

For people living with  
Bardet-Biedl syndrome (BBS)



# Discover a World Beyond Obesity

Actor portrayals.

**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

MC4R=melanocortin-4 receptor.

## What is IMCIVREE?

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.

## Important Safety Information

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.





Actor portrayals.

## Important Safety Information (cont'd)

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)

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

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# What is BBS?

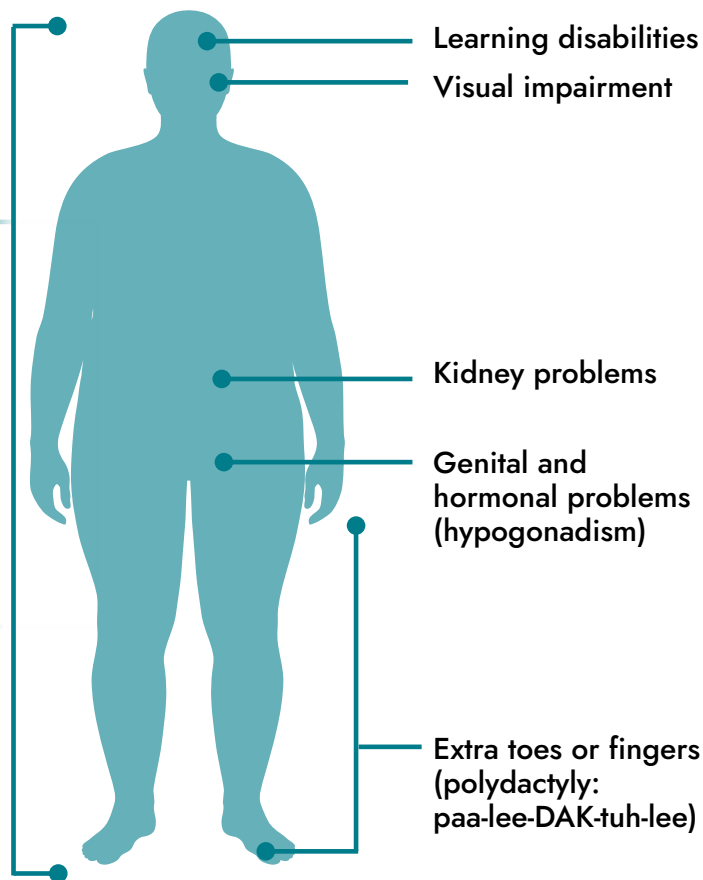
Bardet-Biedl (pronounced BAR-day BEED-el) syndrome, also known as BBS, is a rare genetic disease

**BBS has a wide range of symptoms**

**Obesity**

**Hyperphagia**  
(hai-pr-FAY-jee-uh)

Hyperphagia is insatiable hunger, also described as an intense, hard-to-control hunger.



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**

## Important Safety Information (cont'd)

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

- ◆ Have or have had depression, or suicidal thoughts or behavior

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.



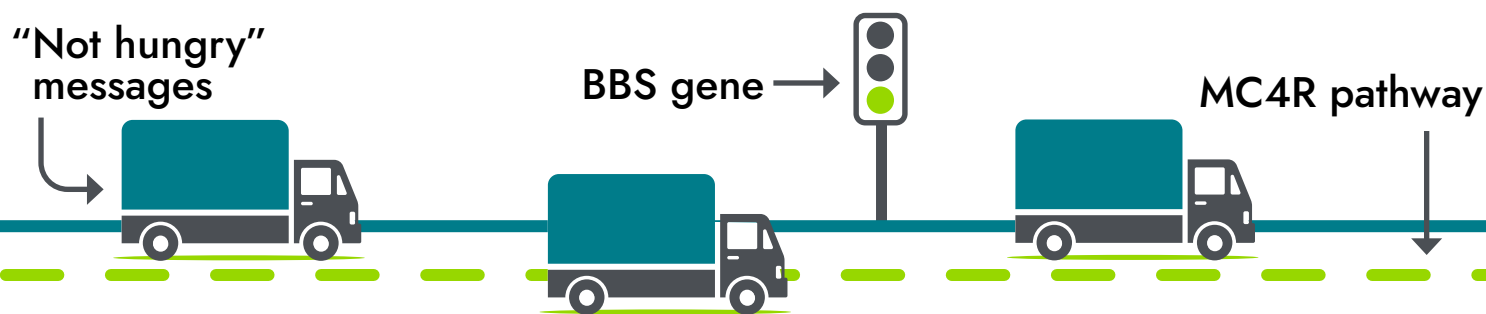
The trucks on this road deliver messages between the body and the brain. These messages control hunger.



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



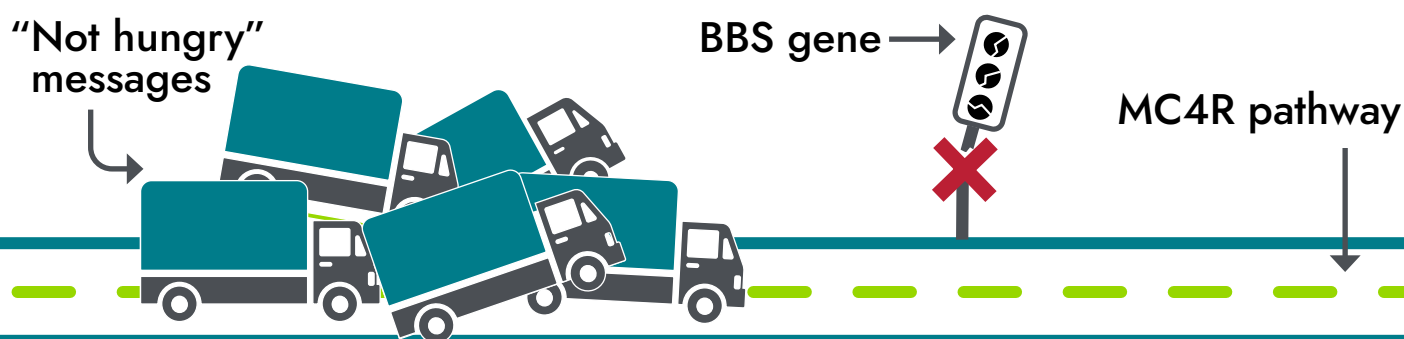
When the BBS gene is normal, without a variant (or change), the traffic light works correctly. The road (MC4R pathway) is open, and the trucks can deliver messages to the brain that the body is satisfied and doesn’t need more food.

## Important Safety Information (cont’d)

Before you use IMCIVREE, tell your healthcare provider about all your medical conditions, including if you: (cont’d)

- ◆ Have kidney problems
- ◆ 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

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.

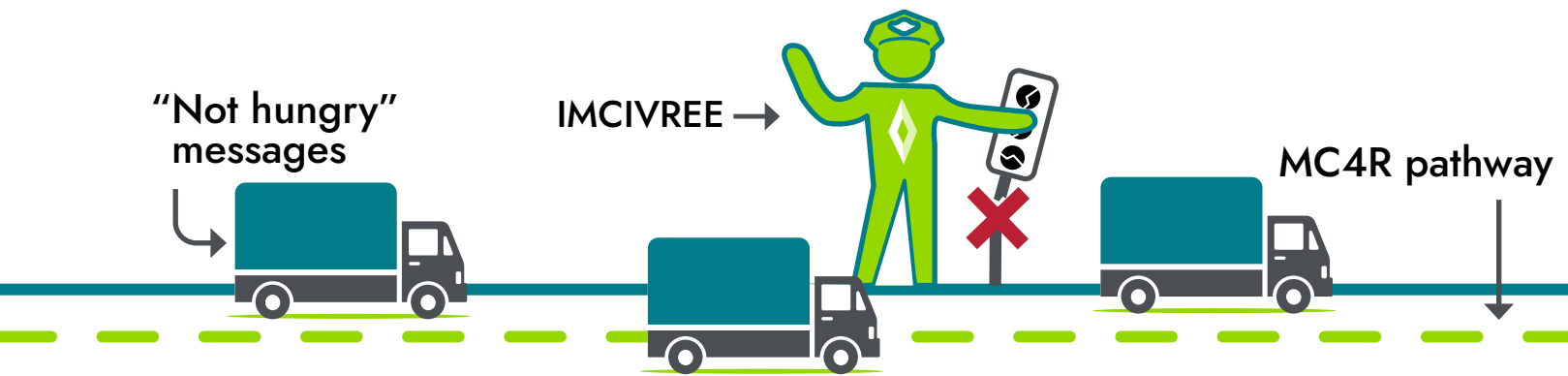
**IMCIVREE is the first and only treatment to target an impaired MC4R pathway, a root cause of hunger and obesity in people living with BBS**

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

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# 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 helps the pathway work properly.

## Important Safety Information (cont'd)

Before you use IMCIVREE, tell your healthcare provider about all your medical conditions, including if you: (cont'd)

- ◆ 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



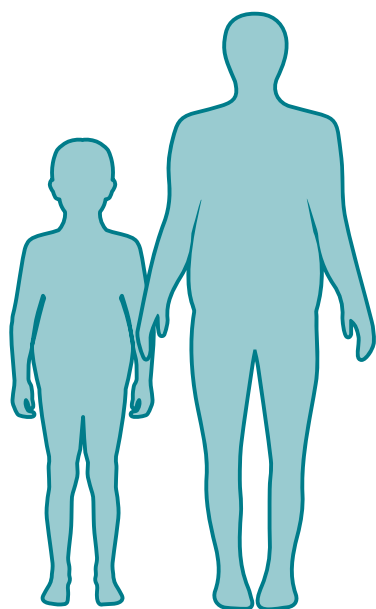
# What are the IMCIVREE study results?

IMCIVREE was studied in both children and adults in a year-long 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.

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# How did IMCIVREE help reduce measures of weight in children in the clinical trial?

A Body Mass Index, or 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.

He is no longer digging through the fridge or garbage, so we do not lock them anymore. He isn't asking for food constantly between meals and snacks, and I sometimes find myself realizing it's been a few hours and asking him if he's ready for a snack.

— Rachel, caregiver of a child living with BBS

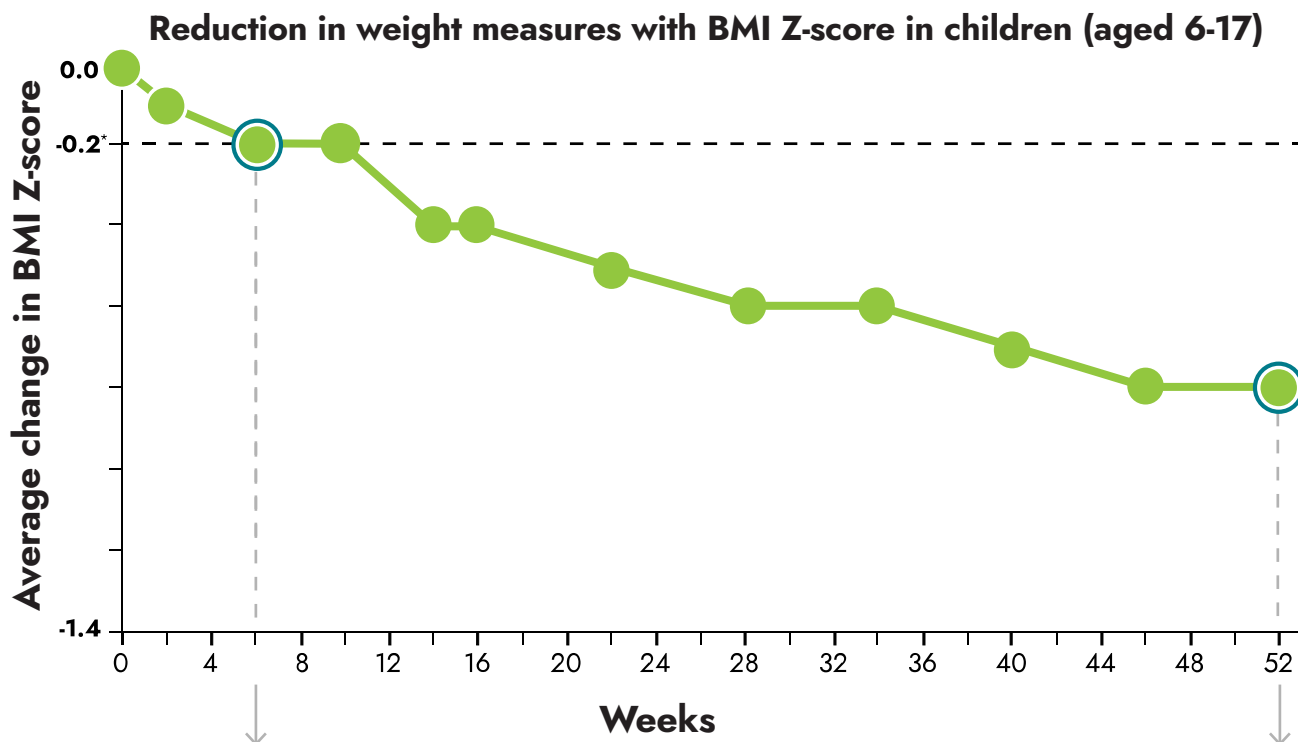


## Important Safety Information (cont'd)

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 helped children reach steady and long-lasting reduction in weight measures



## Meaningful reduction in weight measures starting in <2 months

On average, children saw a meaningful reduction in weight measures (generally considered 0.2 reduction) after 6 weeks\*

## Steady reduction in weight measures during year 1

Children continued to see a reduction in weight measures by BMI Z-score over the course of their first year of treatment

◆ 16 children between the ages of 6 to 17 were evaluated as part of the study.

\*A clinically meaningful reduction is generally defined as a reduction of greater than or equal to 0.2 in BMI Z-score.

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# IMCIVREE is the first and only treatment to significantly reduce BMI Z-score in children with obesity due to BBS



Actor portrayals.

86% ↓

of children had a meaningful reduction in BMI Z-score over 1 year

**No change in diet or exercise:** In the clinical trial, people were not required to change their diet or exercise routine

## 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



# After 2 years, IMCIVREE helped children maintain meaningful reductions in BMI Z-score\*

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 people had a meaningful reduction in BMI Z-score after 2 years

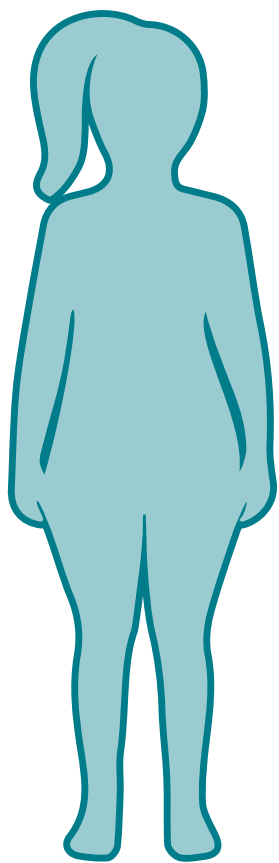
- ◆ There was a 0.72 average reduction in BMI Z-score
- ◆ 12 children between the ages of 6 to 17 years were evaluated as part of the 2 year follow-up study

He weighs so much less...he doesn't struggle to carry that weight anymore. — Caregiver of a child taking IMCIVREE

\*A clinically meaningful reduction is generally defined as a reduction of greater than or equal to 0.2 in BMI Z-score.

# IMCIVREE reduced the severity of obesity in children living with BBS

You may be more familiar with viewing a child's growth as a percentile on a chart from the doctor. These same charts can be used for BMI.



This growth chart is a hypothetical representation of what a 12-year-old female with BBS who is taking IMCIVREE may experience in BMI reduction after 1 and 2 years, based on results from the clinical study.

- ◆ At the start of the clinical trial, BMI was 145% of the 95th percentile
- ◆ At the end of the clinical trial, BMI was 128% of the 95th percentile
  - 17-percentage-point reduction
- ◆ After 2 years in a long-term extension of the clinical trial, BMI was 115% of the 95th percentile
  - 30-percentage-point reduction

With 2 continuous years of treatment, **IMCIVREE helped children living with BBS achieve a healthier BMI**

## Important Safety Information (cont'd)

What are the possible side effects of IMCIVREE? IMCIVREE may cause serious side effects, including: (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

## Hypothetical growth chart based on clinical study data of IMCIVREE

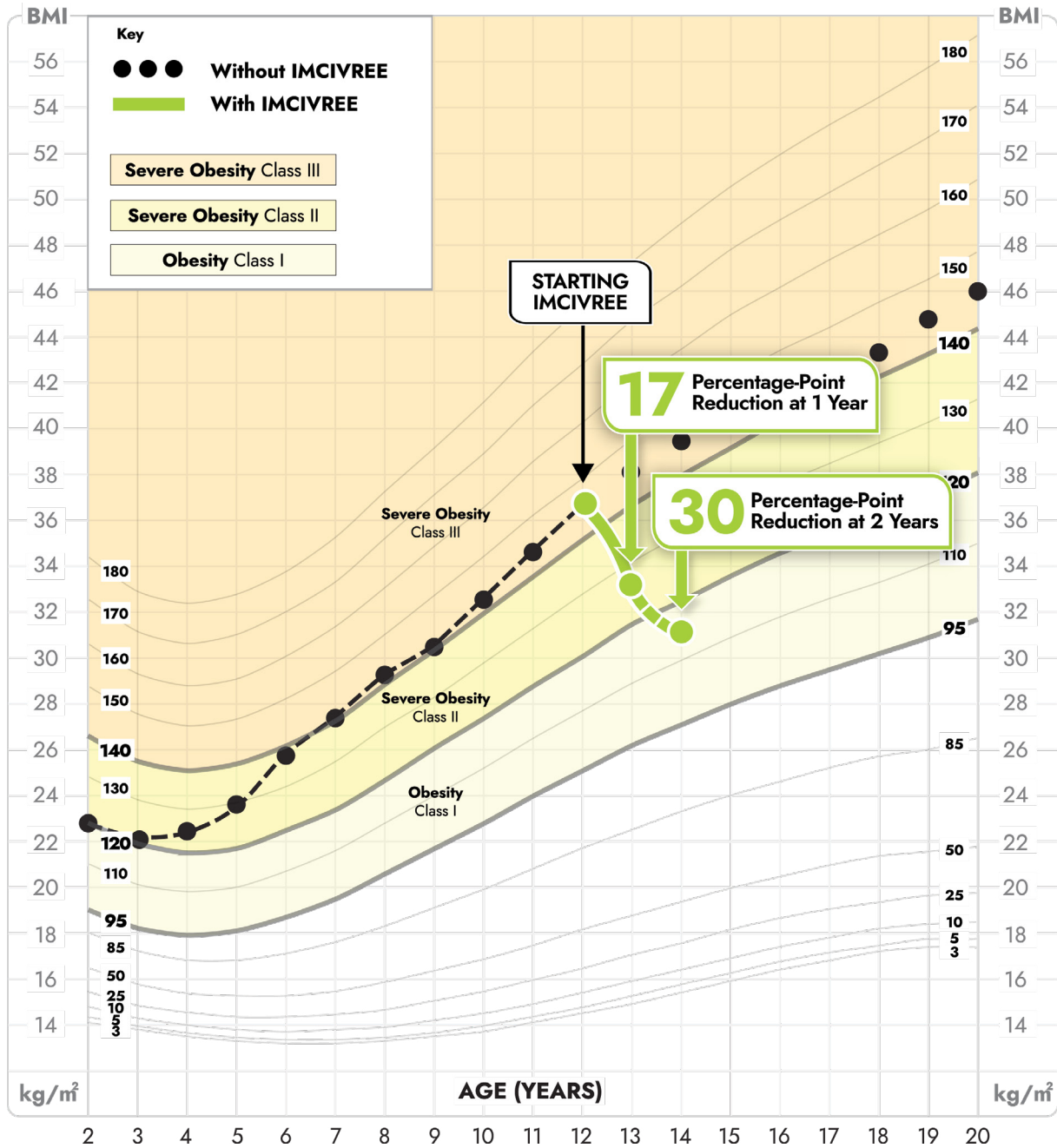
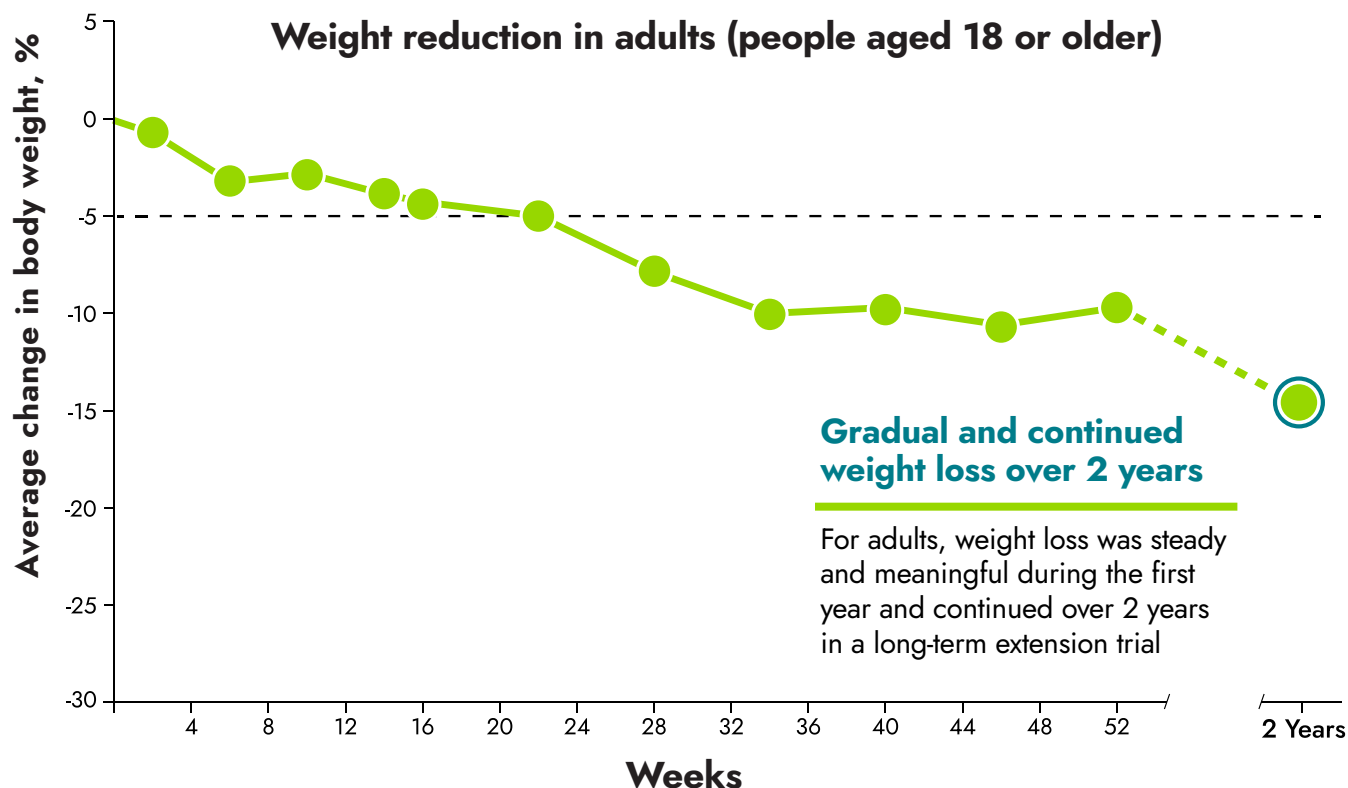


Figure modeled after Gulati AK, Kaplan DW, Daniels SR. Clinical tracking of severely obese children: a new growth chart. *Pediatrics*. 2012 Dec;130(6):1136-40.

Not an actual patient. Growth chart is based on females 2 to 20 years of age and is for illustrative purposes only.

# How did IMCIVREE help adults lose weight in the clinical trial?



- ◆ IMCIVREE reduced body weight over the course of the 1-year clinical trial
- ◆ 15 adults aged 18 years or older were evaluated as part of the study

## Important Safety Information (cont'd)

What are the possible side effects of IMCIVREE? IMCIVREE may cause serious side effects, including: (cont'd)

- ◆ **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 helped adults reach steady and long-lasting weight reduction

14 weeks  
**4%** ↓

Average reductions in weight

11 pounds lost on average

1 year  
**10%** ↓

Average reductions in weight

20 pounds lost on average

2 years  
**15%** ↓

Average reductions in weight

Adults who continued treatment with IMCIVREE lost even more weight over 2 years

◆ 6 adults were part of the study at 24 months

At the end of the clinical trial for IMCIVREE, 19 people continued in a long-term study. 6 of those 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

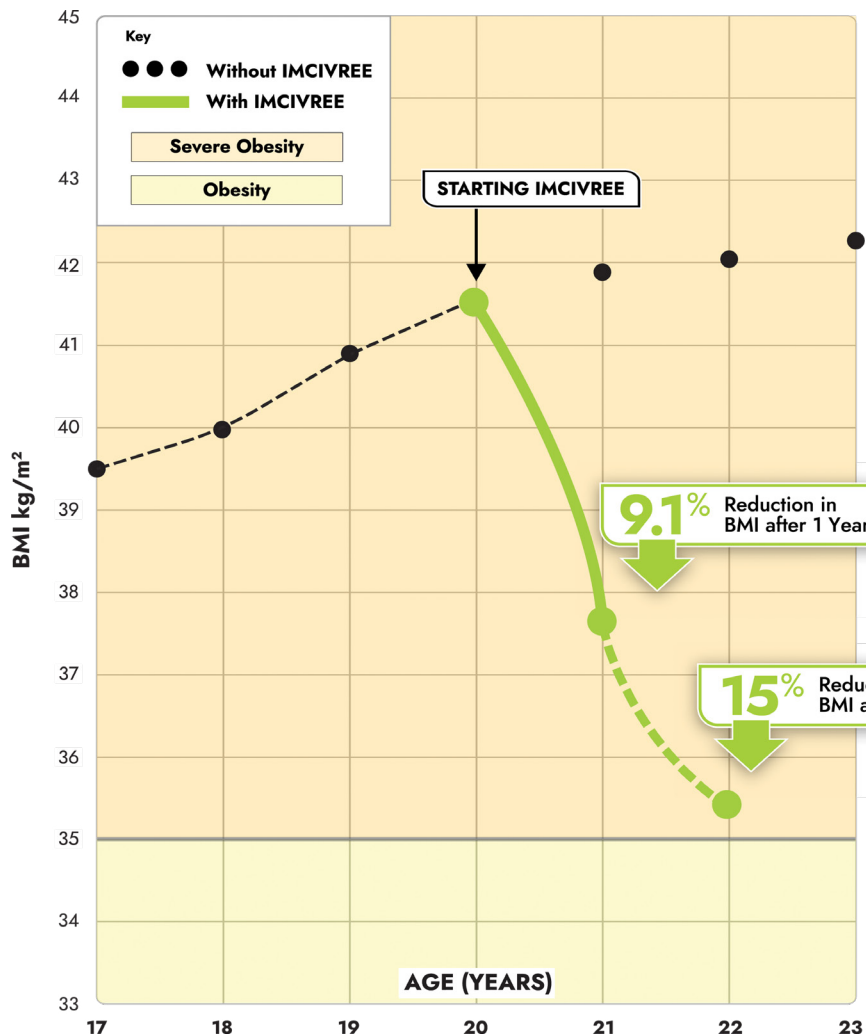
**No change in diet or exercise:** In the clinical trial, people were not required to change their diet or exercise routine

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# IMCIVREE reduced the severity of obesity in adults living with BBS

Hypothetical BMI chart based on clinical study data of IMCIVREE



This BMI chart is a hypothetical representation of the BMI reduction an adult with BBS may experience after 1 and 2 years of treatment on IMCIVREE, based on data from the clinical trial.

## Important Safety Information (cont'd)

What are the possible side effects of IMCIVREE? IMCIVREE may cause serious side effects, including: (cont'd)

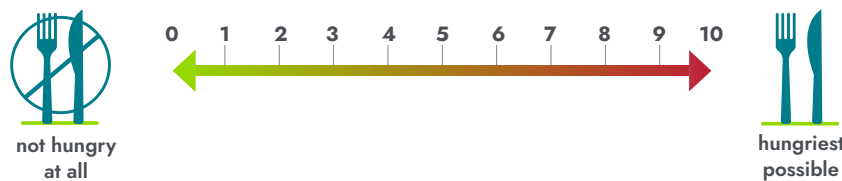
- ◆ Increased skin pigmentation and darkening of skin lesions (moles or nevi) you already have. These changes happen because of how IMCIVREE works in the body and will go away when you stop using IMCIVREE. You should have a full body skin exam before starting and during treatment with IMCIVREE to check for skin changes

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

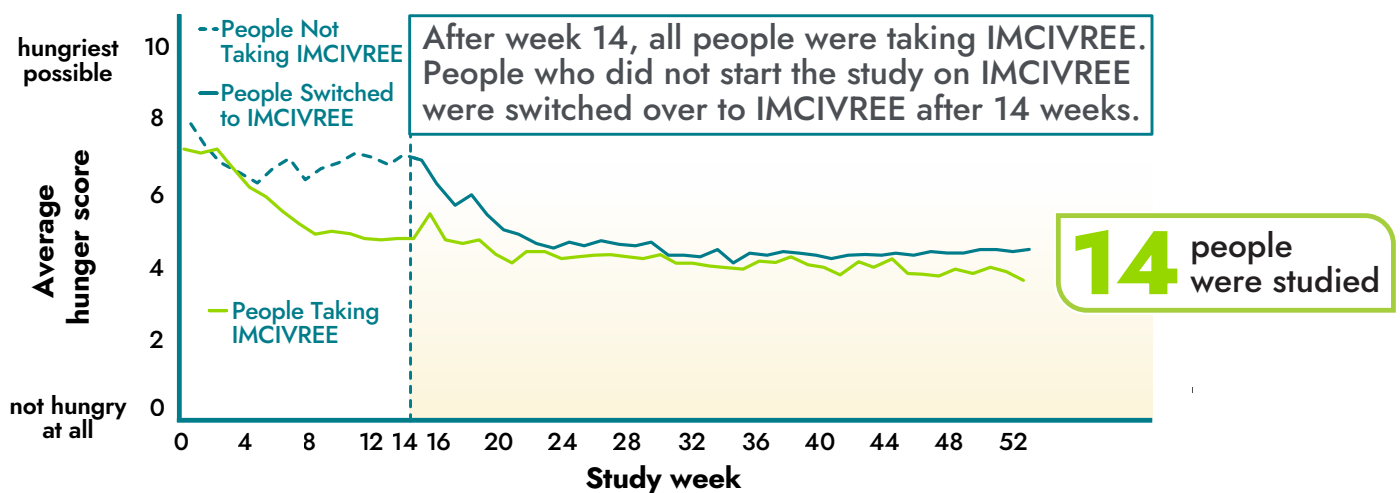
IMCIVREE provided reduction in hunger scores early and continuously throughout treatment

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



## IMCIVREE reduced the most severe feelings of hunger



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

# 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:

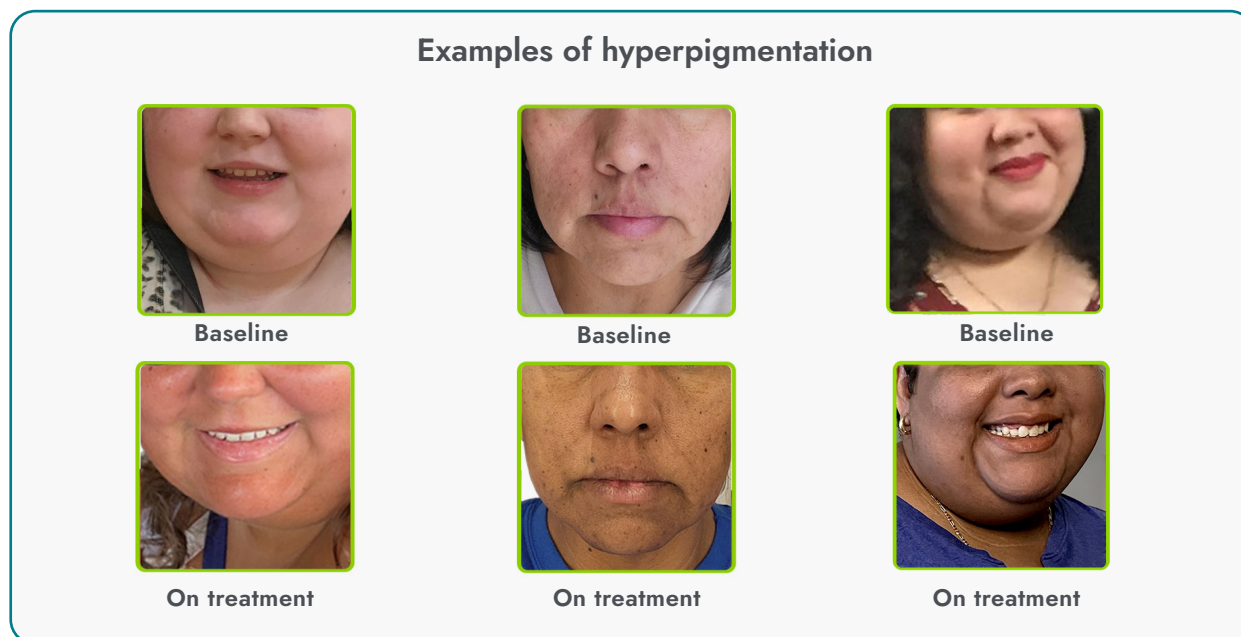
- ◆ Darkening of the skin (hyperpigmentation) (63%)
- ◆ Injection site reactions (51%)
- ◆ Nausea (26%)
- ◆ Erection that happens without any sexual activity in males (25%)
- ◆ Vomiting (19%)
- ◆ Diarrhea (14%)
- ◆ Headache (7%)
- ◆ Stretch marks (7%)
- ◆ Aggression (5%)
- ◆ Fatigue (5%)

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

Contact your doctor if you are experiencing side effects.



**A general darkening of the skin (hyperpigmentation) is common due to the way in which IMCIVREE works**



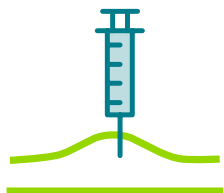
- ◆ Darkening of the skin and/or hair is expected, as IMCIVREE may lead to increased production of melanin (which gives color to your skin)
- ◆ The degree of skin darkening can vary from person to person and can sometimes include darkening of existing skin growths (such as moles)
- ◆ In a clinical trial, hyperpigmentation increased over the first several weeks of IMCIVREE use and leveled off in the initial months of treatment
- ◆ Darkening of the skin went away when people stopped using IMCIVREE
- ◆ You should have a full-body skin exam before starting and during treatment with IMCIVREE to check for skin changes
- ◆ If hyperpigmentation is a concern, talk to your doctor, and they will assess your response to treatment and work with you to create a plan forward with IMCIVREE to check for skin changes

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

# How is IMCIVREE given?

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

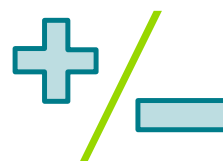
IMCIVREE is given:



As an injection  
under the skin



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



With or  
without food

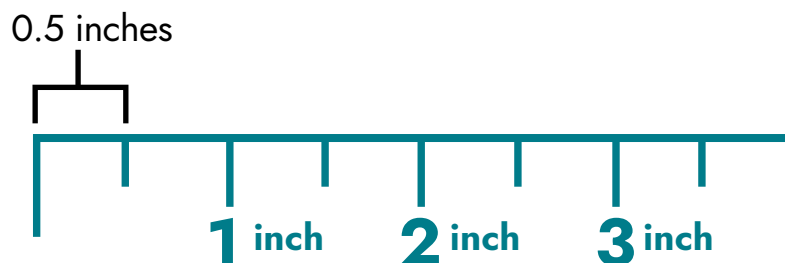
## Important Safety Information (cont'd)

What are the possible side effects of IMCIVREE? IMCIVREE may cause serious side effects, including: (cont'd)

- ◆ **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.



Actor portrayal.

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

— Caregiver of child taking IMCIVREE

# Getting started on IMCIVREE



## Deciding on IMCIVREE

You and your doctor decide whether IMCIVREE is an appropriate treatment. If you agree on IMCIVREE, your doctor will submit a start form along with your consent to enroll in **Rhythm InTune**. Rhythm InTune is your dedicated source for personalized support, which includes helping you understand insurance coverage and exploring financial assistance options for eligible patients. **For more information about Rhythm InTune, please turn to pages 26 and 27.**

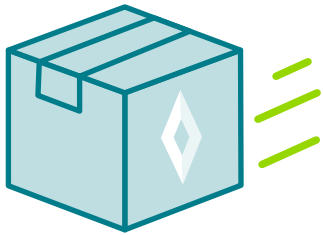


## Learning to inject IMCIVREE

Injection training is offered before you start IMCIVREE. Training can be given by your doctor or coordinated through Rhythm InTune.

## 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.



## Starting on IMCIVREE

IMCIVREE is only available through what is known as a specialty pharmacy. Rhythm InTune will coordinate delivery of IMCIVREE. You should start IMCIVREE at your starting dose, as directed by your doctor.



## Staying on IMCIVREE

Your doctor will monitor you for the first few weeks while you are on IMCIVREE. During this time, they may increase or decrease your dose until you reach the target dose.

**Rhythm InTune provides personalized support and educational resources and programs throughout treatment to help you start and stay on IMCIVREE**



## Your source for personalized support

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

### 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 are encouraged to report negative side effects of prescription drugs to the FDA. Visit [www.fda.gov/medwatch](http://www.fda.gov/medwatch) or call 1-800-FDA-1088.



# What can Rhythm InTune do for you?

Rhythm InTune provides resources, education, and information tailored to fit the unique needs of people living with rare genetic diseases of obesity, including BBS.

Rhythm InTune can help you:



Access educational resources



Connect to a community



Understand your insurance coverage



Get started on a Rhythm treatment

**Patient Education Managers** are employees of Rhythm Pharmaceuticals and do not provide medical care or advice. We encourage you to always speak to your healthcare provider regarding your medical care.

If you're interested in speaking with a Patient Education Manager about the education and support Rhythm InTune can offer you or the person you care for, you can email or call us at:



[patientsupport@rhythmtx.com](mailto:patientsupport@rhythmtx.com)



1-855-206-0815

# Important notes and reminders

This is a space to write down important notes or reminders for yourself or the person you care for living with BBS. These can include any questions you want to remember to ask your doctor about BBS or IMCIVREE, or any resources you would like to request from Rhythm InTune.

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## Important Safety Information (cont'd)

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.



**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**

### **What is IMCIVREE?**

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.

### **Important Safety Information**

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.



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