IMCIVREE®
(setmelanotide) injection

For patients 4 years and older

Target the root cause of acquired HO with IMCIVREE

IMCIVREE is the **first and only** treatment that targets impairment of the hypothalamic MC4R pathway, the root cause of weight gain and increased hunger in acquired hypothalamic obesity (HO)[1,2]

Acquired HO is a distinct disease of MC4R pathway impairment that is characterized by weight gain following hypothalamic injury.[1,2]

Injury to the hypothalamus can impair production of α-MSH, the endogenous MC4 receptor ligand. Deficient α-MSH production leads to decreased MC4 receptor activation and impaired MC4R pathway function, which can disrupt satiety signaling and decrease energy expenditure.

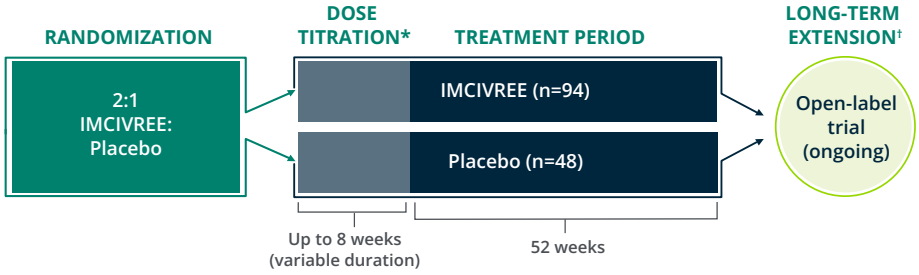
α-MSH=alpha-melanocyte stimulating hormone

IMCIVREE helps reestablish and maintain MC4R pathway function, providing the foundation for effective long-term treatment of acquired hypothalamic obesity.[1,2]

Study design[1]

142 patients participated in the randomized, Phase 3, double-blind, multicenter, placebo-controlled pivotal trial that assessed the safety and efficacy of IMCIVREE in acquired HO. The study enrolled patients 4 years and older with acquired HO due to hypothalamic injury or dysfunction.

MC4R=melanocortin-4 receptor



*Initial doses started at 0.5 mg and escalated in increments of 0.5 mg or 1.0 mg until the patient reached an individual therapeutic regimen.[1]

†Patients who completed the study and study assessments could be eligible to participate in the long-term extension (LTE) (or receive open-label setmelanotide and attend Bridging visits if the LTE was not yet available).[3]

Indication

IMCIVREE is indicated to reduce excess body weight and maintain weight reduction long term in adults and pediatric patients aged 4 years and older with acquired hypothalamic obesity (HO).

Limitations of Use

IMCIVREE is not indicated for the treatment of patients with the following conditions as IMCIVREE would not be expected to be effective:

- Other types of obesity not related to acquired hypothalamic obesity or other FDA-approved indications for IMCIVREE, including obesity associated with other genetic syndromes and general (polygenic) obesity

Important Safety Information

CONTRAINDICATIONS

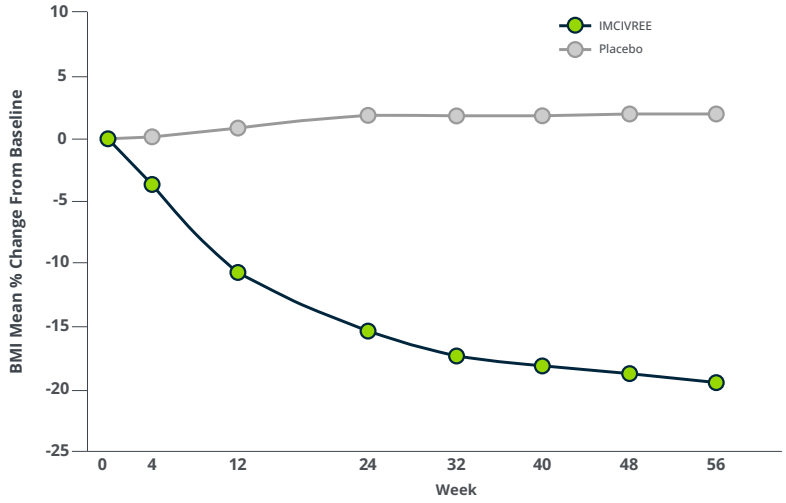
Prior serious hypersensitivity to setmelanotide or any of the excipients in IMCIVREE. Serious hypersensitivity reactions (e.g., anaphylaxis) have been reported.

Please see Important Safety Information throughout and full Prescribing Information.

IMCIVREE clinical trial efficacy

Significant BMI reduction

BMI Mean Percent Change Observed Over Time in Patients 4 Years and Older With Acquired HO[3]



IMCIVREE, n	94	94	90	88	80	85	79	79
Placebo, n	48	47	46	47	43	45	42	44

18.4% placebo-adjusted reduction in BMI at 52 weeks[1]*

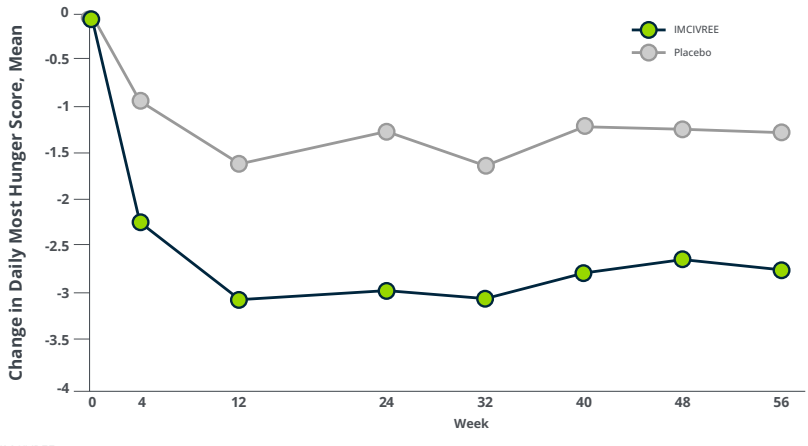
15.8% mean reduction in BMI with IMCIVREE vs a 2.6% mean increase with placebo at 52 weeks (N=142, p<0.0001)[1]

*LSM difference after 52 weeks on a therapeutic dose (95% CI: −21.9, −14.9).[1]

For pediatric patients <18 years old, a reduction was also observed in BMI Z-score (LSM difference: -1.3) and percent of the BMI 95th percentile (LSM difference: -25.5) with IMCIVREE compared with placebo.[3]

Significant hunger reduction

Hunger Mean Change Observed Over Time in Patients 12 Years and Older With Acquired HO[3]



IMCIVREE, n	66	60	61	52	59	55	52	52
Placebo, n	32	25	26	29	30	27	25	25

2.3-point mean reduction in daily most hunger score for IMCIVREE vs 1.4-point mean reduction for placebo at **52 weeks** (LSM difference: -0.8 [95% CI: -1.6, -0.02], n=110, p=0.04)[1†]

†Mean change from baseline in the weekly average of daily "most hunger" score (11-point numerical rating scale, where 0 = "not hungry at all" and 10 = "hungriest possible") after 52 weeks in patients ≥12 years who were able to self-report their hunger.[1,2]

CI=confidence interval, LSM=least squares mean

Important Safety Information (cont'd)

WARNINGS AND PRECAUTIONS

Disturbance in Sexual Arousal: Spontaneous penile erections and increased frequency of penile erections in males have occurred. Inform patients that these events may occur and instruct patients who have an erection lasting longer than 4 hours to seek emergency medical attention.

Please see Important Safety Information throughout and full Prescribing Information.

Safety profile

Adverse Reactions (≥5% and More Frequently Than Placebo) in IMCIVREE-Treated Patients Aged 4 Years and Older with Acquired HO[1]

Adverse Reaction	IMCIVREE N=94 %	Placebo N=48 %	Adverse Reaction	IMCIVREE N=94 %	Placebo N=48 %
Skin hyperpigmentation*	58	10	Constipation	12	6
Nausea	55	25	Dizziness	12	4
Vomiting	38	19	Oropharyngeal pain	11	4
Headache†	37	31	Gastroenteritis	9	2
Melanocytic nevus‡	15	6	Ear infection	5	0

*Includes skin hyperpigmentation, skin discoloration, nail pigmentation, freckles, pigmentation disorder
†Includes headache and migraine
‡Development of new melanocytic nevi and darkening or increase in size of existing melanocytic nevi

The safety of IMCIVREE has been evaluated across multiple indications in more than 700 patients over 10+ years, through clinical trials and real-world experience.[4]

Resources for getting your patients started with IMCIVREE

How IMCIVREE is dosed

IMCIVREE is a once-daily subcutaneous injection. Use the IMCIVREE dosing guide to help determine your patient's dosage and to review monitoring information for acquired HO.

DOWNLOAD OR SCAN THE QR CODE TO REVIEW THE IMCIVREE DOSING GUIDE

Prescribing IMCIVREE for your patients

Use the Start Form to initiate the prescription and help connect your patient with the Rhythm InTune patient support program.

DOWNLOAD OR SCAN THE QR CODE FOR THE PRESCRIPTION START FORM

If e-prescribing, please be sure to:

- Select PANTHERx Rare Pharmacy in the US or Special Care Pharmacy Services in Puerto Rico
- Consider also submitting the Prescription Start Form, which includes the Rhythm InTune patient consent form and additional information fields often required for insurance approval, as these are not typically included when e-prescribing

Important Safety Information (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Depression and Suicidal Ideation: Depression and suicidal ideation have occurred. Monitor patients for new onset or worsening depression or suicidal thoughts or behaviors. Consider discontinuing IMCIVREE if patients experience suicidal thoughts or behaviors, or clinically significant or persistent depression symptoms occur.

Please see Important Safety Information throughout and full Prescribing Information.

Indication and Important Safety Information

Indication

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WARNINGS AND PRECAUTIONS

Disturbance in Sexual Arousal: Spontaneous penile erections and increased frequency of penile erections in males have occurred. Inform patients that these events may occur and instruct patients who have an erection lasting longer than 4 hours to seek emergency medical attention.

Depression and Suicidal Ideation: Depression and suicidal ideation have occurred. Monitor patients for new onset or worsening depression or suicidal thoughts or behaviors. Consider discontinuing IMCIVREE if patients experience suicidal thoughts or behaviors, or clinically significant or persistent depression symptoms occur.

Hypersensitivity Reactions: Serious hypersensitivity reactions (e.g., anaphylaxis) have been reported. If suspected, advise patients to promptly seek medical attention and discontinue IMCIVREE.

Skin Hyperpigmentation, Darkening of Pre-existing Nevi, and Development of New Melanocytic Nevi: Generalized or focal increases in skin pigmentation occurred in the majority of IMCIVREE-treated patients. IMCIVREE may also cause development of new melanocytic nevi or darkening of pre-existing nevi. Perform a full body skin examination prior to initiation and periodically during treatment to monitor pre-existing and new pigmented lesions.

Acute Adrenal Insufficiency with Acquired HO: Patients with acquired HO and secondary adrenal insufficiency reported serious adverse reactions related to acute adrenal insufficiency in 5% of IMCIVREE-treated patients and no placebo-treated patients. In patients with secondary adrenal insufficiency, monitor for clinical signs of acute adrenal insufficiency.

Sodium Imbalance in Patients with Acquired HO and Central Diabetes Insipidus: Patients with acquired HO and concomitant central diabetes insipidus (DI)/arginine vasopressin (AVP) deficiency reported hyponatremia in 6% of IMCIVREE-treated patients and 2% of placebo-treated patients and hypernatremia in 5% of IMCIVREE-treated patients and 4% of placebo-treated patients. Monitor serum sodium levels with changes in fluid intake and hydration status. Adjust the doses of concomitant therapies for DI/AVP deficiency as needed.

ADVERSE REACTIONS

- Most common adverse reactions (incidence ≥20%) included skin hyperpigmentation, nausea, vomiting, and headache

USE IN SPECIFIC POPULATIONS

Treatment with IMCIVREE is not recommended when breastfeeding. Discontinue IMCIVREE when pregnancy is recognized unless the benefits of therapy outweigh the potential risks to the fetus.

Please see full Prescribing Information for additional Important Safety Information.

Visit aHO.IMCIVREEHCP.com or reach out to your Rhythm representative for more information on IMCIVREE and acquired HO.

References: 1. IMCIVREE [prescribing information]. Boston, MA: Rhythm Pharmaceuticals, Inc; 2026. **2.** Roth CL, Scimia C, Shoemaker AH, et al. Setmelanotide for the treatment of acquired hypothalamic obesity: a phase 2, open-label, multicentre trial. *Lancet Diabetes Endocrinol*. 2024;12(6):380-389. doi:10.1016/S2213-8587(24)00087-1 **3.** Data on file. Rhythm Pharmaceuticals, Inc. Boston, MA. **4.** U.S. National Library of Medicine. Identifier: setmelanotide. ClinicalTrials.gov. Accessed January 15, 2025.

Rhythm® PHARMACEUTICALS

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