

▼ **IMCIVREE® (setmelanotide)** 10mg/ml solution for injection. **Active ingredient:** Setmelanotide. **Presentation:** Each vial contains 10mg setmelanotide in 1ml solution for subcutaneous injection. **Indications:** Treatment of obesity and the control of hunger associated with genetically confirmed Bardet-Biedl Syndrome (BBS), loss-of-function biallelic pro-opiomelanocortin (POMC), including PCSK1, deficiency or biallelic leptin receptor (LEPR) deficiency in adults and children 2 years of age and above. **Dosage and method of administration:** IMCIVREE should be prescribed and supervised by a physician with expertise in obesity with underlying genetic aetiology. **POMC, including PCSK1, deficiency and LEPR deficiency (PPL):** Adults and children 12 to 17 years of age: 1mg daily for

2 weeks. If well-tolerated, dose can be increased to 2mg daily. If dose escalation is not tolerated, dose can be maintained at 1mg daily. If additional weight loss is desired in adults, and if weight remains above the 90<sup>th</sup> percentile in children 12 to 17 years of age, dose can be increased to 2.5mg with a maximum dose of 3mg daily. Children aged 6 to <12 years: 0.5mg daily for 2 weeks. If tolerated after 2 weeks, dose can be increased to 1mg daily. If dose escalation is not tolerated, dose can be maintained at 0.5mg daily. If 1mg is tolerated after 2 weeks, dose can be increased to 2mg daily. If weight remains above the 90<sup>th</sup> percentile and additional weight loss is desired, dose may be increased to 2.5mg daily. **BBS: Adults and children more than 16 years of age:** 2mg daily for 2 weeks. If well-tolerated, dose can be increased to 3mg daily. If 2mg starting dose is not tolerated, reduce to 1mg daily. If 1mg daily is tolerated, continue dose titration. Following starting dose, if a subsequent dose is not tolerated, reduce to previous level dose. If reduced dose is tolerated, continue dose titration. Children aged 6 to <16 years: 1mg daily for 1 week. If well-tolerated, dose can be increased to 2mg daily. If well-tolerated, dose can be increased to 3mg daily. If 1mg starting dose is not tolerated, reduce to 0.5mg daily. If 0.5mg dose is tolerated, continue dose titration. Following starting dose, if a subsequent dose is not tolerated, reduce to previous level dose. If reduced dose is tolerated, continue dose titration. **PPL and BBS: Children aged 2 to <6 years: Patients weighing <20kg:** 0.5mg with no upward titration. Patients weighing 20-<30kg: 0.5mg daily for 2 weeks. If dose is tolerated but clinical response is insufficient, dose can be increased to 1mg daily. Patients weighing 30-<40kg: 0.5mg daily for 2 weeks. If dose is tolerated but clinical response is insufficient, dose can be increased by 0.5mg every 2 weeks to a maximum of 1.5mg daily. Patients weighing ≥40kg: 0.5mg daily for 2 weeks. If dose is tolerated but clinical response is insufficient, dose can be increased by 0.5mg every 2 weeks to a maximum of 2.5mg daily. For all 2 to <6 year olds - if 0.5mg dose is not tolerated, reduce to 0.25mg daily. If 0.25mg dose is tolerated, continue dose titration. **Renal impairment: Mild-to-moderate:** no dose adjustments are necessary. **Severe:** For all patients: Following starting dose, if a subsequent dose is not tolerated, reduce to previous level dose. If reduced dose is tolerated, continue dose titration. **PPL (adults and children 12 to 17 years of age) and BBS (adults and children 16 to 17 years of age):** 0.5mg daily for 2 weeks. If well-tolerated, dose can be increased to 1mg daily. If well-tolerated and clinical response is insufficient, increase to 2mg daily. If well-tolerated and clinical response is insufficient, increase to 2.5mg daily. If well-tolerated and clinical response is insufficient, increase to 3mg daily. If 0.5mg dose is not tolerated, reduce to 0.25mg daily. **PPL (children aged 6 to <12 years) and BBS (children 6 to <16 years of age):** 0.25mg daily for 2 weeks. If not tolerated, discontinue treatment. If well-tolerated, dose can be increased to 0.5mg daily for 2 weeks. If well-tolerated, increase to 1mg daily. If well-tolerated and clinical response is insufficient, increase to 2mg daily. **PPL and BBS (children aged 2 to <6 years): Patients weighing <20kg:** 0.25mg with no upward titration. Patients weighing 20-<30kg: 0.25mg daily for 2 weeks. If dose is tolerated but clinical response is insufficient, dose can be increased to 0.5mg daily. Patients weighing 30-<40kg: 0.25mg daily for 2 weeks. If dose is tolerated but clinical response is insufficient, dose can be increased to 0.5mg daily for 2 weeks. 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Patients should be monitored closely. **End-stage renal disease:** Setmelanotide should not be administered to patients with end-stage renal disease. **Hepatic impairment:** Setmelanotide should not be administered to patients with hepatic impairment. **Method of administration:** For subcutaneous use. **Contraindications:** Hypersensitivity to the active ingredient or any excipients. **Special warnings and precautions:** Skin monitoring - full body skin examinations should be conducted annually to monitor pre-existing and new skin pigmentary lesions before and during treatment with setmelanotide. Heart rate and blood pressure monitoring – monitor as part of standard clinical practice at each medical visit (at least every 6 months). Prolonged penile erection - patients experiencing penile erection lasting longer than 4 hours should be instructed to seek emergency medical attention for potential treatment for priapism. Depression - patients with depression should be monitored at each medical visit during treatment with IMCIVREE. Consideration should be given to discontinuing IMCIVREE if patients experience suicidal thoughts or behaviours. Paediatric population - prescribing physician should periodically assess response to setmelanotide therapy. Growing children should be monitored for height and weight using age- and sex-appropriate growth curves. Excipients - medicine contains benzyl alcohol and may cause allergic reactions. Patients aged 2 years old should be monitored for any sign of metabolic acidosis while under treatment. This medicine contains less than 1mmol sodium (23mg) per dose, that is to say essentially “sodium-free”. **Adverse reactions:** Based on observation from clinical studies. Very common: hyperpigmentation disorders, injection site reactions, fatigue, nausea, vomiting, headache, spontaneous penile erection, erection increased, melanocytic naevus. Common: pruritus, rash, dry skin, skin lesion, alopecia, asthenia, pain, diarrhoea, abdominal pain, dry mouth, dyspepsia, constipation, abdominal discomfort, gastroesophageal reflux disease, dizziness, vulvovaginal discomfort, depression, insomnia, disturbance in sexual arousal, libido increased, eosinophilia, back pain, myalgia, muscle spasms, cough. For more information on other adverse reactions, see Summary of Product Characteristics. Marketing Authorisation Holder: Rhythm Pharmaceuticals Netherlands B.V., Radarweg 29, 1043NX Amsterdam, Netherlands. Tel: +31 20 8546071.

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Adverse events should be reported to Rhythm Pharmaceuticals Netherlands B.V., Radarweg 29, 1043NX Amsterdam, Netherlands.  
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