The safety and efficacy of setmelanotide for chronic weight management in patients with obesity due to POMC, PCSK1, and LEPR deficiency were assessed in 2 identically designed, 1-year, open-label studies, each with an 8-week, double-blind withdrawal period. Study 1 (NCT02896192) enrolled patients aged 6 years and above with obesity and genetically confirmed or suspected POMC or PCSK1 deficiency, and Study 2 (NCT03287960) enrolled patients aged 6 years and above with obesity and genetically confirmed or suspected LEPR deficiency. In Study 1, 80% of patients with obesity due to POMC or PCSK1 deficiency met the primary endpoint, achieving a ≥10% weight loss after 1 year of treatment. In Study 2, 46% of patients with obesity due to LEPR deficiency achieved a ≥10% weight loss after 1 year of treatment.[1]

Safety

Setmelanotide contains the following Black Box Warnings: none

Quick Code Search

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Please type a procedure code

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Diagnosis

Please type a diagnosis code

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REVISIONS

12-05-2023
Policy reviewed at Medical Policy Committee meeting on 11/8/2023 – no changes to policy


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