Generic Name: setmelanotide

Brand Name: Imcivree™

Preferred: N/A

VSI-Excluded Drugs: Imcivree™ (setmelanotide)

Date of Origin: 8/18/2025

Date Last Reviewed / Revised: N/A

PRIOR AUTHORIZATION CRITERIA

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

I. Documented diagnosis of 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:

   A. Diagnosis confirmed by FDA-approved genetic testing.

      i. Demonstrated variant(s) in POMC, PCSK1, or LEPR gene(s) interpreted as pathogenic, likely pathogenic, or of uncertain significance (VUS).

   B. Obesity is defined as:

      i. Age 16 and older: baseline BMI ≥ 30 kg/m^2.

      ii. Age 2-15 years: BMI in ≥ 95th percentile for age and sex.

II. Minimum patient age: 2 years.

III. 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.

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

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

VI. 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.
- Use for other types of obesity not related to BBS or POMC, PCSK1, or LEPR deficiency, including obesity associated with other genetic syndromes and general (polygenic) obesity.
- End-stage renal disease (eGFR < 15).

Other Criteria

Recommended Dosing Schedule

- Adults & Children ≥12 years:
  - Start at 2 mg (0.2 mL) SC daily for 2 weeks.
  - If tolerated, titrate to 3 mg (0.3 mL) daily (maintenance dose).
- Children 6–12 years:
  - Start at 1 mg (0.1 mL) SC daily for 2 weeks.
  - If tolerated, titrate to 2 mg (0.2 mL) daily for 2 weeks.
  - If tolerated, titrate to 3 mg (0.3 mL) daily (maintenance dose).
- Children 2–6 years:
  - Start at 0.5 mg (0.05 mL) SC daily for 2 weeks.
  - If tolerated, titrate to maintenance dose daily based on body weight:
    - 15–20 kg: 0.5 mg (0.05 mL)
    - 20–30 kg: 1 mg (0.1 mL)
    - 30–40 kg: 1.5 mg (0.15 mL)
    - ≥40 kg: 2 mg (0.2 mL)
- In patients with severe renal impairment (eGFR 15-29), additional dose reduction is required.

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.

APPENDIX

N/A

REFERENCES

1. Imcivree™ [Prescribing Information], Boston, MA; Rhythm Pharmaceuticals, Inc.; Updated March 2025. https://rhythmtx.com/IMCIVREE/prescribing-information.pdf
2. 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
3. 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
4. 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
5. 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