October 27, 2022

Dear Members of the Iowa Pharmacy &
Therapeutics Committee:

We write today to urge you to add Imcivree (setmelanotide) as a specialty medication available by prior authorization on the Iowa Medicaid preferred drug list (PDL) for the FDA approved indications of Bardet-Biedl syndrome (BBS), proopiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1) or leptin receptor (LEPR) deficiency.

These disease states are so rare that only about 50 cases of POMC deficiency have been reported in medical literature[1], BBS is estimated to occurs at a rate of approximately 1 in 100,000 in the United States, and LEPR deficiency has only identified less than 90 patients worldwide as of 2020.[2]

Currently, there are no other FDA approved treatment options for any of these rare genetic conditions caused by an impaired MC4R (melanocortin 4 receptor) pathway, nor any effective non-FDA approved treatment options. MC4R receptors in the brain are involved in the regulation of hunger, satiety, and energy expenditure. Patients with rare homozygous or biallelic variants in POMC, PCSK1 or LEPR have disrupted signaling in the MC4R pathway and the result is insatiable hunger, or hyperphagia, and severe early-onset obesity, as well as other endocrine disorders.[3,4] Hyperphagia presents often within the first few weeks of life, with severe obesity within the first few years.[3] Setmelanotide is an MC4R receptor agonist and reestablishes the impaired pathway in these genetic conditions, allowing these patients to feel satiety and reduced hunger for the first time in their lives.

Lifestyle modifications and dietary restrictions are currently the mainstay of treatment for these patients with rare genetic causes of obesity. Data has repeatedly demonstrated these genetics conditions are highly resistant to lifestyle interventions, even under the best of conditions. This is likely due to the MC4R's effect on energy expenditure as well as the patient's constant feeling of unsatiable hunger.

We understand that this medication has a cost to it – we ask the Iowa P&T Committee to consider and analyze the burden and long-term cost of not intervening and adding to the formulary – the cost to both the patient and to the health system. Patients with the FDA approved indications have a bleak outlook to their diagnoses.

For example - patients with BBS have vision loss as a major feature of their disease, often becoming legally blind by adolescence or early adulthood. With obesity as another characteristic feature of BBS, through the mechanism described above, severe abnormal weight gain typically begins early in childhood and continues to be an issue throughout life.

Complications typically seen in BBS patients include type 2 diabetes mellitus, hypertension, and hypercholesteremia. Many BBS patients also suffer from kidney abnormalities (e.g., developmental defects, cyst formation), which can be worsened by the progression of type 2 diabetes or hypertension. Approximately 8% of BBS patients progress to end-stage renal failure, requiring dialysis or transplant, with renal disease as the major cause of morbidity and mortality.[7] The complications from untreated or undertreated BBS and its comorbidities leads to a severe disability and a shortened life – both which can be ameliorated by the intervention with setmelanotide.

In two open-label phase 3 clinical trials (NCT02896192 and NCT03287960), setmelanotide demonstrated significant reductions in body weight and hunger scores, along with general improvements in cardiometabolic parameters. Patients with obesity due to POMC (*n* = 9) or LEPR (*n* = 11) deficiency received setmelanotide treatment for 52 weeks (including 4 weeks of placebo); 80% of patients in the POMC trial and 45% in the LEPR trial had at least 10% weight loss after approximately 1 year.[8] Additionally, 43% of patients in the POMC trial and 86% in the LEPR trial achieved at least 25% reduction in peak hunger score. From the results of these clinical trials, setmelanotide was approved by the US Food and Drug Administration in November 2020 for the treatment of patients at least 6 years of age with POMC, LEPR, or proprotein convertase subtilisin/kexin type 1 deficiency. In June 2022, the additional indication of BBS was approved by the FDA based on phase 3 clinical trial data.[9]

The quality-of-life impacts of setmelanotide therapy were published in 2022.[10] The researchers recognized that managing these FDA approved indications for setmelanotide are burdensome for both the patient and the caretaker, however the impacts of the quality of life are under-recognized and were not well characterized for their rare disease states. Prior to setmelanotide therapy, the patients included in the study described "abnormal sensations of hunger with none indicating feeling satiated after meals and also reported that the burden of hyperphagia impacted their families, emotions, and work and/or school functioning." Following the initiation of setmelanotide, all patients included in the study reported reductions in hunger, weight, caloric intake, and reported feelings of satiety. All patients reported feeling very satisfied with the impact of setmelanotide on their quality of life and would be upset if they were required to discontinue setmelanotide therapy.

When patients in this study were asked specifically how their genetic condition had affected their ability to participate in normal daily life, one patient reported being removed from their parent's home and being placed in foster care at the age of 4 due to concerns of maternal neglect (prior to diagnosis) due to their severe obesity. One patient reported that severe obesity and joint pain prevent them from standing and attending recess as a child. The same patient reported that as an adult, continual hospital visits have prevented them from maintaining employment. All patient in the study experienced considerable weight loss following treatment with setmelanotide, and the patient that had not been able to previously work reported the following – "for me, not being able to work was the worst thing, to be honest. I simple could not, and this has changed with the study and with the weight loss…I've been working steadily for 2 years now, without interruption and I'm doing well in my job….It is really unbelievable."[10]

This therapeutic option goes beyond simple weight loss. This is fixing the receptor pathway that is broken to give these patients a chance to live each day in a normal way. Please review the data and consider approval for these very few patients that qualify for this medication due to the genetic conditions of BBS, POMC, PSCK1, or LEPR deficiency so that they have a chance to fully function in society to the best of their ability and maximize their lifespan with high quality of life.

For the reasons listed above, we are requesting the following:

Addition to the PDL the requirement of prior authorization, Imcivree (setmelanotide) available for patients 6 years of age and older that meet the FDA approved indication of monogenic or syndromic obesity due to POMC, PCSK1 or LEPR deficiency as determined by an FDA approved test determining genes interpreted as pathogenic, likely pathogenic or of uncertain significance (VUS), or patients with BBS.

References

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