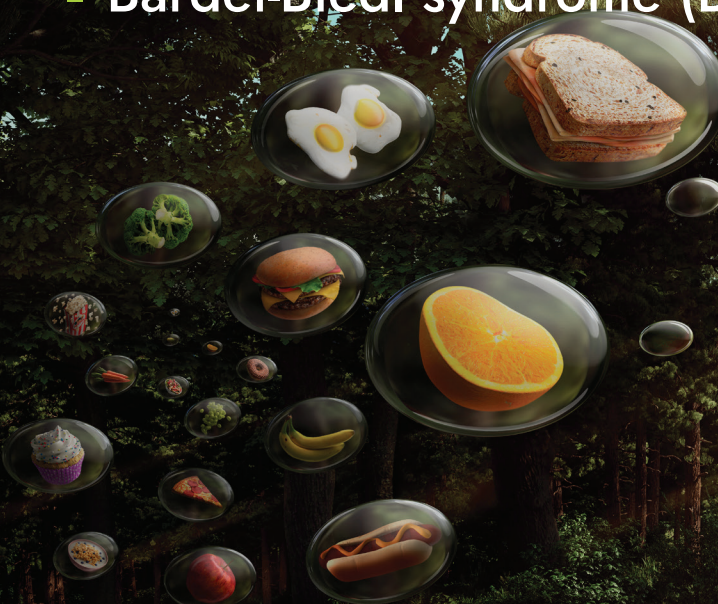


For people living with  
Bardet-Biedl syndrome (BBS)



Actor portrayals.

# Discover a World Beyond Obesity

**IMCIVREE**<sup>®</sup>  
(setmelanotide) injection

**The first and only FDA-approved** treatment to target an impaired MC4R pathway, a root cause of hunger and obesity in people living with BBS

## Your Guide to Getting Started

MC4R=melanocortin-4 receptor.

IMCIVREE is a prescription medicine used in adults and children 6 years of age and older with obesity due to Bardet-Biedl syndrome (BBS) to help them lose weight and keep the weight off.

IMCIVREE is not for use in people with the following conditions because it may not work:

- ◆ Other types of obesity not related to BBS or other FDA-approved uses of IMCIVREE, including obesity associated with other genetic conditions and general obesity

It is not known if IMCIVREE is safe and effective in children under 6 years of age.

Do not use IMCIVREE if you have had a serious allergic reaction to it or any of its ingredients. Serious allergic reactions, including anaphylaxis, can happen.

Please see full [Prescribing Information](#) and [Patient Information](#), as well as Important Safety Information throughout.



# Your guide to starting treatment with **IMCIVREE**

You've made the decision with your doctor to begin treatment with IMCIVREE.

Inside you'll find everything you need to know about starting on IMCIVREE, including an overview of the clinical trial, what to expect, and helpful tips for giving injections.



Please see full [Prescribing Information](#) and [Patient Information](#), as well as Important Safety Information throughout.

Actor portrayals.

# Table of contents

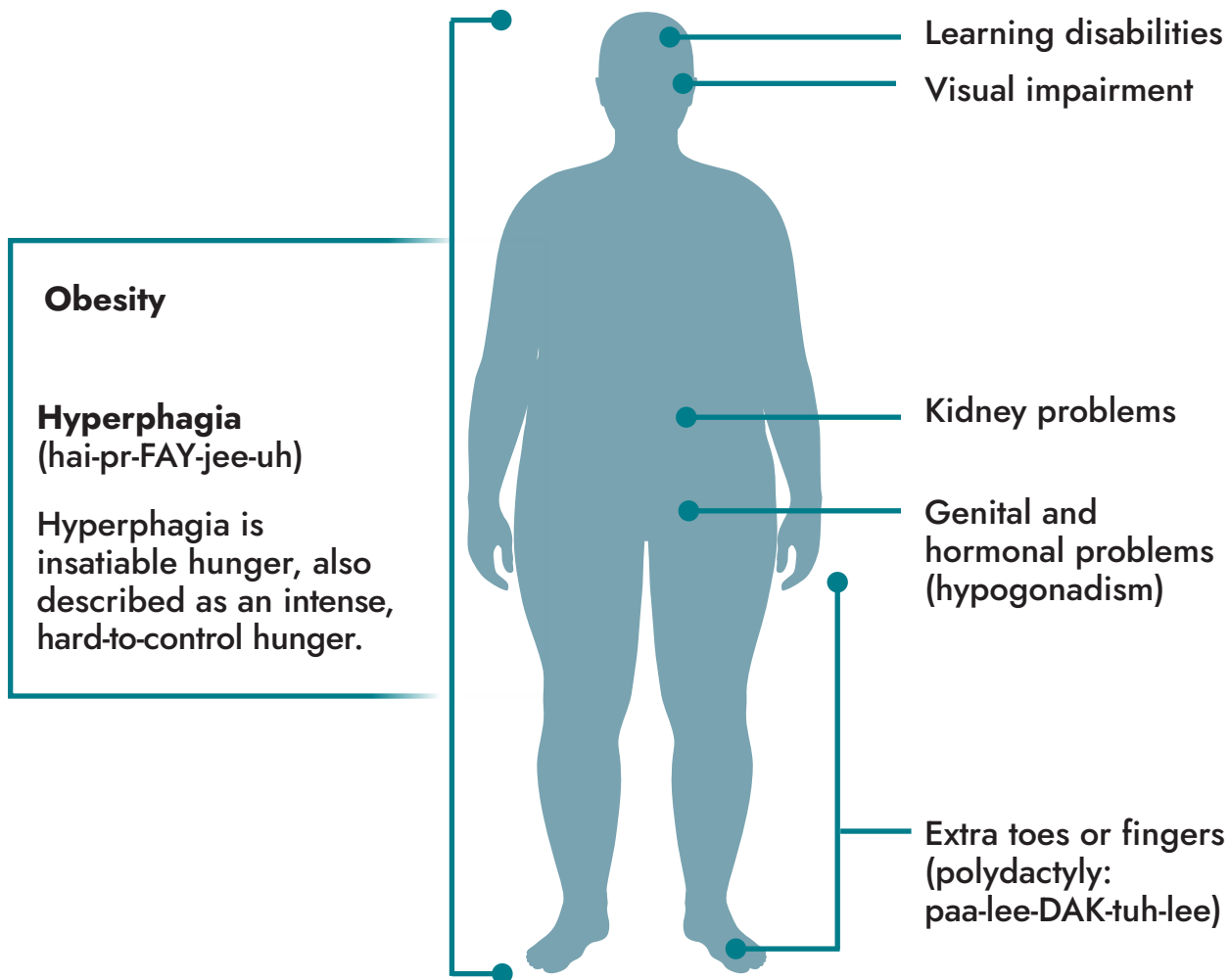
---

◆ What is BBS? .....	4
◆ What causes hunger and obesity in BBS?.....	6
◆ How does IMCIVREE work?.....	8
◆ How can IMCIVREE help with the reduction of weight measures in children? .....	10
◆ How can IMCIVREE help with weight reduction in adults? .....	12
◆ How did IMCIVREE help with hunger reduction in the clinical trial? .....	14
◆ What are the possible side effects of IMCIVREE?.....	16
◆ Rhythm InTune: Your source for personalized support ...	18
◆ How is IMCIVREE given? .....	20
◆ Understanding your dose .....	22
◆ Helpful tips for giving IMCIVREE.....	24
◆ Frequently asked questions.....	26

# What is BBS?

Bardet-Biedl (pronounced BAR-day BEED-el) syndrome, also known as BBS, is a rare genetic disease

BBS has a wide range of symptoms



BBS is inherited. It can be passed from parent to child if both parents have variants, or changes, in a BBS gene.

People living with BBS may experience intense, hard-to-control hunger. This feeling is not their fault. Changes in BBS genes can stop a key area of the brain that controls hunger from working properly



The key area of the brain that communicates being hungry or satisfied is known as the hypothalamus

Think of the hypothalamus as a neighborhood within the brain.



Hypothalamus



In this neighborhood, there are roads that allow trucks to travel to and from the brain. One road is called the melanocortin-4 receptor, or **MC4R**, pathway.



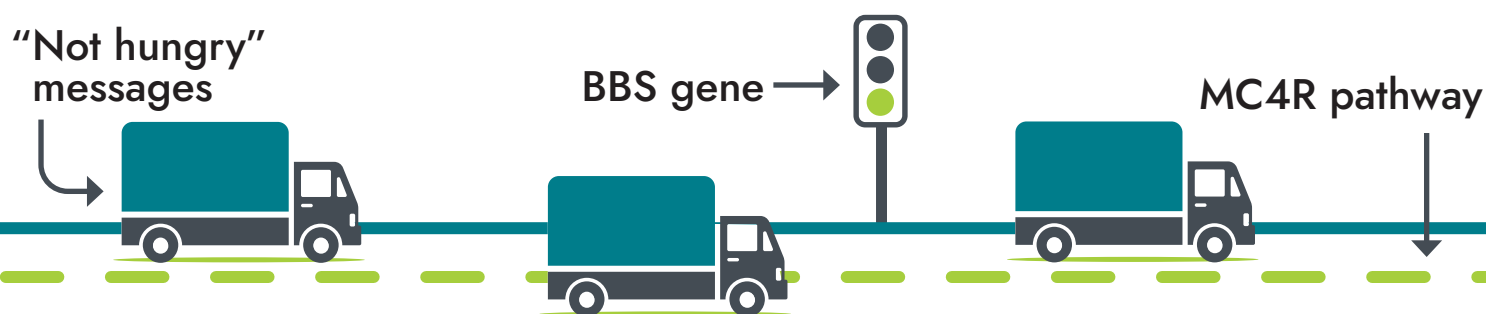
The trucks on this road deliver messages between the body and the brain. These messages control hunger.



On this road, there is a traffic light, or a **BBS** gene, that helps guide the trucks to deliver their messages.

# What causes hunger and obesity in BBS?

In people living with BBS, the signals that turn hunger “off” don’t work correctly in the brain



When the BBS gene is normal, without a variant (or change), the traffic light works correctly. The road (MC4R pathway) is open, and the trucks can deliver messages to the brain that the body is satisfied and doesn’t need more food.

## Important Safety Information

Before you use IMCIVREE, tell your healthcare provider about all your medical conditions, including if you:

- ◆ Have or have had areas of darkened skin, including skin discoloration (hyperpigmentation)
- ◆ Have or have had depression, or suicidal thoughts or behavior
- ◆ Have kidney problems



In people living with BBS, the traffic light is broken due to the change in the BBS gene

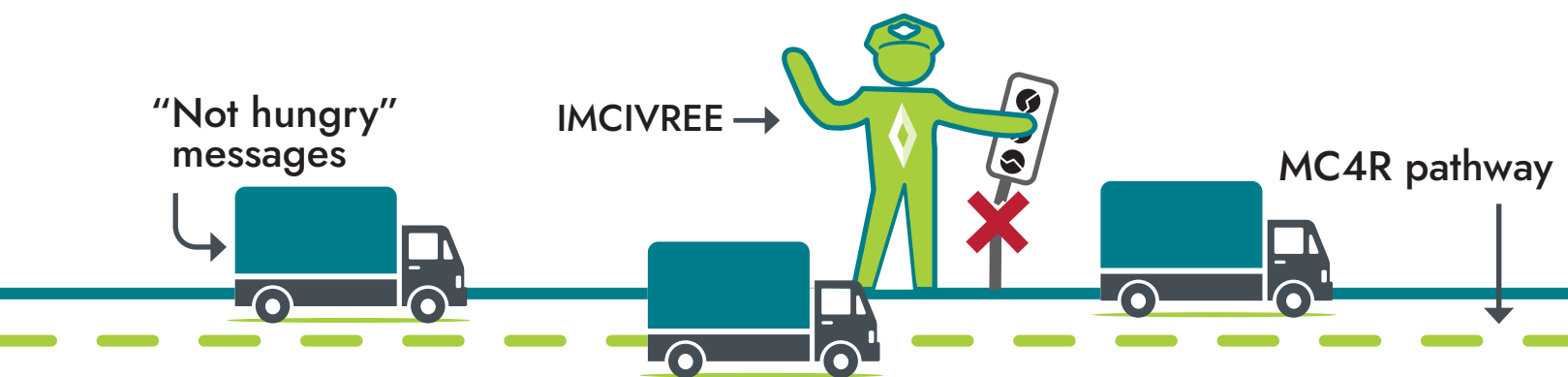


When the BBS gene has a variant (or change), the traffic light is broken, which causes a traffic jam. The trucks can no longer travel along the road (MC4R pathway) to properly deliver messages to the brain that the body is satisfied and doesn't need more food. Instead, the body believes that it's still hungry.

**IMCIVREE is the first and only treatment to target an impaired MC4R pathway, a root cause of hunger and obesity in people living with BBS**

# How does IMCIVREE work?

IMCIVREE is designed to re-establish function to the “road” (MC4R pathway) so trucks can deliver messages to the brain that the body is satisfied



Think of IMCIVREE as a traffic officer. When the traffic light is broken, the traffic officer directs trucks on the road (MC4R pathway), allowing them to deliver messages to the brain that the body is satisfied and doesn't need more food.

This is how IMCIVREE works to help the pathway work properly.

## Important Safety Information (cont'd)

- ◆ Are pregnant or planning to become pregnant. Losing weight while pregnant may harm your unborn baby. Your healthcare provider may stop your treatment with IMCIVREE if you become pregnant. Tell your healthcare provider if you become pregnant or think you might be pregnant during treatment with IMCIVREE
- ◆ Are breastfeeding or plan to breastfeed. It is not known if IMCIVREE passes into your breast milk. You should not breastfeed during treatment with IMCIVREE

**IMCIVREE**<sup>®</sup>  
(setmelanotide) injection

Please see full [Prescribing Information](#) and [Patient Information](#), as well as **Important Safety Information** throughout.



# How was IMCIVREE studied?

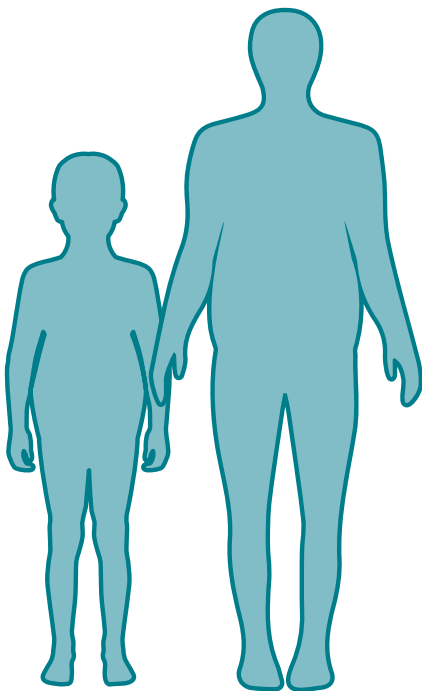
## IMCIVREE was studied in both children and adults in a yearlong clinical trial

The clinical trial was the largest ever to assess weight and hunger reduction in people living with BBS.

- ◆ 31 people were evaluated in the clinical trial
  - All people were 6 years and older with obesity and a clinical diagnosis of BBS
- ◆ Children and adults included in the clinical trial had to have a certain weight or body mass index (BMI). BMI is a measure of body fat based on height and weight
  - Children had to have a weight in the 97th percentile or higher
  - Adults had to have a BMI of 30 or more

## IMCIVREE reduced BMI over the course of the 1-year clinical trial

- ◆ ~8% average reduction in BMI in people 6 years and older



### People taking IMCIVREE had general improvements in other areas

Blood pressure, lipids, and waist size improved with IMCIVREE. Due to a limited number of people studied and the lack of a control group in the study, these treatment effects could not be accurately measured.

# How can IMCIVREE help with the reduction of weight measures in children?\*

## IMCIVREE reduced BMI Z-scores in children over the course of the 1-year clinical trial

A BMI Z-score was used to measure the reduction in BMI in children. BMI Z-scores are reliable measures of weight in children who are still growing because they take into account height, age, and gender.

**86%**

of children had a meaningful reduction in BMI Z-score<sup>†</sup>

In the clinical trial, people were not required to change their diet or exercise routine.

**IMCIVREE is the first and only treatment to significantly reduce BMI Z-score in children with obesity and a clinical diagnosis of BBS**

\*N=14. N is the number of people evaluated. Children were 6 to 17 years of age.

<sup>†</sup>A clinically meaningful reduction is generally defined as a reduction of greater than or equal to 0.2 in BMI Z-score.

## Important Safety Information (cont'd)

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

See the detailed Instructions for Use that come with your IMCIVREE to learn how to prepare and inject IMCIVREE, and how to properly throw away (dispose of) used syringes and needles.

**IMCIVREE**<sup>®</sup>  
(setmelanotide) injection

Please see full [Prescribing Information](#) and [Patient Information](#), as well as Important Safety Information throughout.



# In a long-term study, children who continued taking IMCIVREE maintained reductions in BMI Z-scores<sup>‡</sup>

Some people chose to continue taking IMCIVREE in a separate long-term clinical trial. After they received 2 years of treatment, their results were analyzed.

**100%**

of patients at 2 years had a meaningful reduction in BMI Z-score<sup>†§</sup>

- ◆ There was a 0.72 reduction in BMI Z-score<sup>†</sup>

Children who continued IMCIVREE for 2 years maintained meaningful reductions in BMI Z-score

He weighs so much less...  
he doesn't struggle to carry  
that weight anymore.

— Caregiver of an IMCIVREE-treated  
patient from the BBS clinical trial



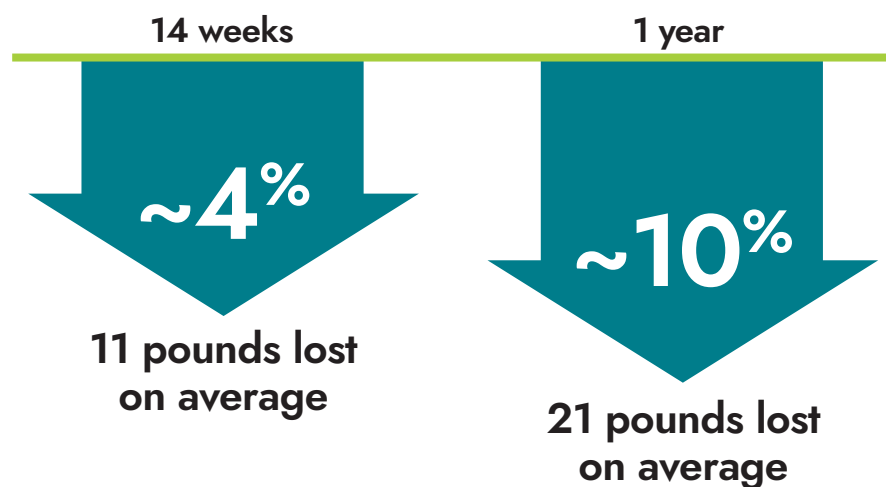
<sup>‡</sup>Change in BMI Z-score could not be calculated for one 20-year-old person who was 17 years old at the beginning of the original trial.

<sup>§</sup>N=12.

# How can IMCIVREE help with weight reduction in adults?\*

IMCIVREE showed early, significant, and continued weight reduction

Average reductions in weight over the course of the 1-year clinical trial†



In the clinical trial, people were not required to change their diet or exercise routine.

\*Adults were 18 years of age or older.

†14 weeks: N=10, 1 year: N=12.

## Important Safety Information (cont'd)

What are the possible side effects of IMCIVREE?

IMCIVREE may cause serious side effects, including:

- ◆ **Male and female sexual function problems.** IMCIVREE can cause an erection that happens without any sexual activity in males (spontaneous penile erection) and unwanted sexual reactions (changes in sexual arousal that happen without any sexual activity) in females. If you have an erection lasting longer than 4 hours, get emergency medical help right away

**IMCIVREE**<sup>®</sup>  
(setmelanotide) injection

Please see full [Prescribing Information](#) and [Patient Information](#), as well as **Important Safety Information** throughout.



## In a long-term study, adults who continued taking IMCIVREE for a total of 2 years lost even more weight

Average reduction in weight at 2 years in the long-term study<sup>‡</sup>



At the end of a clinical trial for IMCIVREE, 19 people continued in a long-term study. 6 of these people were adults. People are being assessed every 3 months until the end of the study (up to 5 years or study withdrawal).

IMCIVREE has mainly helped me lose and control my weight. I know I couldn't have done it without this medication.

— Adult patient enrolled in the IMCIVREE clinical trial

IMCIVREE reduced weight early and continuously over the course of 2 years of treatment

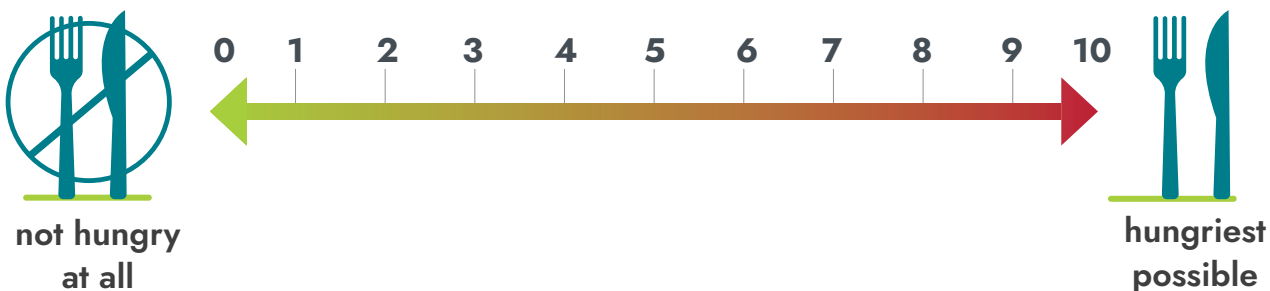
<sup>‡</sup>N=6.

# How did IMCIVREE help with hunger reduction in the clinical trial?

IMCIVREE provided reduction in hunger scores early and continuously throughout treatment

The effect of IMCIVREE on reducing hunger was studied in people 12 years and older living with BBS who could self-report their hunger.

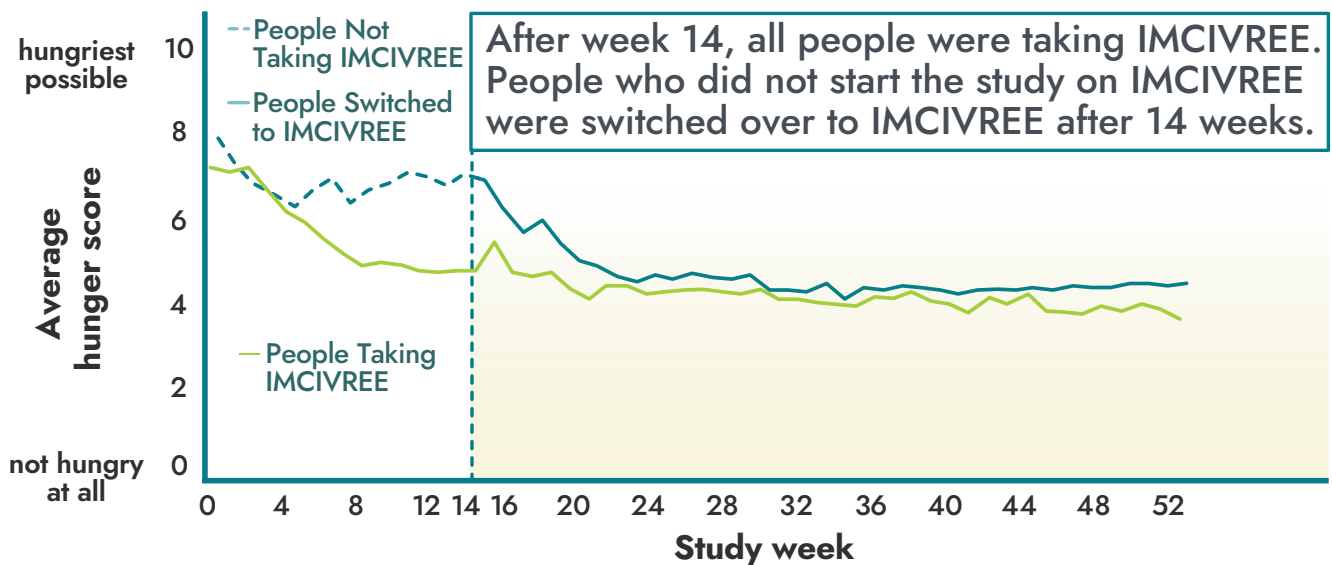
- ◆ They completed a questionnaire every day for 1 year to determine changes in their hunger
- ◆ People scored their hunger on a daily basis using a scale from 0 to 10



## Important Safety Information (cont'd)

- ◆ **Depression and suicidal thoughts or actions.** You or a caregiver should call your healthcare provider right away if you have any new or worsening symptoms of depression, suicidal thoughts or behaviors, or any unusual changes in mood or behavior
- ◆ **Serious allergic reactions.** Stop taking IMCIVREE and get medical help right away if you have any symptoms of a serious allergic reaction including: swelling of your face, lips, tongue, or throat; problems breathing or swallowing; severe rash or itching; fainting or feeling dizzy; rapid heartbeat

## IMCIVREE reduced the most severe feelings of hunger



**A majority of people experienced a reduction in hunger score within 2 weeks of taking IMCIVREE**

Before IMCIVREE, I didn't realize how much time I spent focusing on food, and how much that was affecting my day-to-day and the other things I could be accomplishing.

— Kathryn, who is living with BBS





# What are the possible side effects of IMCIVREE?

IMCIVREE was well studied and most side effects were generally mild and improved over time

The safety of IMCIVREE has been evaluated over ~10 years of clinical trials.

The most common side effects in people with obesity and a clinical diagnosis of BBS included:

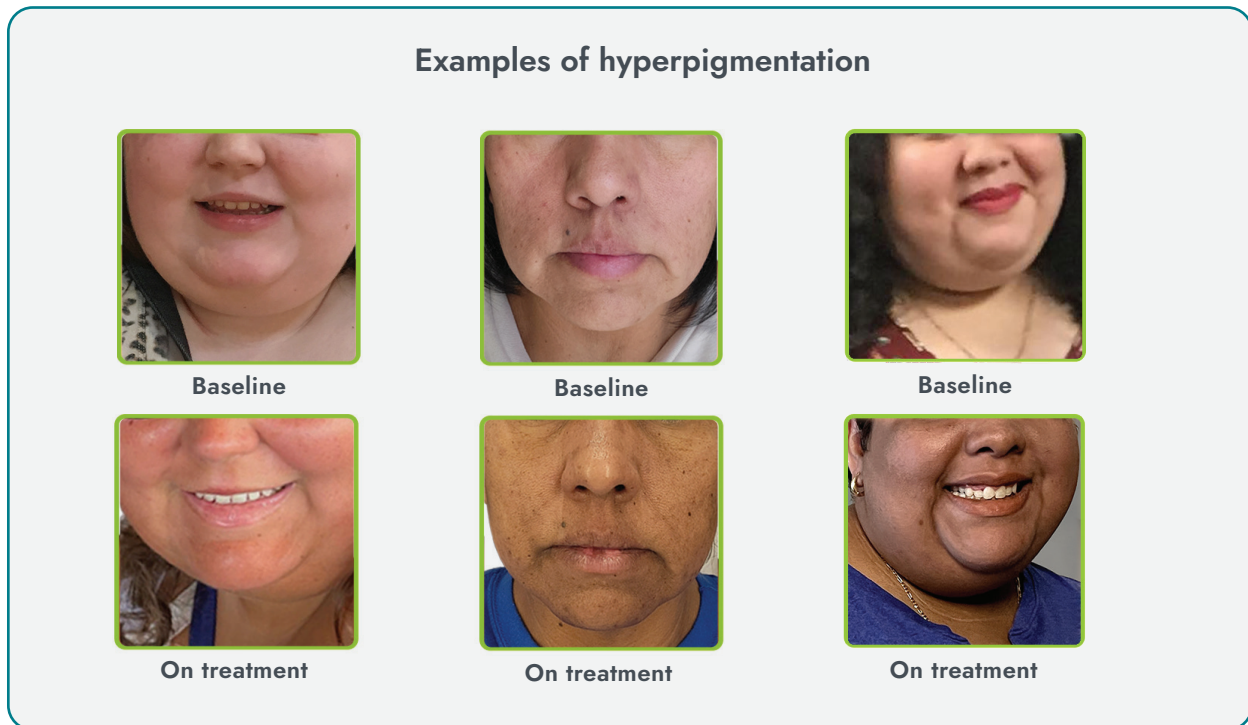
- ◆ Darkening of the skin\* (hyperpigmentation) (63%)
- ◆ Injection site reactions (51%)
- ◆ Nausea (26%)
- ◆ Erection that happens without any sexual activity in males (25%)
- ◆ Vomiting (19%)
- ◆ Diarrhea (14%)
- ◆ Headache (7%)
- ◆ Stretch marks (7%)
- ◆ Aggression (5%)
- ◆ Fatigue (5%)

Most nausea and vomiting events were mild, and none were severe. Nausea and vomiting were primarily reported within the first month of treatment and then sharply declined. These symptoms typically lasted no more than a few days.

No serious side effects were reported related to IMCIVREE in the BBS trial.

Contact your doctor if you are experiencing side effects.

**A general darkening of the skin (hyperpigmentation) was common and rarely led to a stop in treatment**



- ◆ IMCIVREE may also lead to an increased production of melanin (which gives color to your skin)
  - This usually occurs within the first month of starting IMCIVREE
  - Darkening of the skin may vary
- ◆ IMCIVREE can cause darkening of existing skin growths, such as moles
- ◆ You should have a full-body skin exam before starting and during treatment with IMCIVREE to check for skin changes
- ◆ Changes in skin color went away when treatment with IMCIVREE was stopped

These are not all the possible side effects of IMCIVREE. Please review all the possible side effects of IMCIVREE in the [Patient Information](#) and talk to your doctor about any questions you may have.



## Your source for personalized support

Rhythm InTune is a support program designed for caregivers and people living with rare genetic diseases of obesity

A **Patient Education Manager** provides personal, one-on-one support and is your single point of contact at Rhythm InTune. You'll be automatically connected to them whenever you reach out with questions or requests.

Your Patient Education Manager will:



Ensure you have the answers you need before and after starting treatment



Assist with starting IMCIVREE and establishing a treatment routine



Provide insurance support, and offer copay assistance (for eligible patients)



Provide educational materials and resources throughout treatment with IMCIVREE

Contact your Patient Education Manager at [patientsupport@rhythmtx.com](mailto:patientsupport@rhythmtx.com) or 1-855-206-0815 whenever you have questions or need support.



Please see full [Prescribing Information](#) and [Patient Information](#), as well as **Important Safety Information** throughout.

## What to expect when starting with Rhythm InTune

**STEP 1** You will receive a phone call from your Patient Education Manager welcoming you to the program.

---

**STEP 2** Your Patient Education Manager will confirm insurance coverage and enroll you in copay support (if eligible) to help you start IMCIVREE as prescribed.

---

**STEP 3** Your Patient Education Manager will make sure you have all the information you need on how to give IMCIVREE once you've received your first shipment.

---

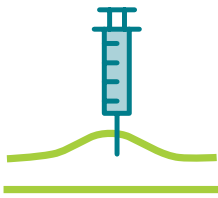
**Your Patient Education Manager will check in with you throughout your IMCIVREE treatment journey**



# How is IMCIVREE given?

IMCIVREE is a once-daily injection used to help reduce weight in people living with BBS

IMCIVREE is given:



As an injection  
under the skin



Once daily at the beginning  
of the day, and can be  
given at home



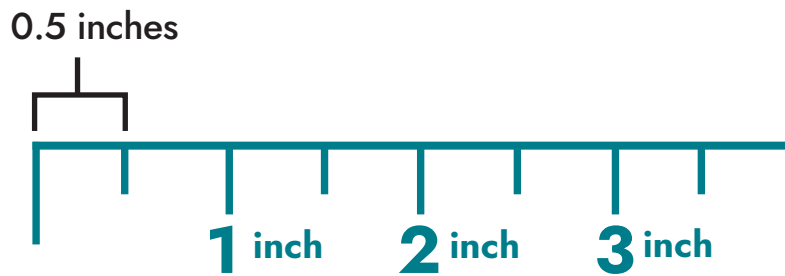
With or  
without food

## Important Safety Information (cont'd)

- ◆ **Increased skin pigmentation and darkening of skin lesions (moles or nevi) you already have.** These changes happen because of how IMCIVREE works in the body and will go away when you stop using IMCIVREE. You should have a full body skin exam before starting and during treatment with IMCIVREE to check for skin changes
- ◆ **Benzyl alcohol toxicity.** Benzyl alcohol is a preservative in IMCIVREE. Benzyl alcohol can cause serious side effects, including death, in premature and low-birth weight infants who have received medicines that contain benzyl alcohol. IMCIVREE should not be used in premature and low-birth weight infants

Because IMCIVREE is injected under the skin, the needle is short and thin

- ◆ The IMCIVREE needle is half an inch long



Please see the [How to Give IMCIVREE Guide](#) for illustrated, step-by-step instructions for giving an IMCIVREE injection.

**The first time I gave her the injection, she was scared and thought it was going to hurt. But now it doesn't faze her at all.**

*— Caregiver of child taking IMCIVREE*

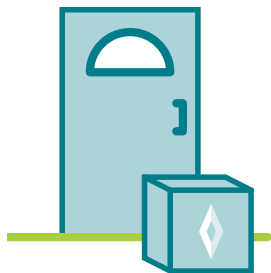


Actor portrayal.

# Understanding your dose

## Starting treatment

---



When you start treatment, your doctor will determine the starting dose for you.

For most people 12 years and older, this dose is 2 mg per day. For people between the ages of 6 and 12 years, the starting dose is typically 1 mg per day.

## Your first few weeks

---



Over the first few weeks of treatment, your doctor will evaluate if your dose needs to change.

If any side effects occur, your doctor may adjust your dose.

## Important Safety Information (cont'd)

The most common side effects of IMCIVREE include darkening of the skin, injection site reactions, nausea, headache, diarrhea, stomach pain, vomiting, depression, and an erection that happens without any sexual activity in males.

## Ongoing treatment

---



Once you've reached the target dose, your doctor will continue to check on your progress.

### Important Safety Information (cont'd)

These are not all the possible side effects of IMCIVREE. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088 or to Rhythm Pharmaceuticals at 1-833-789-6337.



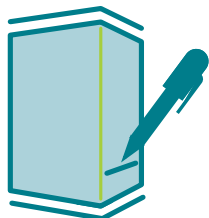
Actor portrayals.

# Helpful tips for giving IMCIVREE

## Keeping track of the injections



- ◆ Use the **IMCIVREE Treatment Journal** or a planner, calendar, phone, or other method to record the location, date, and time for each injection



- ◆ When you first open the vial, write the date on the IMCIVREE carton so you can be sure to dispose of any unused medicine after 30 days

If you miss a dose of IMCIVREE, inject your next dose at the regularly scheduled time the next day



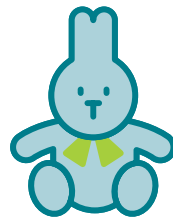
## Assisting children

Distraction can often help reduce fear when giving injections to children.

Have your child try:



◆ Deep (tummy) breathing



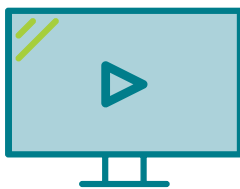
◆ Squeezing a stuffed animal



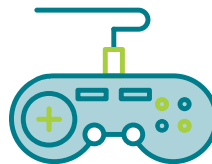
◆ Reading



◆ Listening to music



◆ Watching TV or a movie



◆ Playing a video game

# Frequently asked questions

## Do I need to take my IMCIVREE every day?

---

Yes, IMCIVREE should be injected once daily at the beginning of the day.

## What time of day should I take IMCIVREE?

---

IMCIVREE should be injected once daily, at the beginning of the day, and can be given at home, with or without food.

## Why is it important to take IMCIVREE every day?

---

IMCIVREE was studied and approved as a daily injection.

## What should I do if I miss a dose?

---

If a dose of IMCIVREE is missed, inject the next one at the regularly scheduled time the next day. Do not take the missed dose of IMCIVREE.

## **Do I have to take IMCIVREE for an entire year before I start to lose weight?**

---

Please note that each person is different, and results can vary from one person to another. Please talk to your doctor about your own treatment expectations. In the yearlong clinical trial that studied IMCIVREE for weight reduction in people with obesity and a clinical diagnosis of BBS, people taking IMCIVREE started losing weight early on in treatment and continued to lose weight over the course of their treatment.

## **Will nausea and vomiting get better the longer I take IMCIVREE?**

---

We encourage you to reach out to your doctor for more information about nausea and vomiting. Responses vary, but reports of nausea and vomiting side effects in the clinical trials mostly occurred within the first month of treatment, and then sharply declined after 4 weeks. These side effects typically lasted a few days.

In the yearlong clinical trial that studied IMCIVREE for weight reduction in people with obesity and a clinical diagnosis of BBS, nausea was reported by 26% of people taking IMCIVREE, and vomiting was reported by 19% of people taking IMCIVREE.

It's also important to know that most nausea or vomiting events in the clinical trials of IMCIVREE were mild and none were severe.

## **I have questions. Who should I contact?**

---

Please reach out to your doctor if you have any questions about IMCIVREE. For questions or personalized support, please contact Rhythm InTune.

## **How do I get more supplies if I'm running low?**

---

If you're low on supplies, contact Rhythm InTune to order more.

**IMCIVREE is the first and only FDA-approved treatment to target an impaired MC4R pathway, a root cause of hunger and obesity in people living with BBS.**

**Want to learn more about BBS or IMCIVREE?**

Talk to your doctor. For additional education and support, contact Rhythm InTune at:



**patientsupport@rhythmtx.com**



**1-855-206-0815**

IMCIVREE is a prescription medicine used in adults and children 6 years of age and older with obesity due to Bardet-Biedl syndrome (BBS) to help them lose weight and keep the weight off.

IMCIVREE is not for use in people with the following conditions because it may not work:

- ◆ Other types of obesity not related to BBS or other FDA-approved uses of IMCIVREE, including obesity associated with other genetic conditions and general obesity

It is not known if IMCIVREE is safe and effective in children under 6 years of age.

**Do not use IMCIVREE if you have had a serious allergic reaction to it or any of its ingredients. Serious allergic reactions, including anaphylaxis, can happen.**

Please see full [Prescribing Information](#) and [Patient Information](#), as well as Important Safety Information throughout.