# Setmelanotide: Adis Evaluation

## Clinical Considerations

- First treatment approved for obesity due to POMC, PCSK1 or LEPR deficiency resulting from genetic variants
- Setmelanotide is effective in reducing weight and hunger in patients aged ≥ 6 years
- Generally well tolerated

## Plain Language Summary


### *Background and rationale*

- The causes of obesity are multifactorial, one of which is genetic mutations leading to deficiencies in key ligands and receptors involved in the leptin-melanocortin pathway in the brain that regulates hunger and body weight
- While lifestyle interventions and bariatric surgery are available, there is a lack of pharmacological treatment options for obesity arising from genetic factors
- Subcutaneous setmelanotide (IMCIVREE®) is the first treatment to be approved in the EU and the USA for patients aged ≥ 6 years with obesity due to pro-opiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1) or leptin receptor (LEPR) deficiency

### *Clinical findings*

- Setmelanotide works by activating the melanocortin-4 receptor, a crucial protein receptor in the leptin-melanocortin pathway, facilitating weight loss through hunger reduction and increased energy expenditure
- In phase III trials, approximately one year of treatment with subcutaneous setmelanotide was associated with at least 10% weight reduction in a significant number of patients with POMC, PCSK1 or LEPR deficiency obesity
- Improvements in other outcomes related to weight loss and self-reported hunger scores were also evident
- Setmelanotide was generally well tolerated

### *Conclusion*

Setmelanotide represents an important advancement in the management of patients with POMC, PCSK1 or LEPR deficiency obesity.