Imcivree® (setmelanotide) – New orphan indication

- On June 16, 2022, Rhythm Pharmaceuticals announced the FDA approval of Imcivree (setmelanotide), for chronic weight management in adult and pediatric patients 6 years of age and older with monogenic or syndromic obesity due to Bardet-Biedl syndrome (BBS).

- Imcivree is also approved for chronic weight management in adult and pediatric patients 6 years of age and older with monogenic or syndromic obesity due to Pro-opiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (LEPR) deficiency as determined by an FDA-approved test demonstrating variants in *POMC*, *PCSK1*, or *LEPR* genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance (VUS).

- BBS is a rare genetic disease that affects approximately 1,500 to 2,500 people in the U.S. People living with BBS may experience insatiable hunger, also known as hyperphagia, and severe obesity beginning early in life. BBS may also be associated with cognitive impairment, polydactyly, renal dysfunction, hypogonadism, and visual impairment.

- The approval of Imcivree for the new indication was based on a 66-week clinical study, which included a 14-week randomized, double-blind, placebo-controlled period and a 52-week open-label period. Efficacy analyses were conducted in 44 patients at the end of period 1 (week 14, placebo-controlled data) and in 31 patients during the active-treatment period, defined as the period from randomization to week 52 in patients initially randomized to Imcivree, and from week 14 to week 66 in patients initially randomized to placebo.

    — The mean percent change in body mass index (BMI) after 52 weeks of Imcivree treatment was -7.9% (95% CI: -10.4, -5.5). Additionally, 61.3% (95% CI: 42.2, 78.2) of patients achieved a ≥ 5% BMI decrease from baseline, and 38.7% (95% CI: 21.8, 57.8) had a ≥ 10% decrease in BMI.
    — During the 14-week double-blind, placebo-controlled portion of the study, there was a statistically significant difference in BMI reduction between the Imcivree-treated group and the placebo-treated group (placebo-adjusted difference -4.5, 95% CI: -6.5, -2.5).

- In adult and pediatric patients 12 years of age and older, the recommended starting dosage of Imcivree is 2 mg injected subcutaneously (SC) once daily for 2 weeks, and the recommended target dosage is 3 mg injected SC once daily. Patients should be monitored for gastrointestinal (GI) adverse reactions. If the starting dosage is:

    — Not tolerated, the dosage should be reduced to 1 mg once daily. If the 1 mg once daily dosage is tolerated for at least 1 week, the dosage should be increased to 2 mg once daily.
    — Tolerated for 2 weeks, the dosage should be increased to 3 mg once daily. If the 3 mg once daily dosage is not tolerated, the dosage should be decreased to 2 mg once daily.

- In pediatric patients aged 6 to less than 12 years, the recommended starting dosage is 1 mg injected SC once daily for 2 weeks, and the recommended target dosage is 3 mg injected SC once daily. Patients should be monitored for GI adverse reactions. If the starting dosage is:

    — Not tolerated, the dosage should be reduced to 0.5 mg once daily. If the 0.5 mg once daily dosage is tolerated for at least 1 week, the dosage should be increased to 1 mg once daily.

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— Tolerated for 2 weeks, the dosage should be increased to 2 mg once daily. If the 2 mg daily dosage is: not tolerated, the dosage should be reduced to 1 mg once daily; if it is tolerated, the dosage should be increased to 3 mg once daily.