IMCIVREE® (setmelanotide) 10 mg/ml solution for injection ‖ QUALITATIVE AND QUANTITATIVE COMPOSITION: Each vial contains 10 mg setmelanotide in 1 ml of solution for subcutaneous injection. 1 ml of solution contains 10 mg benzyl alcohol. ‖ PHARMACEUTICAL FORM: Clear to slightly opalescent, colourless to slightly coloured solution. ‖ THERAPEUTIC INDICATIONS: treatment of obesity and the control of hunger in adults and children 4 years of age and above with acquired hypothalamic obesity (aHO) due to hypothalamic injury or impairment; 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.‖ POSOLOGY AND METHOD OF ADMINISTRATION: Imcivree should be prescribed and supervised by physicians experienced in the diagnosis and management of rare forms of obesity with genetic or hypothalamic origin. **aHO**: Dose titration may be performed both upward and downward based on individual tolerability and clinical response. Dose can be reduced to 0.25 mg if needed. *Adults and children 6 years of age and above*: 0.5 mg daily for 1 week. If well-tolerated, dose can be increased to 1 mg daily. If 1 mg daily is tolerated, dose can be increased to 2 mg daily. If 2 mg daily is tolerated, dose can be increased to 3 mg daily. *Children from 4 to less than 6 years of age*: start with 0.5 mg daily for 1 week. *Patients weighing < 20 kg*: If dose is tolerated but clinical response is insufficient, dose can be increased by 0.5 mg every week to a maximum of 1.5 mg daily. *Patients weighing 20 ≤ 25 kg:* If dose is tolerated but clinical response is insufficient, dose can be increased by 0.5 mg every week to a maximum of 2 mg daily. *Patients weighing 25 kg ≤ 30 kg*: If dose is tolerated but clinical response is insufficient, dose can be increased by 0.5 mg every week to a maximum of 2.5 mg daily. *Patients weighing ≥ 30 kg*: If dose is tolerated but clinical response is insufficient, dose can be increased to 1 mg daily. If dose is tolerated but clinical response is insufficient, dose can be increased to 2 mg daily. If dose is tolerated but clinical response is insufficient, dose can be increased to 3 mg daily. **POMC, including PCSK1, deficiency and LEPR deficiency (PPL):** *Adults and children 12 years of age and above*: 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 90th 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 less than 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 90th percentile and additional weight loss is desired, dose may be increased to 2.5mg daily. **BBS:** *Adults and children 16 years of age and above:* 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 less than 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 less than 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: no dose adjustments are necessary. Moderate*: PPL and BBS*: no dose adjustments are necessary. *aHO*: follow dose titration for patients with severe renal impairment. Severe: For all patients: Dose titration may be performed both upward and downward based on individual tolerability and clinical response. If starting dose is not tolerated, discontinue treatment. *PPL or aHO (adults and children 12 years of age and above) and BBS (adults and children 16 years of age and above):* 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 or aHO (children 6 to less than 12 years of age) and BBS (children 6 to less than 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. *All children less than 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. P*atients 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. If dose is tolerated but clinical response is insufficient, dose can be increased to 1mg daily. *Patients weighing ≥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. 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. 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. Setmelanotide should be injected once daily, at the beginning of the day, without regard to the timing of meals. Setmelanotide should be injected subcutaneously in the abdomen, alternating the abdominal area each day. ‖ CONTRAINDICATIONS: Hypersensitivity to the active substance or to any of the excipients. ‖ UNDESIRABLE EFFECTS: Frequencies are defined as: very common (≥1/10), common (≥1/100 to <1/10) and uncommon (≥ 1/1 000 to < 1/100). Adverse reactions are – 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, flatulence, gastrooesophageal reflux disease, Alanine aminotransferase increased, dizziness, Vulvovaginal discomfort, depression, insomnia, disturbance in sexual arousal, libido increased, eosinophilia, back pain, myalgia, arthralgia, ; uncommon: Erythema, skin striae, hyperhidrosis, lipodystrophy acquired, urticaria, skin exfoliation, hair colour

changes, nail discolouration, acanthosis nigricans, temperature intolerance, chills, abdominal distension, salivary hypersecretion, abdominal discomfort, aspartate aminotransferase increased, blood bilirubin increased, gamma-glutamyltransferase increased, hepatic enzyme increased, blood alkaline phosphatase increased, somnolence, migraine, parosmia, dysguesia, female sexual arousal disorder, genital pain, genital discomfort, genital disorder female, genital hyperaesthesia, dysmenorrhoea, sleep disorder, nightmare, libido decreased, dysplastic naevus, muscle spasms, musculoskeletal pain, pain in extremity, blood creatine phosphokinase increased, yawning, rhinorrhoea, cough, scleral discolouration, hot flush, vertigo, appetite disorder, thirst. Healthcare professionals are asked to report any suspected adverse reactions via the Federal Agency for Medicines and Health Products, Vigilance Division, website: www.notifieruneffetindesirable.be , email: adr@fagg-afmps.be ‖ MARKETING AUTHORISATION HOLDER: Rhythm Pharmaceuticals Netherlands B.V., Radarweg 29, 1043NX Amsterdam, Netherlands ‖ MARKETING AUTHORISATION NUMBER: EU/1/ 21/1564/001-002 ‖ DATE OF REVISION OF THE TEXT: 04/2026 ‖ DELIVERY STATUS: prescription.