Applicable Drugs: Imcivree (setmelanotide)

Preferred: N/A

VSI-Excluded Drugs: Imcivree (setmelanotide)

Date of Origin: 8/18/2025

Date Last Reviewed / Revised: 8/6/2026

PRIOR AUTHORIZATION CRITERIA

(May be considered medically necessary when criteria I through V are met)

I. Documented diagnosis of one of the following conditions A or B AND must meet all criteria listed under the applicable diagnosis:

A. Obesity due to Bardet-Biedl syndrome (BBS), Pro-opiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (LEPR) deficiency and must meet ALL of the following criteria i–iii:

i. Diagnosis confirmed by FDA-approved genetic testing.

1. Genetic testing must demonstrate variant(s) in POMC, PCSK1, or LEPR gene(s) that are interpreted as pathogenic, likely pathogenic, or of uncertain significance (VUS).

ii. Obesity is defined as:

1. Age 16 and older: baseline BMI ≥ 30 kg/m^2.
2. Age 2-15 years: BMI in ≥ 95th percentile for age and sex.

iii. Minimum patient age: 2 years.

B. Acquired hypothalamic obesity (HO) and must meet ALL of the following criteria i–iii:

i. Diagnosis confirmed by all of the following:

1. Documentation of a structural lesion, injury, or intervention involving the hypothalamic-pituitary region (e.g., tumor, neurosurgery, cranial irradiation, vascular injury, inflammation, etc.) supported by MRI or other neuroimaging.
2. Rapid, clinically significant weight gain within 12 months of the hypothalamic injury (≥1.0 BMI SDS increase in pediatric patients or ≥5% BMI increase in adults), with persistent obesity despite appropriate management and no alternative cause for the weight gain.

ii. Obesity is defined as:

1. Age 16 and older: baseline BMI ≥ 30 kg/m^2.
2. Age 2-15 years: BMI in ≥ 95th percentile for age and sex.

iii. Minimum patient age: 4 years

II. Documented (health care provider attestation) trial of reduced-calorie diet (approximately 500 kcal/day deficit) and exercise plan (recommended increase in physical activity of a minimum 150 minutes per week) for at least 3 months.

III. Documentation that the requested medication will be used as an adjunct to a reduced-calorie diet and exercise plan, as described in criterion II.

IV. Requested medication is prescribed by an endocrinologist or geneticist.

V. Refer to plan document for the list of preferred products. If requested agent is not listed as a preferred product, must have a documented failure, intolerance, or contraindication to the preferred product(s).

EXCLUSION CRITERIA

- Obesity due to suspected POMC, PCSK1, or LEPR deficiency with POMC, PCSK1, or LEPR variants classified as benign or likely benign.
- Untreated endocrine disorders that could account for weight gain (eg, uncontrolled hypothyroidism, uncontrolled Cushing syndrome, etc.)
- Use for other types of obesity not related to acquired HO, BBS, or POMC, PCSK1, or LEPR deficiency, including obesity associated with other genetic syndromes and general (polygenic) obesity.
- End-stage renal disease (eGFR < 15).

QUANTITY / DAYS SUPPLY RESTRICTIONS

- Age 6 years and older: 9 mL per 30 days
- Age 2 to 6 years:
    - 15–20 kg: 2 mL per 30 days
    - 20–30 kg: 3 mL per 30 days
    - 30–40 kg: 5 mL per 30 days
    - ≥40 kg: 6 mL per 30 days

APPROVAL LENGTH

- **Authorization:** 6 months
- **Re-Authorization:** 6 months. Requires an updated letter of medical necessity or progress notes confirming the medication is effective and well tolerated. Efficacy is defined as ≥5% weight reduction from baseline at 6 months, ≥10% at 12 months, or sustained ≥10% reduction beyond 12 months. Patient adherence must be documented, along with current weight and BMI.

REFERENCES

1. Imcivree [Prescribing Information], Boston, MA; Rhythm Pharmaceuticals, Inc.; Updated March 2026. https://rhythmtx.com/IMCIVREE/prescribing-information.pdf
2. Clement, K, et. al., 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;8(12):960-970. DOI:10.1016/S2213-8587(20)30364-8
3. Dollfus, H, et. al., Bardet-Biedl syndrome improved diagnosis criteria and management: Inter European Reference Networks consensus statement and recommendations. *Eur J Hum Genet*. 2024;32:1347-1360. DOI: 10.1038/s41431-024-01634-7
4. Haqq, AM, et. al., Efficacy and safety of setmelanotide, a melanocortin-4 receptor agonist, in patients with Bardet-Biedl syndrome and Alström syndrome: a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial with an open-label period. *Lancet Diabetes Endocrinol*. 2022;10(12): 859-868. DOI:10.1016/S2213-8587(22)00277-7
5. Müller HL, Tanaka T, Hasegawa T, et. al. Diagnostic criteria for acquired hypothalamic obesity: international expert guidance document. *Endocr J*. 2026;73(2):341-353. DOI:10.1507/endocrj.EJ25-0408
6. Trapp, CM, et. al., Setmelanotide: a promising advancement for pediatric patients with rare forms of genetic obesity. *Curr Opin Endocrinol Diabetes Obes*. 2023;30(2):136-140. DOI:10.1097/MED.0000000000000798

DISCLAIMER: Medication Policies are developed to help ensure safe, effective and appropriate use of selected medications. They offer a guide to coverage and are not intended to dictate to providers how to practice medicine. Refer to Plan for individual adoption of specific Medication Policies. Providers are expected to exercise their medical judgement in providing the most appropriate care for their patients.