


For Bardet-Biedl syndrome (BBS)



Discover a World Beyond Obesity

Actor portrayals.

IMCIVREE[®]
(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.

Important Safety Information

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.

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



Actor portrayals.

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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.

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

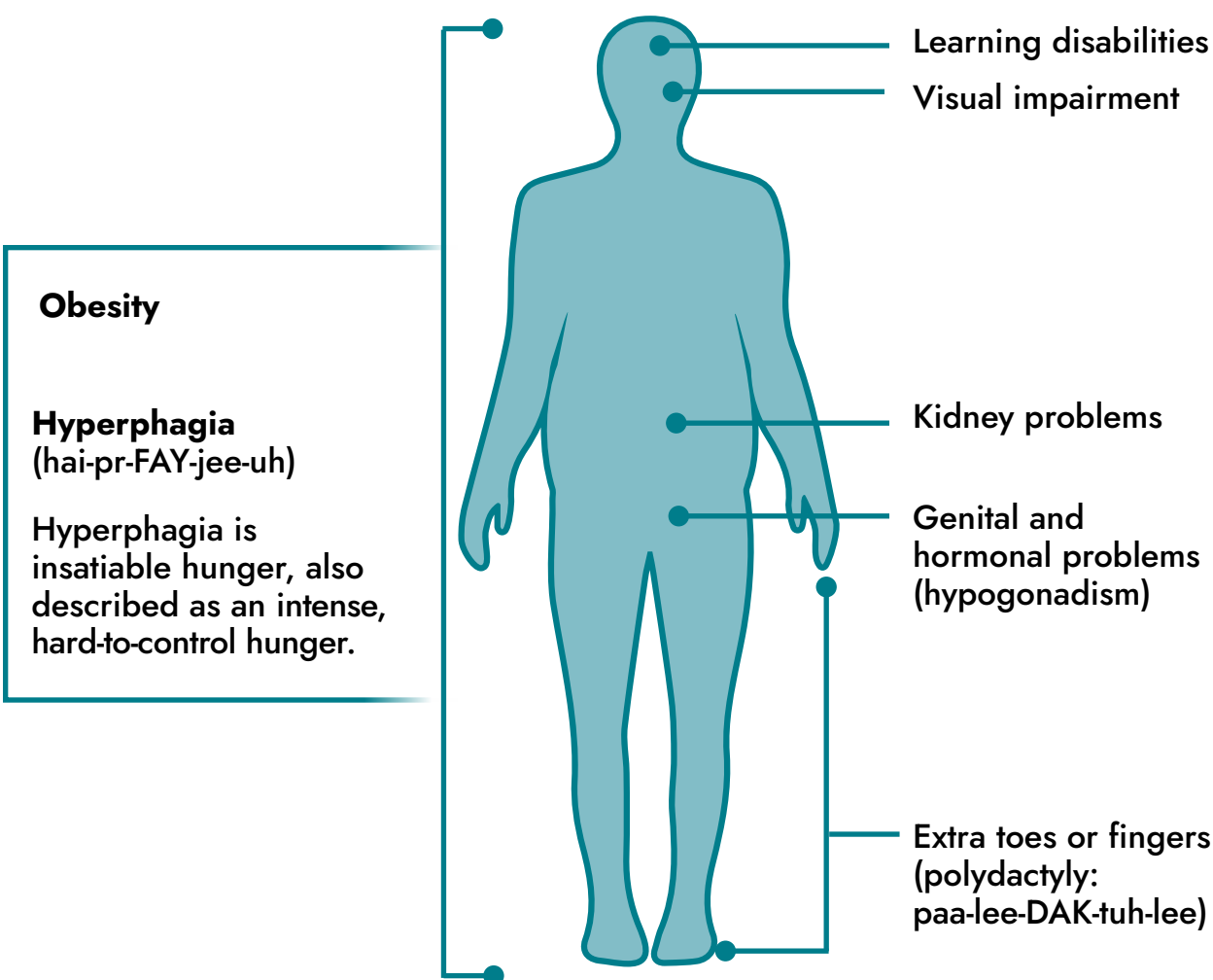
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What is BBS?

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

BBS has a wide range of symptoms



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.



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.



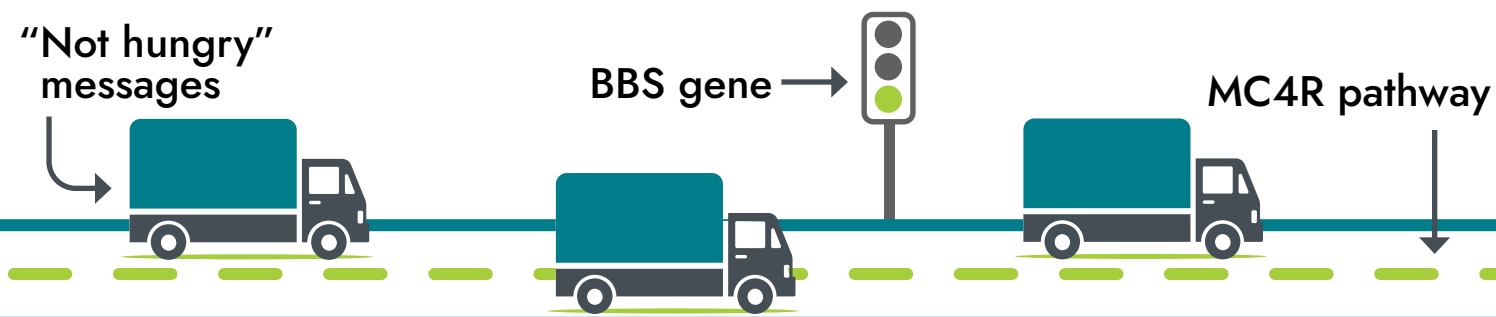
The trucks on this road deliver messages between the body and the brain. These messages control hunger.



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

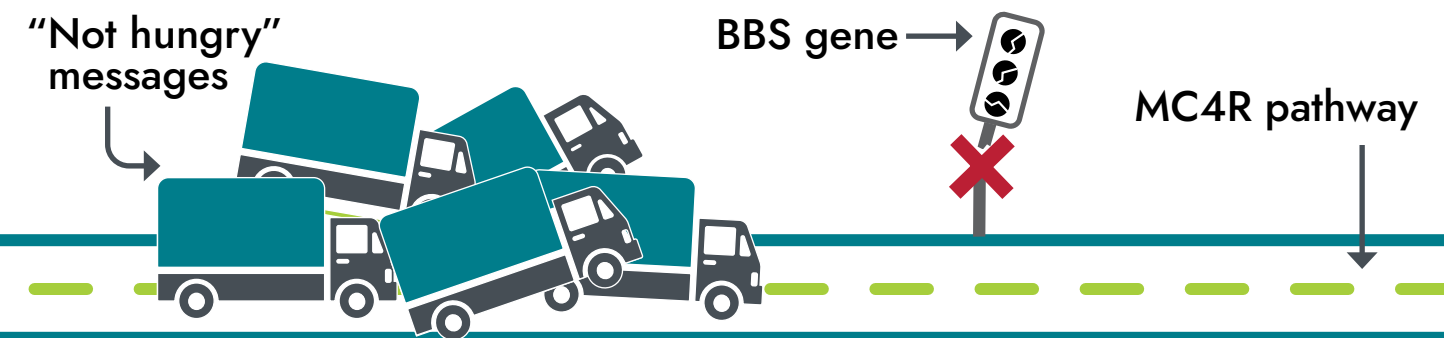
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In people living with BBS, the traffic light is broken due to the change in the BBS gene



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)

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

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
- ◆ 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

How was IMCIVREE studied?

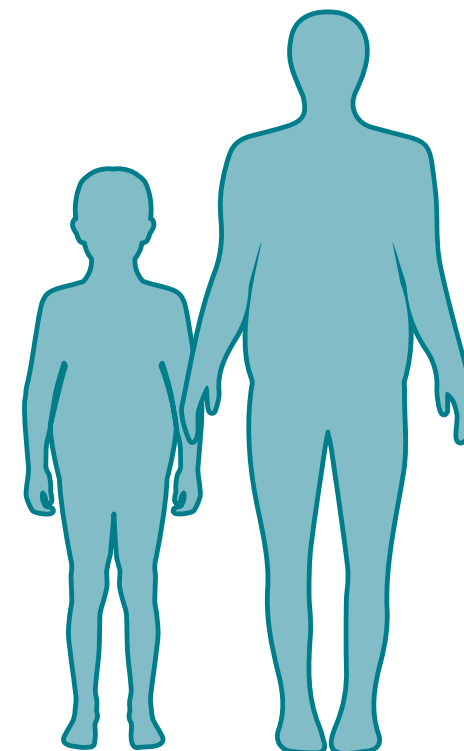
IMCIVREE was studied in both children and adults in a yearlong clinical trial

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.



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.
[†]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)

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



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[‡]

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.



- ◆ There was a 0.72 reduction in BMI Z-score[†]

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 a child taking IMCIVREE

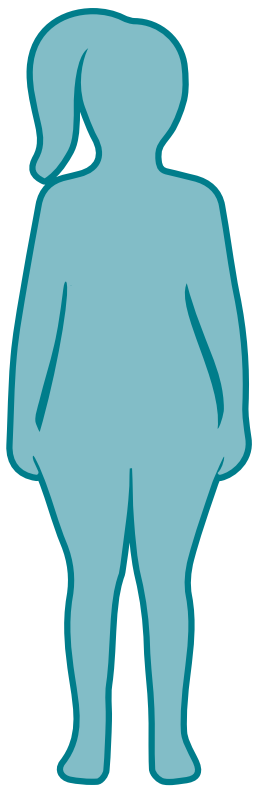


[‡]Change in BMI Z-score could not be calculated for one 20-year-old patient who was 17 years old at the beginning of the original trial.
[§]N=12

Actor portrayals.

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 represents what a 12-year-old female* with BBS who is taking IMCIVREE may experience in BMI reduction after 1 year, based on results from the clinical study.

- ◆ At the start of the clinical trial, average BMI was 145% of the 95th percentile
- ◆ At the end of the clinical trial, average BMI was 127% of the 95th percentile
- 17-percentage-point reduction

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.

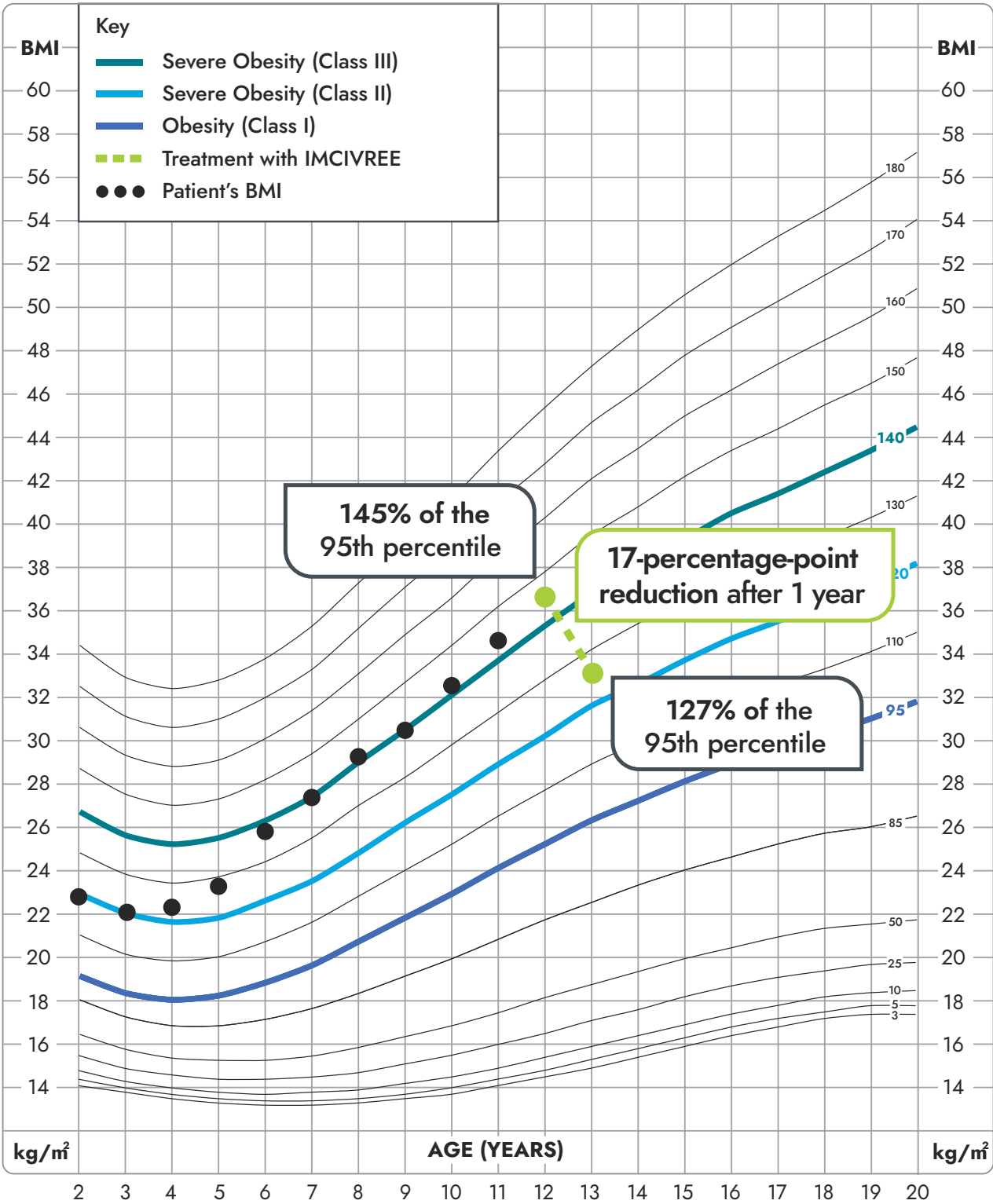


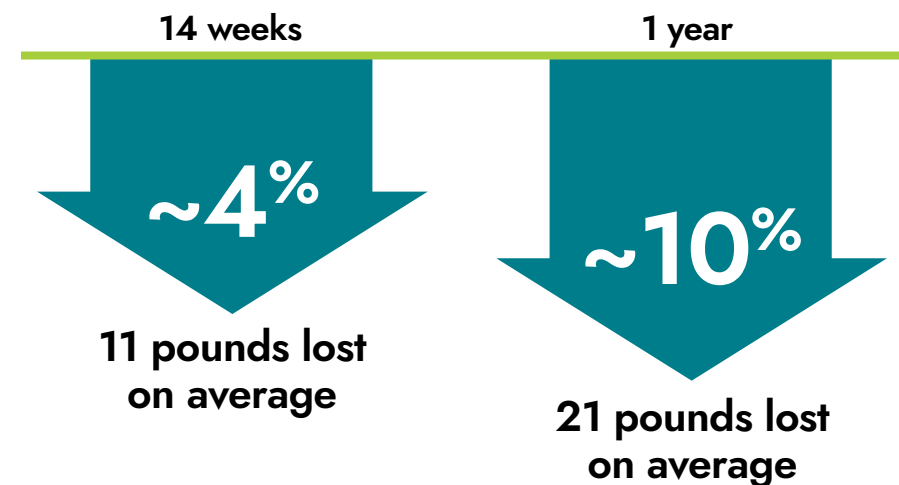
Figure modeled after Gulati AK, Kaplan DW, Daniels SR. Clinical tracking of severely obese children: a new growth chart. *Pediatrics*. 2012 Dec;130(6):1136-40

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

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:

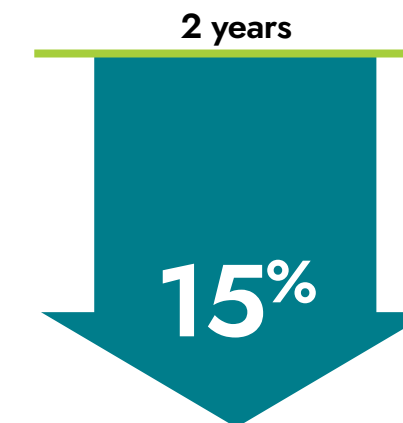
- ◆ Male and female sexual function problems. IMCIVREE can cause an erection that happens without any sexual activity in males (spontaneous penile erection) and unwanted sexual reactions (changes in sexual arousal that happen without any sexual activity) in females. If you have an erection lasting longer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



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‡



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

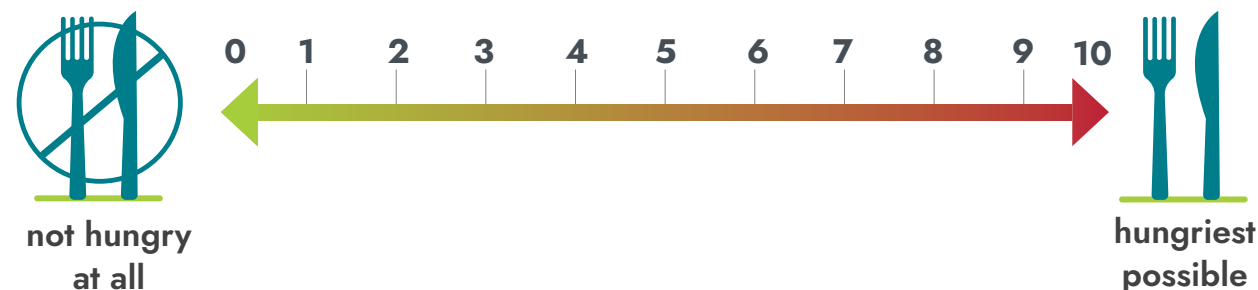
‡N=6.

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)

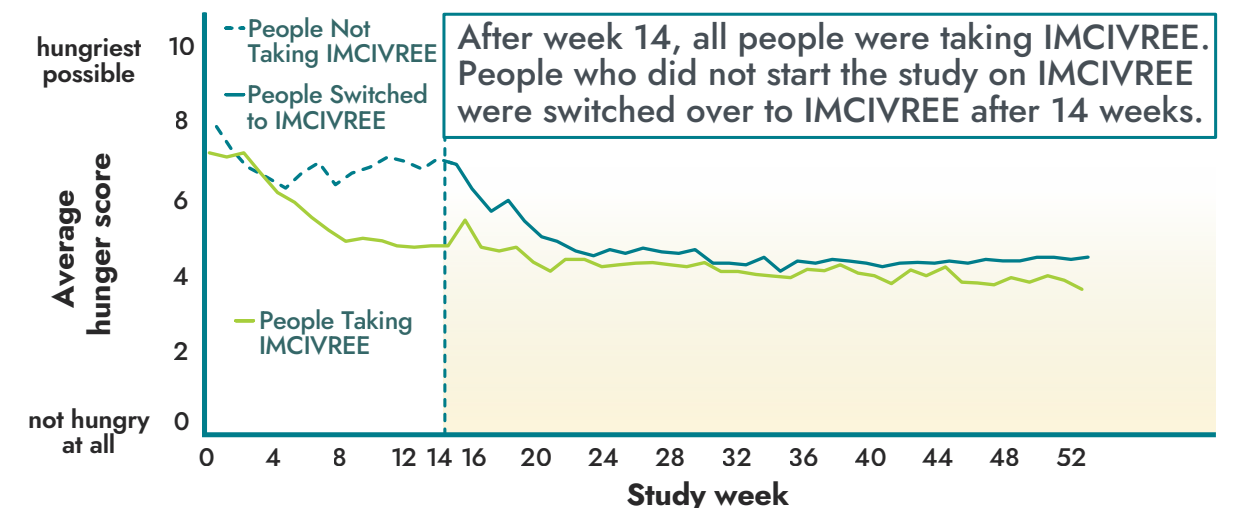
IMCIVREE may cause serious side effects, including: (cont'd)

- ◆ 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



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

IMCIVREE reduced the most severe feelings of hunger



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

He was feeling full and that was a new feeling for him. He didn't quite know how to describe it. He started eating less and started talking about food less.

— Caregiver of a child enrolled in the IMCIVREE clinical trial



Actor portrayals.

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* (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%)

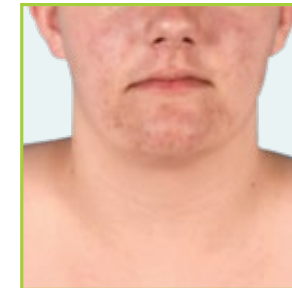
Most nausea and vomiting events were mild, and none were severe. Nausea and vomiting were primarily reported within the first month of treatment and then sharply declined. These symptoms typically lasted no more than a few days.

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

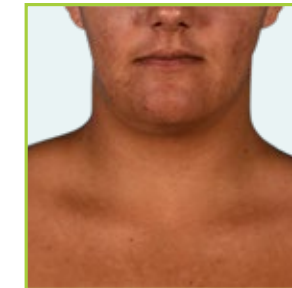
Contact your doctor if you are experiencing side effects.

*Hyperpigmentation.

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



Before IMCIVREE



During IMCIVREE treatment



After stopping IMCIVREE

Example of hyperpigmentation

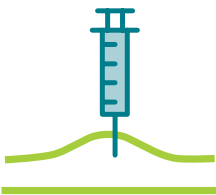
- ◆ IMCIVREE may also lead to an increased production of melanin (which gives color to your skin)
 - This usually occurs within the first month of starting IMCIVREE
 - Darkening of the skin may vary
- ◆ IMCIVREE can cause darkening of existing skin growths, such as moles
- ◆ You should have a full-body skin exam before starting and during treatment with IMCIVREE to check for skin changes
- ◆ No cases of melanoma have been reported in connection with the administration of IMCIVREE in any of the clinical trials, which included more than 500 people
- ◆ 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.

How is IMCIVREE given?

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

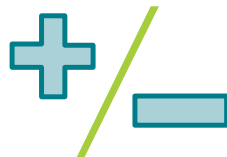
IMCIVREE is given:



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)

IMCIVREE may cause serious side effects, including: (cont'd)

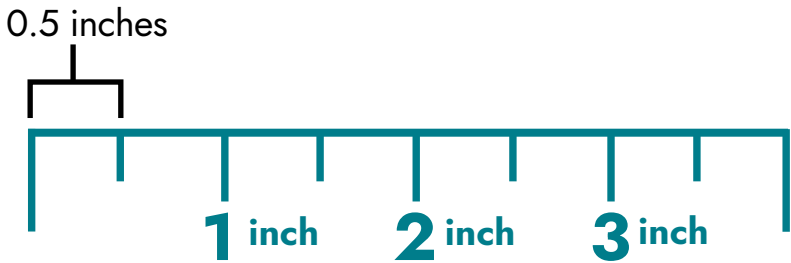
- ◆ Increased skin pigmentation and darkening of skin lesions (moles or nevi) you already have. These changes happen because of how IMCIVREE works in the body and will go away when you stop using IMCIVREE. You should have a full body skin exam before starting and during treatment with IMCIVREE to check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



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

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.

Getting started on IMCIVREE



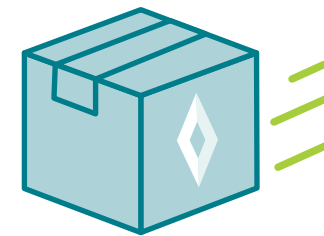
Deciding on IMCIVREE

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 24 and 25.**



Learning to inject IMCIVREE

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



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.

Important Safety Information (cont'd)

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

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)

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.

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.



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

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



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.

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



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Important Safety Information (cont'd)

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PHARMACEUTICALS

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US-SET-2200121 11/2022

Actor portrayals.

