Clinical Policy: Setmelanotide (Imcivree)

Reference Number: LA.PHAR.491
Effective Date:
Last Review Date: 07.21.23
Line of Business: Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Please note: This policy is for medical benefit

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
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of Louisiana Healthcare Connections® 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 (*see Appendix D*);
5. Documentation of baseline weight (in past 60 days) in kilograms;
6. Documentation of estimated Glomerular Filtration Rate (eGFR) ≥ 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. Documentation that member is actively enrolled in a weight loss program that involves a reduced calorie diet and increased physical activity adjunct to therapy;
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:
POMC, PCSK1, or LEPR deficiency – 4 months
BBS – 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: LA.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Currently receiving medication via Louisiana Healthcare Connections benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy as evidenced by one of the following (a, b, or c):

a. Initial re-authorization for POMC, PCSK1, or LEPR deficiency: After 12-16 weeks of treatment, reduction of at least 5% of baseline body weight or 5% of baseline BMI;
b. Initial re-authorization for BBS: After 1 year of treatment, reduction of at least 5% of baseline body weight or 5% of baseline BMI;
c. 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. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: LA.PMN.53 for Medicaid.

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 – LA.PMN.53 for Medicaid or evidence of coverage documents;
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
eGFR: estimated glomerular filtration rate
FDA: Food and Drug Administration
LEPR: leptin receptor
PCSK1: proprotein convertase subtilisin/kexin type 1
POMC: pro-opiomelanocortin

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

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 injected subcutaneously once daily for 2 weeks; if tolerated, titrate up to 3 mg SC once daily Age 6 to < 12 years: 1 mg injected subcutaneously once daily for 2 weeks; if tolerated, titrate up to 3 mg injected subcutaneously once daily	3 mg/day

VI. Product Availability

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

VII. References

1. Imcivree Prescribing Information. Boston, MA: Rhythm Pharmaceuticals, Inc.; June 2022. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/213793s001lbl.pdf. Accessed July 21, 2023.
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.

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	LDH Approval Date
Policy created	05.01.23	
Updated the ages for dose maximums. Reviewed and updated references.	07.21.23	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing

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The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. LHCC retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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