In hereditary angioedema (HAE),
this is big.

In your day,
this is small.

Proven attack prevention
in the palm of your hand.

Capsule not actual size

What is ORLADEYO® (berotralstat)?

ORLADEYO (or-luh-DAY-oh) is a prescription medicine used to prevent attacks of hereditary angioedema (HAE) in adults and children 12 years of age and older. It is not known if ORLADEYO is safe and effective in children under 12 years of age.

It is not known if ORLADEYO is safe and effective to treat an acute HAE attack, therefore ORLADEYO should not be used to treat an acute HAE attack.

Do not take more than one capsule of ORLADEYO per day because extra doses can cause heart rhythm problems.

Please see Important Safety Information on page 13 and accompanying full Prescribing Information, including the Patient Information.

orladeyo®
(berotralstat) capsules 150 mg

orladeyo®
(berotralstat) capsules 150 mg

Introduction to this brochure

You may have received this brochure because you or a loved one want to know more about ORLADEYO®, the first and only oral therapy designed specifically to prevent HAE attacks.

If you haven't already, set up time with your healthcare provider to discuss ORLADEYO (or-luh-DAY-oh) and review any questions you may have.

> "The only thing I'd change about my experience with ORLADEYO is finding it sooner."

– Kurtis, a real ORLADEYO patient on treatment since 2021

Individual results may vary

SELECT IMPORTANT SAFETY INFORMATION

Before taking ORLADEYO, tell your healthcare provider about all of your medical conditions, including if you

- have liver problems or are on kidney dialysis.
- are pregnant or planning to become pregnant. It is not known if ORLADEYO can harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if ORLADEYO passes into your breastmilk. Talk to your healthcare provider about the best way to feed your baby while taking ORLADEYO.

Please see Important Safety Information on page 13 and accompanying full Prescribing Information, including the Patient Information.

orladeyo®
(berotralstat) capsules 150 mg

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SELECT IMPORTANT SAFETY INFORMATION

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

Taking ORLADEYO with certain other medicines may affect the way other medicines work and other medicines may affect how ORLADEYO works.

Know the medicines you take and keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

Please see Important Safety Information on page 13 and accompanying full Prescribing Information, including the Patient Information.

orladeyo®
(berotralstat) capsules 150 mg

Living with HAE

Everyone experiences their disease differently, but regardless of where you are in your journey, HAE likely affects—or has affected—your life in a number of ways.

Scan the QR code to see this study come to life.

Treating your HAE

As you may already know, there are 2 types of therapies used to treat HAE, and people living with HAE often use both types.

- **Rescue therapy**, or acute therapy, is used to help manage or lessen symptoms when an attack is coming on or has already started
- **Preventative therapy**, or prophylactic therapy, is taken regularly as a way to help stop HAE attacks from happening

Because treatment with rescue therapy alone is not always enough, people living with HAE often use both types of therapy to manage their disease. Long-term treatment with preventative therapy is the best way to prevent future HAE attacks.

orladeyo®
(berotralstat) capsules 150 mg

As your life changes, your treatment plan might need to change, too

Making decisions with your healthcare team can lead to better results. As you and your healthcare provider discuss the preventative therapy that's right for you, here are some factors to consider:

- **How it's given (injection, infusion, orally)**
- **How safe it is**
- **How it fits into your lifestyle**
- **How well it prevents attacks**
- **How it may help reduce the use of rescue therapy**

In a study of 75 people living with HAE

~90% say **they have learned to tolerate** difficult aspects of their treatment

75% **try not to think about** the demanding nature of their treatment

Some preventative therapies include intravenous infusions, subcutaneous injections, or oral androgens. These options often mean injecting oneself up to **122 times per year** depending on the treatment. So why not try something that may be better suited to your lifestyle?

orladeyo®
(berotralstat) capsules 150 mg

"I hate needles. I do everything I can to avoid needles, so the pill was refreshing."

– Kissa, a real ORLADEYO® patient on treatment since 2018

Individual results may vary

Scan the QR code to hear more patient experiences.

Capsule not actual size

SELECT IMPORTANT SAFETY INFORMATION

What are the possible side effects of ORLADEYO?

Taking more than one capsule of ORLADEYO per day may cause serious side effects, including **heart rhythm problems**. A heart rhythm problem called QT prolongation can happen in people who take more than one capsule of ORLADEYO per day. This condition can cause an abnormal heartbeat. Do not take more than one capsule of ORLADEYO per day.

Please see Important Safety Information on page 13 and accompanying full Prescribing Information, including the Patient Information.

orladeyo®
(berotralstat) capsules 150 mg

Proven attack prevention in a daily pill

Easy administration
One 150 mg[a] capsule, once per day with food

Flexible dosing
As long as it's taken at the same time of day, ORLADEYO® can be taken anywhere

Convenient storage
Room temperature; no refrigeration needed

Innovative design
Not dependent on the availability of human plasma

ORLADEYO works to prevent HAE attacks by decreasing the activity of a certain protein called kallikrein.

[a]Some people, including those with liver problems and those on certain medicines, may need to take a lower dosage—one 110 mg capsule, once per day with food. Your healthcare provider will tell you which dose is appropriate for you.

Scan the QR code to see kallikrein in action.

SELECT IMPORTANT SAFETY INFORMATION

What are the possible side effects of ORLADEYO (cont'd)

The most common side effects of ORLADEYO include abdominal pain, vomiting, diarrhea, back pain, and heartburn. These are not all of the possible side effects of ORLADEYO. For more information, ask your healthcare provider or pharmacist.

Talk to your healthcare provider for medical advice about side effects.

Please see Important Safety Information on page 13 and accompanying full Prescribing Information, including the Patient Information.

orladeyo®
(berotralstat) capsules 150 mg

"One of the main reasons I switched to ORLADEYO is because of the amount of time it took to give myself a shot once a month. As long as [I have my] pill with [me], the freedom is amazing."

– Kurtis, a real ORLADEYO® patient on treatment since 2021

Individual results may vary

Scan the QR code to hear more patient experiences.

SELECT IMPORTANT SAFETY INFORMATION

Before taking ORLADEYO, tell your healthcare provider about all of your medical conditions, including if you

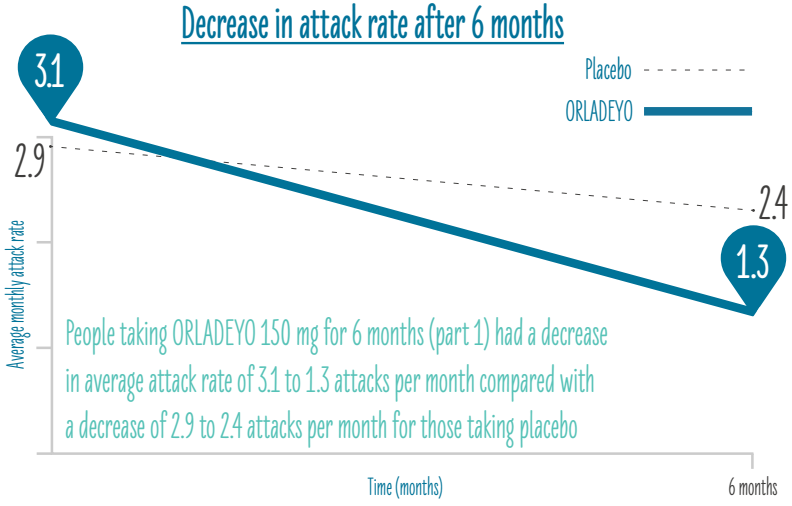
- have liver problems or are on kidney dialysis.
- are pregnant or planning to become pregnant. It is not known if ORLADEYO can harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if ORLADEYO passes into your breastmilk. Talk to your healthcare provider about the best way to feed your baby while taking ORLADEYO.

Please see Important Safety Information on page 13 and accompanying full Prescribing Information, including the Patient Information.

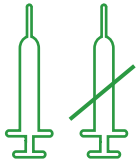
orladeyo®
(berotralstat) capsules 150 mg

Proven HAE attack prevention in the palm of your hand

In a 3-part study of 120 adolescents and adults with HAE, 40 were given ORLADEYO® 150 mg, 41 were given ORLADEYO 110 mg, and 39 were given placebo



Scan the QR code to see this study come to life.



The use of rescue therapy was cut by more than half in people taking ORLADEYO 150 mg compared with people taking placebo[a]

As you know, people living with HAE are all different, and everyone responds differently to treatment (even within families). When it comes to ORLADEYO, see for yourself.

[a]Based on data from an ad-hoc analysis of the first 6 months of the study (part 1).

SELECT IMPORTANT SAFETY INFORMATION

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

Taking ORLADEYO with certain other medicines may affect the way other medicines work and other medicines may affect how ORLADEYO works.

Know the medicines you take and keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

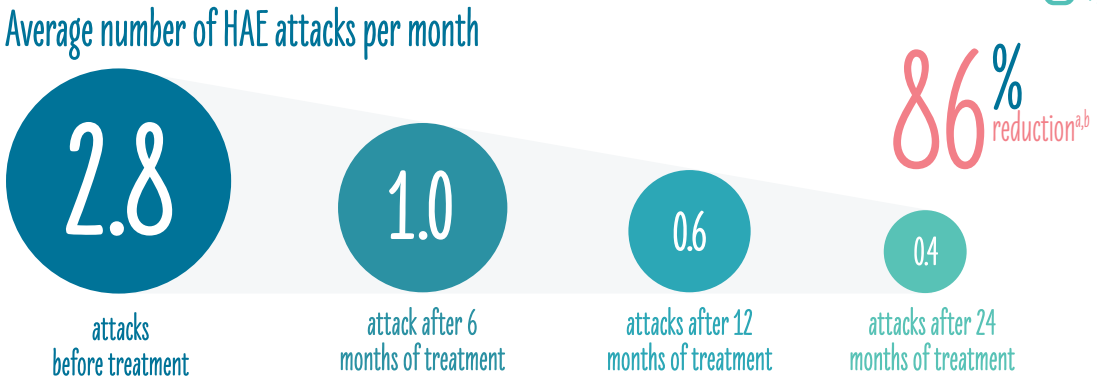
Please see Important Safety Information on page 13 and accompanying full Prescribing Information, including the Patient Information.

orladeyo®
(berotralstat) capsules 150 mg

Continued attack rate reduction over 2 years

Among 21 people with HAE who took ORLADEYO® 150 mg for a total of 24 months their average number of attacks per month dropped considerably[a]

Scan the QR code to see this study come to life.



MORE THAN HALF OF PEOPLE HAD 0 ATTACKS in 16 of the last 17 months of treatment[a]

It's important to stick to the treatment plan you've made with your healthcare provider for the best chance at a successful treatment experience.

[a]Based on data from an ad-hoc analysis of interim data (the trial investigators explored this trend after the trial was designed and before the final data analysis).
[b]At 24 months, average attack rate was lowered by 86% compared with pretreatment for the 21 people who completed the full 24 months of treatment with ORLADEYO 150 mg.

SELECT IMPORTANT SAFETY INFORMATION

What are the possible side effects of ORLADEYO?

Taking more than one capsule of ORLADEYO per day may cause serious side effects, including **heart rhythm problems**. A heart rhythm problem called QT prolongation can happen in people who take more than one capsule of ORLADEYO per day. This condition can cause an abnormal heartbeat. Do not take more than one capsule of ORLADEYO per day.

Please see Important Safety Information on page 13 and accompanying full Prescribing Information, including the Patient Information.

orladeyo®
(berotralstat) capsules 150 mg

Side effects of ORLADEYO® have been studied in multiple clinical studies over several years

In the first 6 months of the clinical study (part 1)

- The most common[a] side effects were abdominal pain, vomiting, diarrhea, back pain, and heartburn. These are not all of the possible side effects of ORLADEYO. For more information, ask your healthcare provider or pharmacist

- Not everyone experienced GI side effects. For those who did, they generally occurred early after starting treatment, became less frequent with time, and typically got better on their own

- No one being treated with ORLADEYO 150 mg discontinued therapy due to gastrointestinal (GI) side effects
- One person being treated with ORLADEYO 110 mg discontinued. If you experience GI side effects that don't go away, your healthcare provider may prescribe a reduced dosage of ORLADEYO (110 mg, once daily with food)
- No new types of side effects were seen in those who continued ORLADEYO for 2 years
- Another clinical study of 227 people looked at the safety of ORLADEYO and found results that support the findings from the previous study

What to avoid when taking ORLADEYO

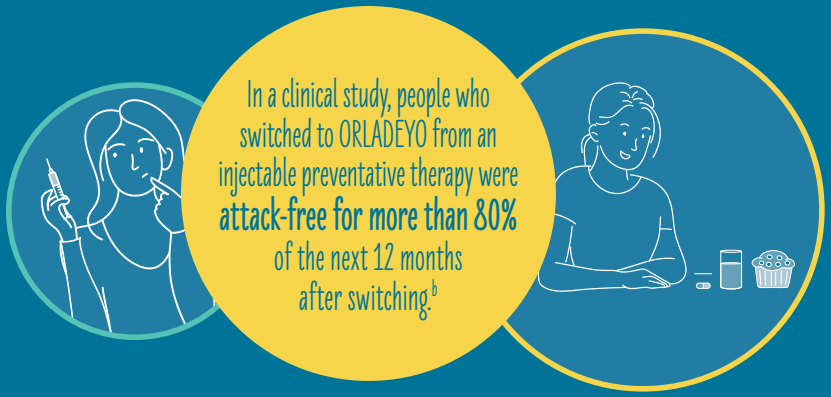
- Do not take ORLADEYO to treat an acute swelling attack; it is not known if ORLADEYO is safe or effective in treating acute attacks
- Do not take additional doses of ORLADEYO to treat an acute swelling attack
- Do not take more than 1 capsule of ORLADEYO per day because extra doses can cause **heart rhythm problems**. If you do, call your healthcare provider right away
- Do not start taking ORLADEYO without telling your healthcare provider about all the medicines you take. Taking ORLADEYO with certain other medicines may affect the way those medicines work and other medicines may affect how ORLADEYO works

Don't forget to give your body time to adjust to new medication–even if you were on a previous preventative therapy.

[a]Side effects that occurred in at least 10% of people taking ORLADEYO and more frequently than in those taking placebo.

orladeyo®
(berotralstat) capsules 150 mg

Almost half of people who are currently on ORLADEYO® were previously taking another preventative therapy, including an injectable[a]



In a clinical study, people who switched to ORLADEYO from an injectable preventative therapy were **attack-free for more than 80%** of the next 12 months after switching.[b]

These same patients reported improved convenience and similar effectiveness as their previous therapy.[b,c]

Join more than 2000 others who have been prescribed ORLADEYO, the fastest-growing therapy in HAE.[d]

[a]Data current as of February 2023.
[b]These data are from an analysis of 34 US patients who switched from an injectable prophylaxis to ORLADEYO during a long-term safety study. It is unknown what these patients would have experienced had they remained on injectable prophylaxis.
[c]According to a questionnaire that measures medication satisfaction. The efficacy and safety of ORLADEYO compared with other treatments have not been established.
[d]Based on data on file from a BioCryst Pharmaceuticals, Inc. third-party specialty pharmacy partner.

Scan the QR code to see why people are switching to ORLADEYO.

SELECT IMPORTANT SAFETY INFORMATION

What are the most common side effects of ORLADEYO? (cont'd)

The most common side effects of ORLADEYO include abdominal pain, vomiting, diarrhea, back pain, and heartburn. These are not all of the possible side effects of ORLADEYO. For more information, ask your healthcare provider or pharmacist.

Talk to your healthcare provider for medical advice about side effects.

Please see Important Safety Information on page 13 and accompanying full Prescribing Information, including the Patient Information.

Important Safety Information

WHAT IS ORLADEYO® (berotralstat)?

ORLADEYO (or-luh-DAY-oh) is a prescription medicine used to prevent attacks of hereditary angioedema (HAE) in adults and children 12 years of age and older. It is not known if ORLADEYO is safe and effective in children under 12 years of age.

It is not known if ORLADEYO is safe and effective to treat an acute HAE attack, therefore ORLADEYO should not be used to treat an acute HAE attack.

Do not take more than one capsule of ORLADEYO per day because extra doses can cause heart rhythm problems.

IMPORTANT SAFETY INFORMATION

Before taking ORLADEYO, tell your healthcare provider about all of your medical conditions, including if you

- have liver problems or are on kidney dialysis.
- are pregnant or planning to become pregnant. It is not known if ORLADEYO can harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if ORLADEYO passes into your breastmilk. Talk to your healthcare provider about the best way to feed your baby while taking ORLADEYO.

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

Taking ORLADEYO with certain other medicines may affect the way other medicines work and other medicines may affect how ORLADEYO works.

Know the medicines you take and keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

What are the possible side effects of ORLADEYO?

Taking more than one capsule of ORLADEYO per day may cause serious side effects, including **heart rhythm problems**. A heart rhythm problem called QT prolongation can happen in people who take more than one capsule of ORLADEYO per day. This condition can cause an abnormal heartbeat. Do not take more than one capsule of ORLADEYO per day.

The most common side effects of ORLADEYO include abdominal pain, vomiting, diarrhea, back pain, and heartburn. These are not all of the possible side effects of ORLADEYO. For more information, ask your healthcare provider or pharmacist.

Talk to your healthcare provider for medical advice about side effects.

You are encouraged to report side effects of prescription drugs to BioCryst Pharmaceuticals, Inc at 1-833-633-2279 or to the FDA at www.fda.gov/medwatch or 1-800-FDA-1088.

For more information, please see the accompanying full Prescribing Information, including the Patient Information.

EMPOWER
PATIENT SERVICES

Empower Patient Services is known for customer service and a team that truly cares

You'll be matched with your care team as soon as you enroll. They work with great dedication to support you and your healthcare provider throughout your ORLADEYO® journey. This is about more than just getting you started–they are genuinely invested in helping you achieve your goals. They care about you.

"They go above and beyond...If we have any questions, they are there for us, it's fantastic. That's the only way I could describe them. Empower is fantastic."

– A real ORLADEYO patient

Individual results may vary

In a survey of people with experience taking ORLADEYO,[a]
nearly everyone rated Empower Patient Services

10 OUT OF 10

for excellence

[a]Based on data from a qualitative study of 15 people.

Through Empower Patient Services, you'll have the opportunity to connect with someone who has firsthand experience with ORLADEYO.

orladeyo®
(berotralstat) capsules 150 mg

Scan the QR code to connect with our Empower Patient Services team.

Getting access and getting started—here's how we help

Financial assistance: Your dedicated Empower Patient Services care team will manage the insurance process and coordinate assistance based on eligibility.

- $0 copay if you are commercially insured (up to the annual program maximum to cover out-of-pocket expenses per calendar year)[a]
- Help with finding financial options for other out-of-pocket costs

Get started quickly: Your dedicated care team will work with your healthcare provider's office on insurance approval. To make sure you have therapy as soon as possible, you may be eligible to access ORLADEYO® while they're working through your approval via the Quick Start Program.[b]

Seamless transition: Your dedicated care team will coordinate the process of switching to ORLADEYO from another therapy to help make the transition as seamless as possible.

Custom delivery: Your dedicated care team will schedule refills and deliveries for a time and location that you choose. Empower Patient Services is a specialty pharmacy and support services program all in one.

Support while on therapy: Your dedicated care team will continue to work with you throughout your treatment with ORLADEYO and will connect you with resources that may be helpful.

Empower Patient Services is more than service—it's partnership.
To learn more about our unique offerings, give us a call at 1-866-5-EMPOWER (1-866-536-7693) or visit EmpowerORLADEYO.com.

[a]Subject to terms and conditions of the Co-pay Assistance Program which you can obtain from your Empower Patient Services team. BioCryst reserves the right to rescind, revoke, or amend the Program at any time without notice.

[b]Subject to terms and conditions of the Quick Start program. BioCryst reserves the right to rescind, revoke, or amend the program at any time without notice.

orladeyo®
(berotralstat) capsules 150 mg

Scan the QR code to meet our care team.

Notes

Notes

The preventative therapy that can change the way you treat your HAE

Simple administration
One 150 mg[a] capsule, once per day with food

Attack prevention
ORLADEYO® reduced attacks by 44% compared with placebo[b]

At 24 months, average attack rate was lowered by 86% compared with before starting treatment[c,d]

Established safety
In the first clinical study, GI events generally occurred early after starting treatment, became less frequent with time, and typically got better on their own

1-on-1 support
A dedicated care team will provide customized support for your individual needs

Switching to ORLADEYO
Most people who have been prescribed ORLADEYO were previously taking an injectable preventative therapy[d]

[a]Some people, including those with liver problems and those on certain medicines, may need to take a lower dosage—one 110 mg capsule, once per day with food. Your healthcare provider will tell you which dose is appropriate for you.
[b]In a clinical study of 40 patients who received ORLADEYO 150 mg once daily for 6 months.
[c]Based on data from an ad-hoc analysis of interim data (the trial investigators explored this trend after the trial was designed and before the final data analysis).
[d]At 24 months, average attack rate was lowered by 86% compared with pretreatment for the 21 people who completed the full 24 months of treatment with ORLADEYO 150 mg.

Visit ORLADEYO.com to find out more and ask your healthcare provider if ORLADEYO might be right for you.

SELECT IMPORTANT SAFETY INFORMATION

Before taking ORLADEYO, tell your healthcare provider about all of your medical conditions, including if you

- have liver problems or are on kidney dialysis.
- are pregnant or planning to become pregnant. It is not known if ORLADEYO can harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if ORLADEYO passes into your breastmilk. Talk to your healthcare provider about the best way to feed your baby while taking ORLADEYO.

Please see Important Safety Information on page 13 and accompanying full Prescribing Information, including the Patient Information.

orladeyo® (berotralstat) capsules 150 mg

bioCryst®

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use ORLADEYO® safely and effectively. See full prescribing information for ORLADEYO.

ORLADEYO (berotralstat) capsules, for oral use
Initial U.S. Approval: 2020

----------INDICATIONS AND USAGE----------
ORLADEYO is a plasma kallikrein inhibitor indicated for prophylaxis to prevent attacks of hereditary angioedema (HAE) in adults and pediatric patients 12 years and older. (1)

Limitations of Use:
ORLADEYO should not be used for treatment of acute HAE attacks. (1)

----------DOSAGE AND ADMINISTRATION----------
- Recommended Dosage: One capsule (150 mg) taken orally once daily with food. (2.1)

See Full Prescribing Information for:
- Dosage adjustment in patients with moderate or severe hepatic impairment. (2.2)
- Dosage adjustment in patients with chronic administration of P-gp or BCRP inhibitors. (2.3)
- Dosage adjustment in patients with persistent gastrointestinal reactions. (2.4)

----------DOSAGE FORMS AND STRENGTH----------
Capsules: 150 mg, 110 mg (3)

----------CONTRAINDICATIONS----------
None (4)

----------WARNINGS AND PRECAUTIONS----------
An increase in QT prolongation can occur at dosages higher than the recommended 150 mg once daily dosage. Additional doses or doses of ORLADEYO higher than 150 mg once daily are not recommended. (5.1)

----------ADVERSE REACTIONS----------
Most common adverse reactions (≥10%) are abdominal pain, vomiting, diarrhea, back pain, and gastroesophageal reflux disease. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact BioCryst Pharmaceuticals, Inc. at 1-833-633-2279 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------
P-gp or BCRP inhibitors: Reduce ORLADEYO dosage when co-administered. (7.1, 12.3)

P-gp inducers: Avoid use with ORLADEYO. (7.1)

CYP2D6, CYP3A4 or P-gp Substrates: Appropriately monitor or dose titrate narrow therapeutic index drugs that are predominantly metabolized by CYP2D6, CYP3A4 or are P-gp substrates when co-administered with ORLADEYO. (7.2, 12.3)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 03/2022

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

ORLADEYO® is indicated for prophylaxis to prevent attacks of hereditary angioedema (HAE) in adults and pediatric patients 12 years of age and older.

Limitations of Use:
The safety and effectiveness of ORLADEYO for the treatment of acute HAE attacks have not been established. ORLADEYO should not be used for treatment of acute HAE attacks. Additional doses or doses of ORLADEYO higher than 150 mg once daily are not recommended due to the potential for QT prolongation *[see Warnings and Precautions (5.1)].*

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage

The recommended dosage of ORLADEYO is one 150 mg capsule taken orally once daily with food.

2.2 Recommended Dosage in Patients with Hepatic Impairment

No dosage adjustment of ORLADEYO is recommended for patients with mild hepatic impairment (Child-Pugh Class A) *[see Use in Specific Populations (8.7) and Clinical Pharmacology (12.3)]*.

In patients with moderate or severe hepatic impairment (Child-Pugh B or C), the recommended dosage of ORLADEYO is one 110 mg capsule taken orally once daily with food *[see Use in Specific Populations (8.7) and Clinical Pharmacology (12.3)]*.

2.3 Recommended Dosage for Concomitant Use with P-gp or BCRP Inhibitors

In patients with chronic administration of P-gp or BCRP inhibitors (e.g., cyclosporine), the recommended dosage of ORLADEYO is one 110 mg capsule taken orally once daily with food *[see Drug Interactions (7.1) and Clinical Pharmacology (12.3)]*.

2.4 Dosage Adjustment in Patients with Persistent GI Reactions

Gastrointestinal (GI) reactions may occur in patients receiving ORLADEYO *[see Adverse Reactions (6.1)]*. If GI events persist, a reduced dose of 110 mg once daily with food may be considered.

3 DOSAGE FORMS AND STRENGTHS

Capsules:

- 150 mg: a white opaque body with a black imprint “150” and a light blue opaque cap with a black imprint “BCX”.
- 110 mg: light blue opaque capsules with a white imprint “110” on body and a white imprint “BCX” on cap.

4 CONTRAINDICATIONS

None

5 WARNINGS AND PRECAUTIONS

5.1 Risk of QT Prolongation with Higher-Than-Recommended Dosages

ORLADEYO should not be used for treatment of acute attacks of HAE. Additional doses or doses of ORLADEYO higher than 150 mg once daily are not recommended. An increase in QT was observed at dosages higher than the recommended 150 mg once daily dosage and was concentration dependent *[see Clinical Pharmacology (12.2)].*

6 ADVERSE REACTIONS

The following clinically significant adverse reaction is described elsewhere in the labeling:

- QT Prolongation *[see Warnings and Precautions (5.1)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of ORLADEYO is primarily based on 24-week (Part 1) data from a 3-part, double-blind, parallel-group, placebo-controlled study (Trial 1) in 120 patients with Type I or II HAE randomized and dosed with either ORLADEYO 110 mg, 150 mg or placebo, once daily with food. After Week 24, patients who continued in the study received active treatment through 48 weeks.

In Trial 1, a total of 81 patients aged 12 years and older with HAE received at least one dose of ORLADEYO in Part 1. Overall, 66% of patients were female and 93% of patients were Caucasian with a mean age of 41.6 years. The proportion of patients who discontinued study drug prematurely due to adverse reactions was 7% and 3% for patients treated with 110 mg and 150 mg ORLADEYO, respectively, and 3% for placebo-treated patients. No deaths occurred in the trial.

The safety profile of ORLADEYO was generally similar across all subgroups of patients, including analysis by age, sex, and geographic region.

Table 1 shows adverse reactions occurring in ≥10% of patients in any ORLADEYO treatment group that also occurred at a higher rate than in the placebo treatment group in Trial 1.

Table 1: Adverse Reactions Observed in ≥10% of Patients in any ORLADEYO Treatment Group (Trial 1)

Adverse Reaction	Placebo (N=39)	ORLADEYO		
		110 mg (N=41)	150 mg (N=40)	Total (N=81)
	n (%)	n (%)	n (%)	n (%)
Abdominal Pain*	4 (10)	4 (10)	9 (23)	13 (16)
Vomiting	1 (3)	4 (10)	6 (15)	10 (12)
Diarrhea†	0	4 (10)	6 (15)	10 (12)
Back Pain	1 (3)	1 (2)	4 (10)	5 (6)
Gastroesophageal Reflux Disease	0	4 (10)	2 (5)	6 (7)

* includes Abdominal pain, Abdominal discomfort, Abdominal pain upper, and Abdominal tenderness

† includes Diarrhea and Frequent bowel movements

Gastrointestinal reactions, including abdominal pain, vomiting, and diarrhea occurred more frequently in patients receiving ORLADEYO 150 mg versus ORLADEYO 110 mg or placebo. These reactions generally occurred early after initiation of treatment with ORLADEYO, became less frequent with time, and typically self-resolved. No patients in the ORLADEYO 150 mg dose group and 1 patient in the ORLADEYO 110 mg dose group discontinued treatment due to a gastrointestinal adverse reaction.

Less Common Adverse Reactions

Other adverse reactions that occurred in Part 1 of Trial 1 with an incidence between 5% and <10% at a higher incidence in ORLADEYO-treated patients compared to placebo included headache (9% versus 5%), fatigue (6% versus 3%), and flatulence (6% versus 3%).

A maculopapular drug rash was reported in less than 1% of patients treated with ORLADEYO. The rash resolved, including in subjects who continued dosing.

Safety data are also available from 227 patients enrolled in an ongoing, open-label, long-term safety study (Trial 2) who received ORLADEYO 110 mg (N=100) or 150 mg (N=127) once daily with food and are consistent with the 24-week controlled safety data from Trial 1 (Part 1).

Laboratory Abnormalities

Transaminase elevations

In Part 1 of Trial 1, a single 150 mg ORLADEYO-treated patient discontinued treatment due to asymptomatic elevated transaminases (ALT >8x the upper limit of normal [ULN] and AST >3x ULN). Total bilirubin was normal. No subject receiving 110 mg or placebo developed transaminase levels >3x ULN. In addition to this patient, 2 ORLADEYO-treated patients developed laboratory-related hepatic adverse events compared to 1 placebo-treated patient. No patient reported serious adverse reactions of elevated transaminases.

7 DRUG INTERACTIONS

This section describes clinically relevant drug interactions with ORLADEYO. Drug interaction studies are described elsewhere in the labeling *[see Clinical Pharmacology (12.3)].*

7.1 Potential for Other Drugs to Affect ORLADEYO

P-gp or BCRP inhibitors

ORLADEYO is a P-gp and BCRP substrate. A dose of 110 mg ORLADEYO is recommended for patients with chronic administration of P-gp or BCRP inhibitors (e.g., cyclosporine) *[see Clinical Pharmacology (12.3)].*

P-gp Inducers

Berotralstat is a substrate of P-gp and BCRP. P-gp inducers (e.g., rifampin, St. John’s wort) may decrease berotralstat plasma concentration, leading to reduced efficacy of ORLADEYO. The use of P-gp inducers is not recommended with ORLADEYO.

7.2 Potential for ORLADEYO to Affect Other Drugs

CYP2D6 and CYP3A4 Substrates

ORLADEYO at a dose of 150 mg is a moderate inhibitor of CYP2D6 and CYP3A4. For concomitant medications with a narrow therapeutic index that are predominantly metabolized by CYP2D6 (e.g., thioridazine, pimozide) or CYP3A4 (e.g., cyclosporine, fentanyl), appropriate monitoring and dose titration is recommended *[see Clinical Pharmacology (12.3)]*.

P-gp Substrates

ORLADEYO at a dose of 300 mg is a P-gp inhibitor. Appropriate monitoring and dose titration is recommended for P-gp substrates (e.g., digoxin) when co-administering with ORLADEYO *[see Clinical Pharmacology (12.3)]*.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are insufficient data in pregnant women available to inform drug-related risks with ORLADEYO use in pregnancy. Based on animal reproduction studies, no evidence of structural alterations was observed when berotralstat was administered orally to pregnant rats and rabbits during organogenesis at doses up to approximately 10 and 2 times, respectively, the maximum recommended human daily dose (MRHDD) in adults on an AUC basis (*see Data)*.

The background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Data

Animal Data

In animal reproduction studies, oral administration of berotralstat to pregnant rats and rabbits during the period of organogenesis did not cause fetal structural alterations. The berotralstat dose in rats and rabbits was up to approximately 10 and 2 times, respectively, the MRHDD in adults (on an AUC basis at maternal doses of 75 and 100 mg/kg/day, respectively). In a pre- and postnatal development study in rats, oral administration of berotralstat to pregnant rats during the period of organogenesis and until delivery at doses up to 45 mg/kg/day (approximately 2 times of the MRHDD on a mg/m^2 basis) did not cause fetal structural alterations either. Berotralstat concentrations in the fetal blood were approximately 5-11% of the maternal blood.

8.2 Lactation

Risk Summary

There are no data on the presence of berotralstat in human milk, its effects on the breastfed infant, or its effects on milk production. However, when a drug is present in animal milk, it is likely that the drug will be present in human milk. Low levels of berotralstat were detected in the plasma of rat pups when dams were dosed with the drug orally during the lactation period. The berotralstat concentration in the pup plasma was approximately 2% of the maternal plasma *(see Data)*.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for ORLADEYO and any potential adverse effects on the breastfed infant from ORLADEYO or from the underlying maternal condition.

Data

Animal Data

In the pre- and post-natal development study in rats, berotralstat was administered to dams during the pregnancy and lactation periods at doses up to 45 mg/kg/day (approximately 2 times of the MRHDD on a mg/m^2 basis). Berotralstat was detected in the plasma of pups during the lactation period. The berotralstat concentration in the pup plasma was approximately 2% of the maternal plasma. Both dams and pups at 45 mg/kg/day showed statistically significant decreases in body weight gain ($p<0.05$). No treatment-related effects were observed at 25 mg/kg/day (approximately equal to the MRHDD on a mg/m^2 basis).

8.4 Pediatric Use

The safety and effectiveness of ORLADEYO for prophylaxis to prevent attacks of hereditary angioedema have been established in pediatric patients aged 12 and older. Use of ORLADEYO in this population is supported by evidence from an adequate and well-controlled study (Trial 1) that included adults and a total of 6 adolescent patients aged 12 to <18 years of age. The safety profile

and attack rate on study were similar to those observed in adults *[see Adverse Reactions (6.1), Clinical Pharmacology (12.3), and Clinical Studies (14)]*. An additional 10 adolescent patients aged 12 to <18 years were enrolled in the open-label study (Trial 2).

The safety and effectiveness of ORLADEYO in pediatric patients <12 years of age have not been established.

8.5 Geriatric Use

The safety and effectiveness of ORLADEYO were evaluated in a subgroup of patients (N=9) aged ≥65 years in Trial 1. Results of the subgroup analysis by age were consistent with overall study results. The safety profile from an additional 5 elderly patients aged ≥65 years enrolled in the open-label, long-term safety study (Trial 2) was consistent with data from Trial 1 *[see Adverse Reactions (6.1), Clinical Pharmacology (12.3), and Clinical Studies (14)]*.

8.6 Renal Impairment

No dosage adjustment of ORLADEYO is recommended for patients with mild, moderate or severe renal impairment *[see Clinical Pharmacology (12.3)]*.

ORLADEYO has not been studied in patients with End-Stage Renal Disease (CL_{CR} <15 mL/min or eGFR <15 mL/min/1.73 m^2 or patients requiring hemodialysis), and therefore is not recommended for use in these patient populations *[see Clinical Pharmacology (12.3)].*

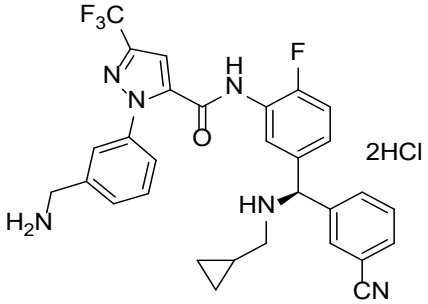
8.7 Hepatic Impairment

No dosage adjustment of ORLADEYO is recommended for patients with mild hepatic impairment (Child-Pugh Class A) *[see Clinical Pharmacology (12.3)]*.

In patients with moderate or severe hepatic impairment (Child-Pugh B or C), the recommended dose of ORLADEYO is 110 mg once daily with food *[see Dosage and Administration (2.2) and Clinical Pharmacology (12.3)]*.

11 DESCRIPTION

ORLADEYO (berotralstat) capsules is a plasma kallikrein inhibitor. Berotralstat is presented as the dihydrochloride salt with the chemical name 1-[3-(aminomethyl)phenyl]-*N*-(5-{(*R*)-(3-cyanophenyl)[(cyclopropylmethyl)amino]methyl}-2-fluorophenyl)-3-(trifluoromethyl)-1*H*-pyrazole-5-carboxamide dihydrochloride. The chemical structure is:



Berotralstat dihydrochloride is a white to off-white powder that is soluble in water at pH ≤4. The molecular formula is $C_{30}H_{26}F_4N_6O$ • 2HCl and the molecular weight is 635.49 (dihydrochloride).

ORLADEYO is supplied as 150 mg (equivalent to 169.4 mg berotralstat dihydrochloride) and 110 mg (equivalent to 124.3 mg berotralstat dihydrochloride) hard gelatin capsules for oral administration. Each capsule contains the active ingredient berotralstat dihydrochloride and the inactive ingredients colloidal silicon dioxide, crospovidone, magnesium stearate, and pregelatinized starch.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Berotralstat is a plasma kallikrein inhibitor that binds to plasma kallikrein and inhibits its proteolytic activity. Plasma kallikrein is a protease that cleaves high-molecular-weight-kininogen (HMWK) to generate cleaved HMWK (cHMWK) and bradykinin, a potent vasodilator that increases vascular permeability resulting in swelling and pain associated with HAE. In patients with HAE due to C1-inhibitor (C1-INH) deficiency or dysfunction, normal regulation of plasma kallikrein activity is not present, which leads to uncontrolled increases in plasma kallikrein activity and results in angioedema attacks. Berotralstat decreases plasma kallikrein activity to control excess bradykinin generation in patients with HAE.

12.2 Pharmacodynamics

Concentration-dependent inhibition of plasma kallikrein, measured as a reduction from baseline of specific enzyme activity, was demonstrated after oral administration of ORLADEYO once daily in patients with HAE.

Cardiac Electrophysiology

At the recommended dose of 150 mg once daily, ORLADEYO does not prolong the QT interval to any clinically relevant extent. At 3-times the recommended dose, the mean (upper 90% confidence interval) increase in QTcF was 15.9 msec (23.5 msec). The observed increase in QTcF was concentration-dependent.

12.3 Pharmacokinetics

Following oral administration of berotralstat 150 mg once daily, the steady state C_{max} and area under the curve over the dosing interval (AUC_{tau}) are 158 ng/mL (range: 110 to 234 ng/mL) and 2770 ng*hr/mL (range: 1880 to 3790 ng*hr/mL), respectively. Following oral administration of berotralstat 110 mg once daily, the steady-state C_{max} and AUC_{tau} are 97.8 ng/mL (range: 63 to 235 ng/mL) and 1600 ng*hr/mL (range: 950 to 4170 ng*hr/mL), respectively.

Berotralstat exposure (C_{max} and AUC) increases greater than proportionally with dose and steady state is reached by days 6 to 12. After once-daily administration, exposure of berotralstat at steady state is approximately 5 times that after a single dose.

The pharmacokinetics of berotralstat are similar between healthy adult subjects and in patients with HAE.

Absorption

The median time to maximum plasma concentration (T_{max}) of berotralstat when administered with food is 5 hours (range: 1 to 8 hours).

Effect of Food

No differences in the C_{max} and AUC of berotralstat were observed following administration with a high-fat meal, however the median T_{max} was delayed by 3 hours, from 2 hours (fasted) to 5 hours (fed).

Distribution

Plasma protein binding is approximately 99%. After a single dose of radiolabeled berotralstat 300 mg, the blood to plasma ratio was approximately 0.92.

Elimination

The median elimination half-life of berotralstat was approximately 93 hours (range: 39 to 152 hours).

Metabolism

Berotralstat is metabolized by CYP2D6 and by CYP3A4 with low turnover *in vitro*. After a single oral radiolabeled berotralstat 300 mg dose, berotralstat represented 34% of the total plasma radioactivity, with 8 metabolites, each accounting for between 1.8 and 7.8% of the total radioactivity.

Excretion

After a single oral radiolabeled berotralstat 300 mg dose, approximately 9% was excreted in urine (3.4% unchanged; range: 1.8 to 4.7%) and 79% was excreted in feces.

Specific Populations

Body weight, age, gender, and race did not have a clinically meaningful influence on the systemic exposure of berotralstat.

Geriatric Patients

Based on the population pharmacokinetic analyses that included elderly patients (≥65 to 74 years, N=25), age does not have a clinically meaningful impact on the systemic exposure of berotralstat *[see Use in Specific Populations (8.5)]*.

Pediatric Patients

Based on population pharmacokinetic analyses that included pediatric patients 12 to <18 years of age, exposure at steady state following oral administration of berotralstat 150 mg once daily was approximately 20% higher compared to adults. The higher exposure in adolescents is not considered to be clinically meaningful.

Patients with Renal Impairment

The pharmacokinetics of a single 200 mg oral dose of berotralstat were studied in subjects with severe renal impairment (CL_{CR} less than 30 mL/min). When compared to a concurrent cohort with normal renal function (CL_{CR} greater than 90 mL/min), no clinically relevant differences were observed; C_{max} was increased by 47%, while $AUC_{0\text{-last}}$ was increased by 14% *[see Use in Specific Populations (8.6)]*.

The pharmacokinetics of berotralstat has not been studied in patients with End-Stage Renal Disease (CL_{CR} less than 15 mL/min or eGFR less than 15 mL/min/1.73 m^2 or patients requiring hemodialysis).

Patients with Hepatic Impairment

The pharmacokinetics of a single 150 mg oral dose of berotralstat were studied in subjects with mild, moderate, and severe hepatic function (Child-Pugh Class A, B, and C, respectively). The pharmacokinetics of berotralstat were unchanged in subjects with mild hepatic impairment compared to subjects with normal hepatic function. In subjects with moderate hepatic impairment, C_{max} was increased by 77%, while $AUC_{0\text{-inf}}$ was increased by 78%. In subjects with severe hepatic impairment, C_{max} was increased by 27%, while $AUC_{0\text{-last}}$ was decreased by 5%. The median half-life of berotralstat was increased by 37% and 22% in patients with moderate and severe hepatic impairment, respectively, in comparison to healthy subjects. The percent of unbound berotralstat increased 2-fold from a mean of 1.2% in healthy subjects to a mean of 2.4% in subjects with severe hepatic impairment *[see Use in Specific Populations (8.7)]*.

Drug Interaction Studies

Effect of Other Drugs on the Pharmacokinetics of ORLADEYO

Berotralstat is a P-gp and BCRP substrate. Cyclosporine, a P-gp and BCRP inhibitor, increased berotralstat C_{max} by 25%, $AUC_{0\text{-last}}$ by 55%, and $AUC_{0\text{-inf}}$ by 69% *[see Drug Interactions (7.1)]*.

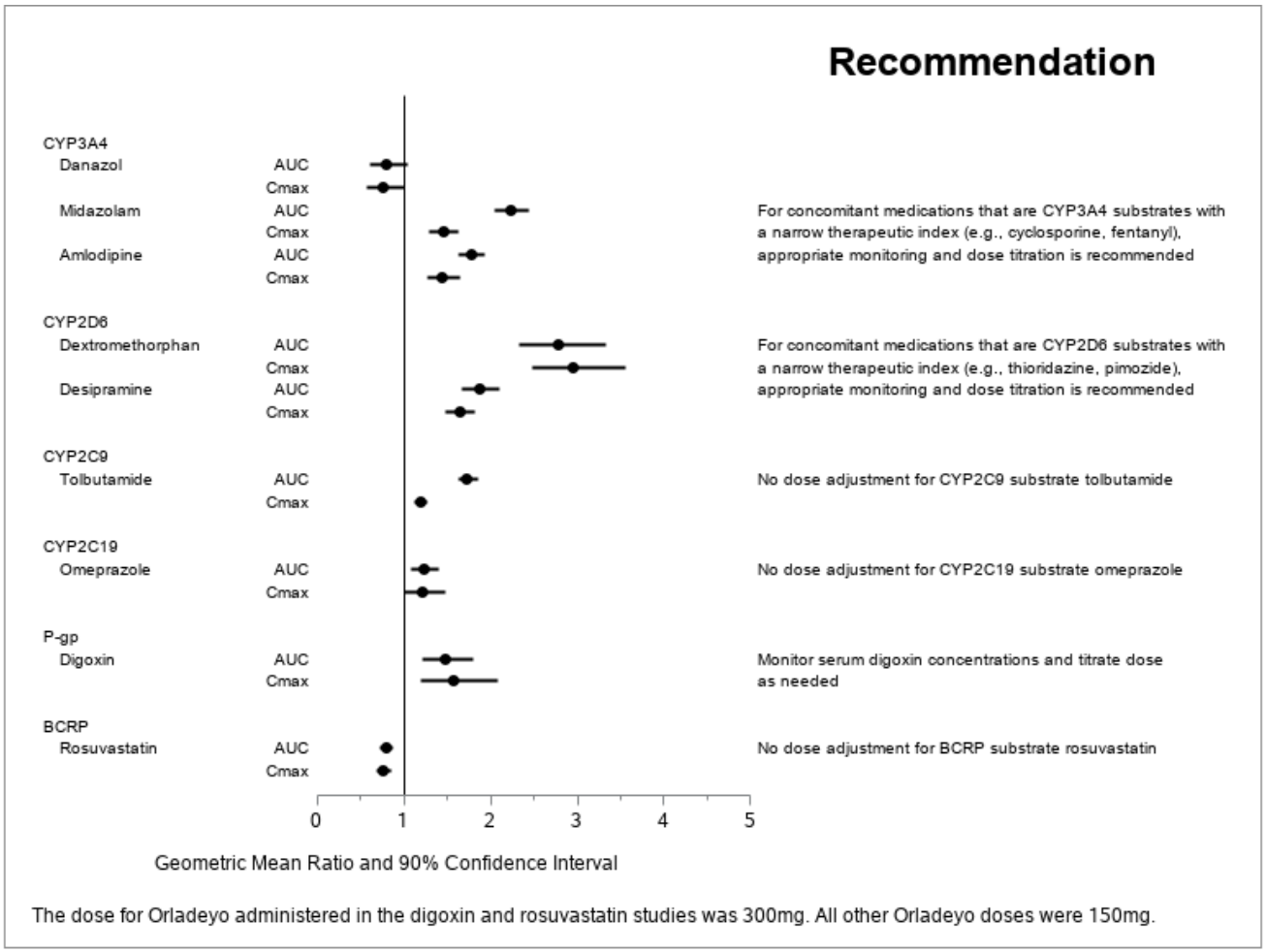
Effect of ORLADEYO on the Pharmacokinetics of Other Drugs

Berotralstat 150 mg once daily is a moderate inhibitor of CYP2D6 and CYP3A4, and a weak inhibitor of CYP2C9 and CYP2C19.

Berotralstat at a 300 mg dose is an inhibitor of P-gp and is not an inhibitor of BCRP (rosuvastatin exposure was decreased by approximately 20%).

The effect of berotralstat on the pharmacokinetics of other drugs are presented in Figure 1 *[see Drug Interactions (7.2)].*

Figure 1: Effect of ORLADEYO on Concomitant Medications



13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Carcinogenicity of berotralstat was evaluated in a 2-year study in Wistar rats and a 26-week study in Tg.rasH2 transgenic mice. The berotralstat doses (oral gavage) were up to 20 and 50 mg/kg/day in rats and mice (approximately 5 and 10 times the MRHDD on a plasma AUC basis, respectively). No evidence of tumorigenicity was observed in either species.

Mutagenesis

Berotralstat tested negative in the *in vitro* bacterial reverse mutation assay (Ames test), the *in vitro* chromosomal aberration assay in human peripheral blood lymphocytes, and the *in vivo* rat micronucleus assay.

Impairment of Fertility

In a fertility study in rats, berotralstat at oral doses up to 45 mg/kg/day (approximately 2 times the MRHDD on a mg/m^2 basis) showed no effect on fertility in males or females.

14 CLINICAL STUDIES

Trial 1 (NCT3485911)

The efficacy of ORLADEYO for the prevention of angioedema attacks in patients 12 years of age and older with Type I or II HAE was demonstrated in Part 1 of a multicenter, randomized, double-blind, placebo-controlled, parallel-group study (Trial 1).

The study included 120 adult and adolescent patients who experienced at least two investigator-confirmed attacks within the first 8 weeks of the run-in period and took at least one dose of study treatment. Patients were randomized into 1 of 3 parallel treatment arms, stratified by baseline attack rate, in a 1:1:1 ratio (berotralstat 110 mg, berotralstat 150 mg, or placebo by oral administration once daily, with food) for the 24-week treatment period (Part 1).

Patients discontinued other prophylactic HAE medications prior to entering the study; however, all patients were allowed to use rescue medications for treatment of breakthrough HAE attacks.

A history of laryngeal angioedema attacks was reported in 74% of patients and 75% reported prior use of long-term prophylaxis. The median attack rate during the prospective run-in period (baseline attack rate) was 2.9/month. Seventy percent of patients enrolled had a baseline attack rate of ≥2 attacks/month.

ORLADEYO 150 mg and 110 mg produced statistically significant reductions in the rate of HAE attacks compared to placebo for the primary endpoint in the Intent-to-Treat (ITT) population as shown in Table 2. The percent reductions in HAE attack rate were greater with ORLADEYO 150 mg and 110 mg relative to placebo, regardless of attack rate during the run-in period.

Table 2. Primary Efficacy Endpoint (Trial 1): Reduction in HAE Attack Rate- ITT Population

	ORLADEYO		Placebo
	110 mg QD	150 mg QD	
Outcome	**N = 41**	**N = 40**	**N = 40***
HAE Attack Rate, rate per 28 days†	1.65	1.31	2.35
% Rate Reduction‡ (95% CI)	30.0% (4.6, 48.7)	44.2% (23.0, 59.5)	-
p-value	0.024	<0.001	-

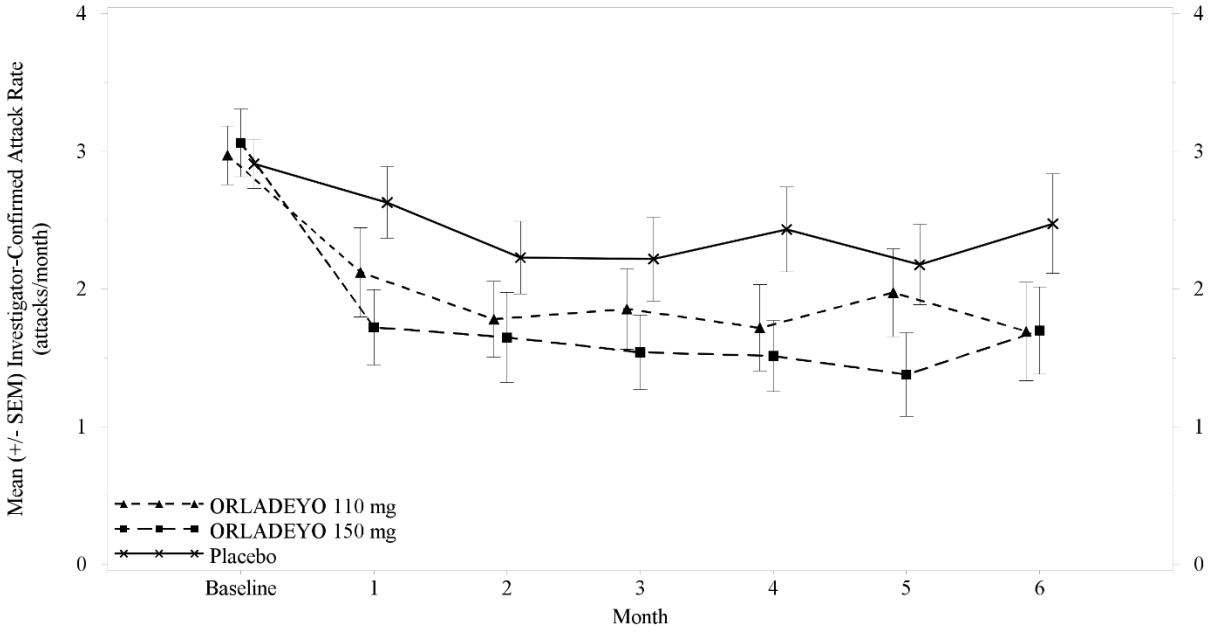
* One patient in the ITT analysis was randomized to placebo but was not treated.

† Statistical analysis based on a negative binomial regression model; number of attacks included as dependent variable, treatment included as fixed effect, baseline attack rate included as covariate, and logarithm of duration on treatment included as offset variable.

‡ Percent reduction relative to placebo.

Reductions in attack rates were observed in the first month of treatment with ORLADEYO 150 mg and 110 mg and were sustained through 24 weeks as shown in Figure 2.

Figure 2. Mean (+/- SEM) HAE Attack Rate/month Through 24 Weeks (Trial 1)- ITT Population



Pre-defined exploratory endpoints included the proportion of responders to study drug, defined as at least a 50% relative reduction in HAE attacks during treatment compared with the baseline attack rate; 58% of patients receiving 150 mg ORLADEYO and 51% of patients receiving 110 mg ORLADEYO had a ≥50% reduction in their HAE attack rates compared to baseline versus 25% of placebo patients. In post-hoc analyses, 50% and 23% of patients receiving 150 mg ORLADEYO, and 27% and 10% of patients receiving 110 mg ORLADEYO, had a ≥70% or ≥90% reduction in their HAE attack rates compared to baseline versus 15% and 8% of placebo patients, respectively. The rate of attacks rated as moderate or severe was reduced by 40% and 10% in patients receiving 150 mg ORLADEYO and 110 mg ORLADEYO, respectively, versus placebo.

16 HOW SUPPLIED/STORAGE AND HANDLING

ORLADEYO (berotralstat) capsules:

- 150 mg: a white opaque body with a black imprint “150” and a light blue opaque cap with a black imprint “BCX”.
- 110 mg: light blue opaque capsules with a white imprint “110” on body and a white imprint “BCX” on cap.
- A 28-day supply of ORLADEYO is provided in a carton containing four child-resistant shellpaks, each containing a 7-capsule blister card. NDC 72769-101-01 (150 mg) and NDC 72769-102-01 (110 mg).
- Each carton contains a tamper evident seal.
- Do not use if tamper evident seal is broken or missing.

Store at 20ºC to 25ºC (68ºF to 77ºF). Excursions permitted between 15ºC and 30ºC (59ºF to 86ºF) *[see USP Controlled Room Temperature]*.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Inform patients of the risks and benefits of ORLADEYO before prescribing or administering to the patient.

Drug Interactions

Advise patients that ORLADEYO may interact with other drugs *[see Drug Interactions (7) and Clinical Pharmacology (12.3)]*. Advise patients to report to their healthcare provider the use of any other prescription or nonprescription medication or herbal products.

Not for Acute Treatment of HAE Attacks

Advise patients to take their usual rescue medication to treat an acute attack of HAE. Inform patients that the safety and effectiveness of ORLADEYO has not been established as an acute treatment for HAE attacks. Advise patients that they should not take daily doses higher than 150 mg once daily or additional doses of ORLADEYO to treat an acute attack of HAE due to risk of QT prolongation *[see Limitations of Use (1) and Warnings and Precautions (5.1)].*

For more information, visit www.ORLADEYO.com

ORLADEYO® is a registered trademark of BioCryst Pharmaceuticals, Inc.

Manufactured for:
BioCryst Pharmaceuticals, Inc.
Durham, NC 27703

214094-BC-001

PATIENT INFORMATION
ORLADEYO® (or-luh-DAY-oh)
(berotralstat)
capsules, for oral use

What is ORLADEYO?

- ORLADEYO is a prescription medicine used to prevent attacks of Hereditary Angioedema (HAE) in adults and children 12 years of age and older.
- ORLADEYO is not used to treat an acute HAE attack.
- Do not take more than one capsule of ORLADEYO a day because extra doses can cause heart rhythm problems.
- It is not known if ORLADEYO is safe and effective to treat an acute HAE attack.
- It is not known if ORLADEYO is safe and effective in children under 12 years of age.

Before you take ORLADEYO, tell your healthcare provider about all of your medical conditions, including if you:

- have liver problems or are on kidney dialysis.
- are pregnant or planning to become pregnant. It is not known if ORLADEYO can harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if ORLADEYO passes into your breastmilk. Talk to your healthcare provider about the best way to feed your baby while taking ORLADEYO.

Tell your healthcare provider about all of the medicines you take, including other medicines for HAE, prescription and over-the-counter medicines, vitamins, and herbal supplements.
Taking ORLADEYO with certain other medicines may affect the way other medicines work and other medicines may affect how ORLADEYO works.
Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

How should I take ORLADEYO?

- Take ORLADEYO exactly as your healthcare provider tells you to take it.
- Take 1 capsule, by mouth, 1 time every day with food.

What are the possible side effects of ORLADEYO?
Taking more than one capsule of ORLADEYO a day may cause serious side effects, including:

- **heart rhythm problems**. A heart rhythm problem called QT prolongation can happen in people who take more than one capsule of ORLADEYO a day. This condition can cause an abnormal heart beat. Do not take more than one capsule of ORLADEYO a day.

The most common side effects of ORLADEYO include:

- abdominal pain
- vomiting
- diarrhea
- back pain
- heartburn

Less common side effects include increases in liver function tests. Rarely, some patients had a brief, itchy rash.

These are not all of the possible side effects of ORLADEYO. For more information, ask your healthcare provider or pharmacist.
Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store ORLADEYO?

- Store ORLADEYO at room temperature between 68ºF to 77ºF (20ºC to 25ºC).
- Each carton contains a tamper evident seal. Do not use ORLADEYO if the tamper evident seal is broken or missing.

Keep ORLADEYO and all medicines out of the reach of children.

General information about the safe and effective use of ORLADEYO.
Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use ORLADEYO for a condition for which it was not prescribed. Do not give ORLADEYO to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about ORLADEYO that is written for health professionals.

What are the ingredients in ORLADEYO?
Active ingredient: berotralstat dihydrochloride
Inactive ingredients: colloidal silicon dioxide, crospovidone, magnesium stearate, and pregelatinized starch

Manufactured for: BioCryst Pharmaceuticals, Inc., Durham, NC 27703

For more information, visit www.ORLADEYO.com or call 1-833-633-2279.

This Patient Information has been approved by the U.S. Food and Drug Administration. 03/2022