SmartPA Criteria Proposal

Drug/Drug Class:	Imcivree Clinical Edit
First Implementation Date:	November 18, 2021
Revised Date:	August 3, 2023
Prepared for:	MO HealthNet
Prepared by:	MO HealthNet/Conduent
Criteria Status:	☒Existing Criteria ☐Revision of Existing Criteria ☐New Criteria

Executive Summary

Purpose: Ensure appropriate utilization and control of Imcivree™ (setmelanotide)

Why Issue Selected: In November of 2020, Imcivree™ (setmelanotide) was FDA approved for chronic weight management in adult and pediatric patients 6 years of age and older with obesity due to proopiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (LEPR) deficiency confirmed by genetic testing demonstrating variants that are interpreted as pathogenic, likely pathogenic, or of uncertain significance (VUS). Deficiencies in POMC, PCSK1, and LEPR, which are ultra-rare and underdiagnosed, are caused by variants in *POMC*, *PCSK1* or *LEPR* genes and impair the MC4 receptor pathway in the hypothalamus. This pathway is responsible for regulating hunger and energy expenditure. Patients with these deficiencies experience symptoms such as extreme hunger and subsequent weight gain manifesting in morbid obesity, often as early as infancy. These patients can also experience many comorbid disorders of the endocrine system like adrenal insufficiency, hypothyroidism, and hypogonadism. Imcivree is a melanocortin-4 receptor (MC4R) agonist that is intended to partially or completely restore signaling at the MC4 receptor, thus directly impacting the cause of the obesity. Until the approval of Imcivree, there were no other FDA-approved treatment alternatives that target the underlying cause of obesity in this patient population. In June of 2022, Imcivree gained FDA-approval for the indication of chronic weight management in adult and pediatric patients aged 6 years and older with obesity due to Bardet-Biedl syndrome.

Due to the high cost and specific approved indication, MO HealthNet will impose clinical criteria to ensure appropriate utilization of Imcivree.

Program-Specific Information:

Date Range FFS 1-1-2022 to 12-31-2022			
Drug	**Claims**	**Spend**	**Avg Spend per Claim**
IMCIVREE 10 MG/ML VIAL	6	$158,453.10	$26,408.85

Type of Criteria:
☐ **Increased risk of ADE**
☒ **Appropriate Indications**
☐ **Preferred Drug List**
☒ **Clinical Edit**

Data Sources:
☐ **Only Administrative Databases**
☒ **Databases + Prescriber-Supplied**

Setting & Population

- Drug class for review: Imcivree™ (setmelanotide)
- Age range: All appropriate MO HealthNet participants aged 6 years or older

Approval Criteria

Initial Therapy:

- Prescribed by or in consultation with an appropriate specialist for the treated disease state **AND**
- Participant is 6 years of age or older **AND**
- Participant has a diagnosis of obesity, defined as:
  - ≥ 95th percentile using growth chart assessments for participants with continued growth potential **OR**
  - BMI of ≥ 30 kg/m^2 **AND**
- Documentation that obesity is due to diagnosis of Bardet-Biedl Syndrome (BBS) confirmed by presence of four primary features associated with BBS OR three primary features plus two secondary features:
  - Primary features associated with BBS:
    - Rod-cone dystrophy
    - Polydactyly
    - Obesity
    - Learning disabilities
    - Hypogonadism in males
    - Renal abnormalities
  - Secondary features associated with BBS:
    - 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 **OR**
- Documentation that obesity is due to a homozygous or presumed compound heterozygous variant in at least one of the following genes, confirmed by genetic testing:
  - Proopiomelanocortin (*POMC*)
  - Proprotein convertase subtilisin/kexin type 1 (*PCSK1*)
  - Leptin receptor (*LEPR*) **AND**
- Documentation of genetic testing demonstrating that the variants in *POMC*, *PCSK1*, or *LEPR* genes are interpreted as pathogenic or likely pathogenic

Continuation of Therapy:

- Initial approval is for 4 months, renewal of prior authorization may be given following documentation of the following:
  - Documentation of benefit of therapy, as evidenced by:
    - At least a 5% reduction in baseline body weight **OR**
    - At least a 5% reduction in baseline BMI for participants with continued growth potential **AND**
  - Documentation of compliance to therapy (90 out of 120 days)

Denial Criteria

- Therapy will be denied if all approval criteria are not met
- Documented history of moderate to severe renal impairment or end stage renal disease
- Prior gastric bypass surgery resulting in > 10% weight loss that was maintained
- For obesity due to *POMC*, *PCSK1*, or *LEPR* deficiency: documentation of genetic testing demonstrating that the variants in *POMC*, *PCSK1*, or *LEPR* genes are interpreted as benign or likely benign
- Participant demonstrates non-compliance to therapy regimen
- Documented diagnosis of Alport syndrome
- Participant is currently pregnant

Required Documentation

Laboratory Results:	X	Progress Notes:	X
MedWatch Form:		Other:	X

Disposition of Edit

Denial: Exception code “0682” (Clinical Edit)
Rule Type: CE

Default Approval Period

4 months

References

- IMCIVREE (setmelanotide) [package insert]. Boston, MA: Rhythm Pharmaceuticals, Inc.; June 2022.
- 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;8(12):960-970. doi:10.1016/S2213-8587(20)30364-8.
- Richards S, Aziz N, Bale S, et al; ACMG Laboratory Quality Assurance Committee. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genet Med. 2015;17(5):405-424. doi:10.1038/gim.2015.30.
- IPD Analytics. New Drug Review: Imcivree (setmelanotide). December 2020.
- Beales P, Elcioglu N, Woolf A, et al. New criteria for improved diagnosis of Bardet-Biedl syndrome: results of a population survey. J Med Genet. 1999 Jun;36(6):437-46. PMID: 10874630; PMCID: PMC1734378.