Clinical Policy: Setmelanotide (Imcivree)

Reference Number: PA.CP.PHAR.491
Effective Date: 11/2022
Last Review Date: 01/2025

Description
Setmelanotide (Imcivree®) is melanocortin-4 receptor pathway activator.

FDA Approved Indication(s)
Imcivree is indicated for chronic weight management in adult and pediatric patients 6 years of age and older with monogenic or syndrome 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)
- Bardet-Biedl syndrome (BBS)

Limitation(s) of use: Imcivree is not indicated for the treatment of patients with the following conditions as Imcivree would not be expected to be effective:

- Obesity due to suspected POMC, PCSK1, or LEPR deficiency with POMC, PCSK1, or LEPR variants classified as benign or likely benign
- Other types of obesity not related to POMC, PCSK1 or LEPR deficiency, or BBS, including obesity associated with other genetic syndromes and general (polygenic) obesity

Policy/Criteria
It is the policy of PA Health & Wellness that Imcivree is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Genetic Obesity Disorders (must meet all)**:**

1. Diagnosis of obesity due to POMC deficiency, PCSK1 deficiency, LEPR deficiency, or BBS (*see Appendix D*);
2. Prescribed by or in consultation with an endocrinologist or expert in rare genetic disorders of obesity;
3. Member meets one of the following (a or b):
   a. Age ≥ 6 and < 18 years with one of the following weight percentiles for age on growth chart assessment (*see Appendix D*) (i or ii):
      i. POMC, PCSK1, or LEPR deficiency: ≥ 95th percentile;
      ii. BBS:≥ 97th percentile;
   b. Age ≥ 18 years of age and body mass index (BMI) ≥ 30 kg/m^2;
4. One of the following (a or b):
   a. Genetic testing confirms that variants in the following genes are interpreted as pathogenic, likely pathogenic, or of uncertain significance (i, ii, or iii):
      i. POMC;
      ii. PCSK1;
      iii. LEPR;
   b. Diagnosis of BBS is confirmed clinically per Beales criteria or genetic testing

(*see Appendix D*);
5. Documentation of baseline weight (in past 60 days) in kilograms;
6. Documentation of creatinine clearance ≥ 15 mL/min/1.73 m^2;
7. If member has had prior gastric bypass surgery, member meets one of the following (a or b):
   a. Member has not had > 10% weight loss from baseline pre-operative weight;
   b. Member has regained weight after an initial response to surgery;
8. Member has documentation of counseling regarding lifestyle changes and behavioral modification (e.g., healthy diet and increased physical activity);
9. Dose does not exceed the following (a and b):
   a. First 2 weeks (i or ii):
      i. Age ≥ 6 and < 12 years: 1 mg per day;
      ii. Age ≥ 12 years: 2 mg per day;
   b. Maintenance: 3 mg per day.

Approval duration: 12 months

B. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

A. Genetic Obesity Disorders (must meet all)**:**
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy as evidenced by one of the following (a or b):
   a. Initial re-authorization: After 1 year of treatment, reduction of at least 5% of baseline body weight or 5% of baseline BMI;
   b. Subsequent re-authorizations for all indications: Maintenance of ≥ 5% reduction in weight or BMI compared with baseline;
3. If request is for a dose increase, new dose does not exceed 3 mg per day.

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care Policy (PA.PHARM.01) applies; or
   Approval duration: 6 months;
   or
2. Refer to PA.CP.PMN.53

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53;

B. Obesity disorders not caused by POMC, PCSK1, or LEPR deficiency or by BBS;

C. Obesity disorder in patients with POMC, PCSK1, or LEPR gene variants that are interpreted as benign or likely benign.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

BBS: Bardet-Biedl syndrome
BMI: body mass index
FDA: Food and Drug Administration
LEPR: leptin receptor
PCSK1: proprotein convertase subtilisin/kexin type 1
POMC: pro-opiomelanocortin
VUS: variant of uncertain significance

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): hypersensitivity to setmelanotide or any of its excipients
- Boxed warning(s): none reported

Appendix D: General Information

- Body mass index calculator: https://globalrph.com/medcalcs/body-mass-index-bmi/
- CDC Clinical Growth Charts from 3rd to 97th percentiles:
  - 2 to 20 years: Boys Stature-for-age and Weight-for-age percentiles https://www.cdc.gov/growthcharts/data/set2clinical/cj41c071.pdf
  - 2 to 20 years: Girls Stature-for-age and Weight-for-age percentiles https://www.cdc.gov/growthcharts/data/set2clinical/cj41c072.pdf
- A clinical diagnosis of BBS is confirmed using Beales criteria. There must be presence of at least 4 primary features, OR 3 primary and 2 secondary features:
  - Primary features: rod-cone dystrophy, polydactyly, obesity, learning disabilities, hypogonadism in males, renal anomalies
  - Secondary features: speech disorder/delay, strabismus/cataracts/astigmatism, brachydactyly/syndactyly, developmental delay, polyuria/polydipsia (nephrogenic diabetes insipidus), ataxia/poor coordination/imbalance, mild spasticity (especially lower limbs), diabetes mellitus, dental crowding/hypodontia/small roots/high arched palate, left ventricular hypertrophy/congenital heart disease, hepatic fibrosis

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Obesity due to POMC, PCSK1, or LEPR deficiency or due to BBS	≥ 12 years and older: 2 mg SC once daily for 2 weeks; if tolerated, titrate up to 3 mg SC once daily Age 6 to 12 years: 1 mg SC once daily for 2 weeks; if tolerated, titrate up to 3 mg SC once daily	3mg/day

VI. Product Availability

Vial: 10 mg/mL (1 mL multi-dose)

VII. References

1. Imcivree Prescribing Information. Boston, MA: Rhythm Pharmaceuticals, Inc.; November 2023. Available at: https://www.imcivree.com/. Accessed October 22, 2024.
2. Styne DM, Arslanian SA, Conner EL, et al. Pediatric Obesity: Assessment, Treatment, and Prevention: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2017; 102: 709–757.
3. Clement K, van den Akker E, Argente J, et al. Efficacy and safety of setmelanotide, an MC4R agonist, in individuals with severe obesity due to LEPR or POMN deficiency: single-arm, open-label, multicenter, phase 3 trials. Lancet Diabetes Endocrinol. 2020; 8: 960-70. DOI: 10.1016/S2213-8587(20)30364-8.
4. Haws RM, Gordon G, Han JC, et al. The efficacy and safety of setmelanotide in individuals with Bardet-Biedl syndrome or Alström syndrome: Phase 3 trial design. Contemporary Clinical Trials Communications. 2021; 22: 100780.
5. Hampl SE, Hassink SG, Skinner AC, et al. Clinical Practice Guideline for the Evaluation and Treatment of Children and Adolescents With Obesity. Pediatrics. 2023 Feb 1;151(2):e2022060640. doi: 10.1542/peds.2022-060640. PMID: 36622115.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
C9399	Unclassified drugs or biologicals
J3490	Unclassified drugs

Reviews, Revisions, and Approvals	Date
Policy created	10/2022
1Q 2023 annual review: no significant changes; references reviewed and updated.	01/2023
1Q 2024 annual review: no significant changes; references reviewed and updated.	01/2024
1Q 2025 annual review: updated contraindications section to include hypersensitivity to setmelanotide or any of its excipients per PI; references reviewed and updated.	01/2025