Imcivree (setmelanotide)

Override(s)	Approval Duration
Prior Authorization Quantity Limit	**Initial authorization for POMC/PCSK1/LEPR deficiency:** 16 weeks **Initial authorization for BBS:** 1 year **Subsequent authorization all diagnoses**: 6 months

Medications	Quantity Limit
Imcivree 10 mg/mL multi-dose vial	May be subject to quantity limit

APPROVAL CRITERIA

Initial requests for Imcivree (setmelanotide) for Proopiomelanocortin (POMC), Proprotein convertase subtilisin/kexin type 1 (PCSK 1), or Leptin receptor (LEPR) deficiency (POMC/PCSK1/LEPR) deficiency may be approved if the following criteria are met:

I. Individual is 2 years of age or older; **AND**
II. Documentation is provided that individual has a diagnosis of obesity, defined as:
    A. BMI of 30 kg/m^2 or greater for adults; **OR**
    B. Bodyweight of more than the 95th percentile for age on growth chart assessment for individuals aged 6 to 17 years; **OR**
    C. Baseline BMI greater than or equal to the 97th percentile for age and sex, and body weight of at least 20 kg for individuals aged 2-5 years;

AND

III. Documentation is provided that obesity is due to POMC, PCSK 1, or LEPR deficiency, confirmed by genetic testing; **AND**
IV. Genetic testing demonstrating variants in POMC, PCSK1, or LEPR genes that are pathogenic, likely pathogenic, or of uncertain significance; **AND**
V. Individual is NOT receiving two medications for weight loss at the same time.

Initial requests for Imcivree (setmelanotide) for Bardet-Biedl syndrome (BBS) may be approved if the following criteria are met:

I. Individual is 2 years of age or older; **AND**
II. Documentation is provided that individual has a diagnosis of obesity, defined as:
    A. BMI of 30 kg/m^2 or greater for individuals 16 years of age and above; **OR**
    B. Bodyweight of more than the 97th percentile for age on growth chart assessment for individuals aged 6-15 years; **OR**

C. Baseline BMI greater than or equal to the 97th percentile for age and sex, and body weight of at least 20 kg for individuals aged 2-5 years;

AND

III. Obesity is due to BBS, as defined by one of the following [A or B] (Haws 2021):
   A. Four (4) primary features of BBS:
      1. Primary Features:
         a. Rod-cone dystrophy
         b. Polydactyly
         c. Obesity
         d. Learning disabilities
         e. Hypogonadism in males
         f. Renal anomalies;

      OR

   B. Three (3) primary features [above] **AND** 2 secondary features of BBS:
      1. Secondary Features:
         a. Speech disorder/delay
         b. Strabismus/cataracts/astigmatism
         c. Brachydactyly/syndactyly
         d. Developmental delay
         e. Polyuria/polydipsia (nephrogenic diabetes insipidus)
         f. Ataxia/poor coordination/imbalance
         g. Mild spasticity (especially lower limbs)
         h. Diabetes mellitus
         i. Dental crowding/hypodontia/small roots/high arched palate
         j. Left ventricular hypertrophy/congenital heart disease
         k. Hepatic fibrosis;

AND

IV. For individuals less than 6 years old, genetic testing demonstrates homozygous or compound heterozygous loss-of-function variants in BBS genes; **AND**

V. Individual is NOT receiving two medications for weight loss at the same time.

Requests for subsequent authorization for Imcivree (setmelanotide) may be approved if the individual meets ALL of the following criteria:

I. Documentation is provided that individual has achieved/maintained weight loss of at least 5% of baseline body weight or 5% of baseline BMI for patients with continued growth potential; **AND**

II. Individual is NOT receiving two medications for weight loss at the same time.

Requests for Imcivree (setmelanotide) may not be approved for any of the following:

I. Obesity with POMC, pCSK1, or LEPR variants classified as benign or likely benign (for POMC/PCSK1/LEPR deficiency requests); **OR**

II. Individual has end stage renal disease (eGFR less than 15 mL/min/1.73 m^2); **OR**

III. Individual is 2 years of age to less than 6 years of age with weight less than 20 kilograms with severe renal impairment (eGFR 15-29 mL/min/1.73 m^2); **OR**

IV. Individual has a history of suicide attempts or has active suicidal ideation; **OR**
V. When the above criteria are not met and for all other indications.

Key References:

1. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm.
2. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
3. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2025; Updated periodically.
4. Argente J, Verge CF, Okorie U, et al. Setmelanotide in patients aged 2-5 years with rare MC4R pathway-associated obesity (VENTURE): a 1 year, open-label, multicenter, phase 3 trial. *Lancet Diabetes Endocrinol*. 2025;13(1):29-37. doi:10.1016/S2213-8587(24)00273-0.
5. Clément 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 POMC deficiency: single-arm, open-label, multicentre, phase 3 trials. *Lancet Diabetes Endocrinol*. 2020 Dec;8(12):960-970. doi: 10.1016/S2213-8587(20)30364-8. Epub 2020 Oct 30. PMID: 33137293.
6. Haqq AM, Chung WK, Dollfus H, 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 [published correction appears in Lancet Diabetes Endocrinol. 2023 Feb;11(2):e2. doi: 10.1016/S2213-8587(22)00360-6.]. *Lancet Diabetes Endocrinol*. 2022;10(12):859-868. doi:10.1016/S2213-8587(22)00277-7.
7. Haws RM, Gordon G, Han JC, et al. The efficacy and safety of setmelanotide in individuals with Bardet-Biedl syndrome or Alstrom syndrome: Phase 3 trial design. Contemp Clin Trials Commun. 2021 May 3; 22:100780.
8. "About Child & Teen BMI." *Centers for Disease Control and Prevention*, Centers for Disease Control and Prevention, 29 June 2020, www.cdc.gov/healthyweight/assessing/bmi/childrens_bmi/about_childrens_bmi.html.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.