THE #1 PRESCRIBED HAE PREVENTIVE TREATMENT*—APPROVED IN PATIENTS AS
YOUNG AS 2 YEARS OF AGE. OVER 5 YEARS OF PATIENT EXPERIENCE AND 3250+ PATIENTS
PRESCRIBED SINCE 2018.1+



*Based on total patients on HAE preventive treatments according to US third-party industry healthcare data.

INDICATION

TAKHZYRO is indicated for prophylaxis to prevent attacks of hereditary angioedema (HAE) in patients ≥2 years of age.

IMPORTANT SAFETY INFORMATION

Hypersensitivity reactions have been observed. In case of a severe hypersensitivity reaction, discontinue TAKHZYRO administration and institute appropriate treatment.

Please see additional <u>Important Safety Information</u> throughout and full <u>Prescribing Information</u>.



[†]The number of patients prescribed TAKHZYRO is based on third-party US specialty pharmacy data.

What is HAE?

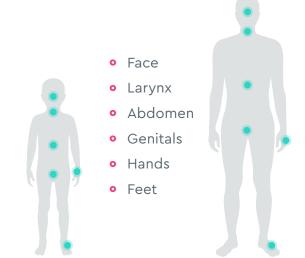
AN UNPREDICTABLE AND POTENTIALLY LIFE-THREATENING GENETIC DISEASE

HAE is a rare genetic disease that causes recurrent, debilitating, and potentially life-threatening attacks of angioedema in the body. HAE affects about 1 in 50,000 people of all ages.^{3,4}

An accurate and early diagnosis is an important first step in developing an effective management plan for your patients with HAE.

The frequency and severity of HAE attacks may vary for each individual over time regardless of age, meaning past attacks do not predict the severity of future attacks.⁵

For both adult and pediatric patients, attacks can occur in the...6



Attacks in the larynx can be life-threatening, and they are especially dangerous for children who lack the ability to self-administer treatment during an attack or who may be unable to describe their symptoms.^{6,7}

TAKHZYRO is not indicated for acute treatment.

Long-term prevention should be individualized and considered in all patients with HAE.8

IMPORTANT SAFETY INFORMATION (cont'd)

Adverse Reactions: The most commonly observed adverse reactions (≥10%) associated with TAKHZYRO were injection site reactions consisting mainly of pain, erythema, and bruising at the injection site; upper respiratory infection; headache; rash; dizziness; diarrhea; and myalgia. Less common adverse reactions observed included elevated levels of transaminases; one patient discontinued the trial for elevated transaminases.

CRAFT AN EFFECTIVE HAE MANAGEMENT PLAN

Your patients' needs and disease may change over time, and they may need a reminder that their management plan can change.³

- The 2020 US HAEA guidelines recommend:
 - Reviewing management plans for patients with HAE on a regular basis, including the need for preventive treatment³
 - TAKHZYRO as one of the first-line therapies for long-term prevention in adult and adolescent patients ≥12 years of age³
- The 2021 international WAO/EAACI guidelines state:
 - High HAE disease activity often comes with impact on daily life⁸
 - The daily lives of some patients with low attack rates are also impacted, thought to be linked to the unpredictability and continuous fear of HAE attacks⁸

Since most attacks are unpredictable and not prompted by triggers, guidelines suggest that physicians should not support excessive avoidance of suspected triggers, which can limit a patient's normal life.⁸



HAE can be unpredictable and attacks could happen with no warning."

Andrew
 Real TAKHZYRO patient since 2018

EAACI=European Academy of Allergy and Clinical Immunology; HAEA=Hereditary Angioedema Association; WAO=World Allergy Organization.

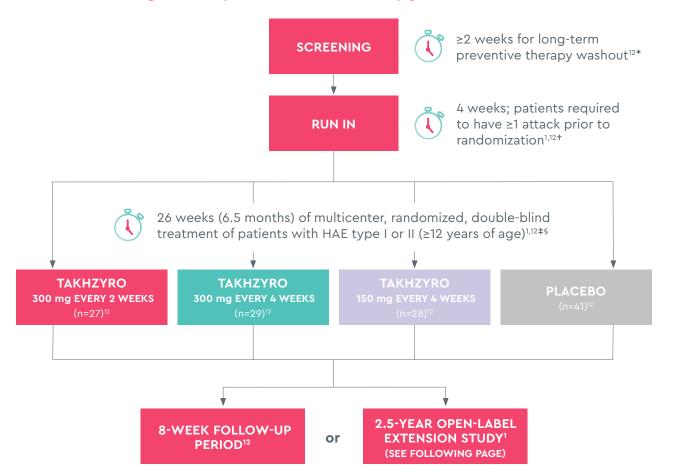
Please see additional <u>Important Safety Information</u> throughout and full <u>Prescribing Information</u>.



HELP study

WITH 125 PATIENTS, HELP IS ONE OF THE LARGEST STUDIES IN HAE PREVENTION WITH THE LONGEST ACTIVE TREATMENT 1,2,9-11

44% of patients at baseline in HELP had not previously received long-term preventive therapy¹²



^{*}Long-term preventive therapy washout was only for patients ≥18 years of age.¹³

IMPORTANT SAFETY INFORMATION (cont'd)

Use in Specific Populations: The safety and efficacy of TAKHZYRO in pediatric patients <2 years of age have not been established.

No data are available on TAKHZYRO in pregnant women. No data are available on the presence of lanadelumab in human milk or its effects on breastfed infants or milk production.

To report SUSPECTED ADVERSE REACTIONS, contact Dyax Corp., a Takeda company, at 1-877-TAKEDA-7 (1-877-825-3327), or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

HELP open-label extension (OLE) study

ABOUT 97% OF PATIENTS IN THE HELP STUDY ENROLLED IN THE 2.5-YEAR EXTENSION STUDY²

41% of patients at baseline in HELP OLE had not previously received long-term preventive therapy²

Rollover (n=109)¹

Total: 212 patients ≥12 years of age Nonrollover (n=103)¹

Baseline attack rate of the HELP study (4-week run-in period) was used as the baseline. Attack rate requirement: at least 1 attack in 4 weeks.^{2,12}

of 29.6 (SD=8.2) months²

Baseline was defined as the number of investigator-confirmed attacks reported in the last 3 months. Attack rate requirement: 1 attack in 3 months.²

SINGLE DOSE OF TAKHZYRO 300 mg
PATIENTS FOLLOWED UNTIL THE FIRST
HAE ATTACK OCCURRED²

SCREENING (4 WEEKS, NO LONG-TERM



- Patients were given TAKHZYRO 300 mg every 2 weeks for a mean duration
- 81.6% of patients completed the study or enrolled in commercial product²

The long-term safety of TAKHZYRO was the primary endpoint in this study.²

Please see additional <u>Important Safety Information</u> throughout and full <u>Prescribing Information</u>.



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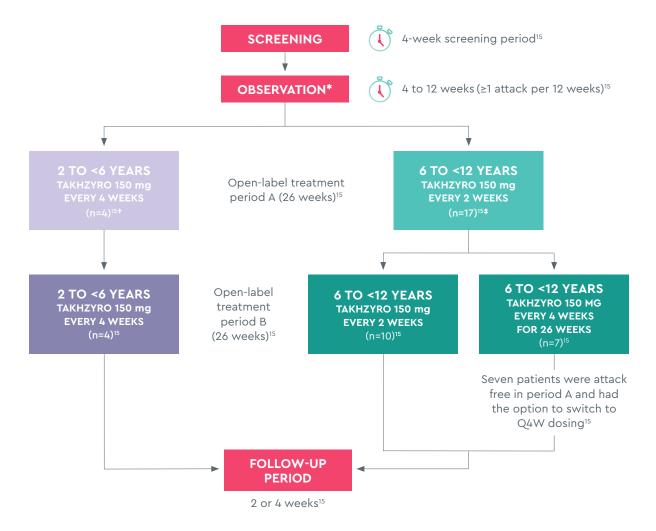
^{*}Run-in period could be shortened if the patient experienced ≥3 HAE attacks before completion of the 4 weeks, and the period could be extended to 8 weeks if the patient did not experience any attacks during the 4 weeks. During the 8 weeks, the patient needed to have ≥2 attacks to proceed to enrollment and randomization.¹²

^{*}Treatments were administered as 2 separate 1-mL injections in the upper arm every 2 weeks to maintain the blind.12

[§]One month was defined as 28 days in the trial.¹²

AN OPEN-LABEL, MULTICENTER STUDY IN PATIENTS WITH HAE AS YOUNG AS 2 YEARS OF AGE¹

TAKHZYRO was studied in 21 pediatric patients 2 to <12 years of age with HAE type I or II¹



The safety and pharmacokinetics of TAKHZYRO were the co-primary endpoints in the SPRING study.¹⁵

Q4W=every 4 weeks.



IMPORTANT SAFETY INFORMATION

Hypersensitivity reactions have been observed. In case of a severe hypersensitivity reaction, discontinue TAKHZYRO administration and institute appropriate treatment.

Please see additional <u>Important Safety Information</u> throughout and full <u>Prescribing Information</u>.



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Efficacy

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Dosing

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^{*}Eligible patients underwent a 4- to 12-week baseline observation period before initiating treatment with TAKHZYRO.15

[†]Patients aged 2 to <6 years received 150 mg every 4 weeks for the 52-week treatment period.¹⁵

[‡]Patients aged 6 to <12 years were to receive 150 mg every 2 weeks for 52 weeks and had an option to switch to every 4 weeks if they were attack free for 26 weeks.¹⁵

HELP primary endpoint

REDISCOVER EFFECTIVE PREVENTION

Significant reduction in mean attack rate* vs placebo at 6.5 months in the HELP study^{1,12}

87% REDUCTION IN ATTACKS

vs placebo

 $(Adjusted P < 0.001)^{1+}$

- TAKHZYRO 300 mg every 4 weeks resulted in a 73% reduction in attacks vs placebo (Adjusted P<0.001)1+
 - Please see page 10 for additional subanalysis of the Q4W cohort
- Mean monthly attack rate at baseline (during the run-in period): 3.52 for TAKHZYRO every 2 weeks (n=27); 3.71 for TAKHZYRO every 4 weeks (n=29); 4.02 for placebo (n=41)¹²
- Mean monthly attack rate (during treatment): 0.26 for TAKHZYRO every 2 weeks; 0.53 for TAKHZYRO every 4 weeks; 1.97 for placebo¹

All data presented are for TAKHZYRO 300 mg every 2 weeks unless otherwise indicated.

IMPORTANT SAFETY INFORMATION (cont'd)

Adverse Reactions: The most commonly observed adverse reactions (≥10%) associated with TAKHZYRO were injection site reactions consisting mainly of pain, erythema, and bruising at the injection site; upper respiratory infection; headache; rash; dizziness; diarrhea; and myalgia. Less common adverse reactions observed included elevated levels of transaminases; one patient discontinued the trial for elevated transaminases.



Significant reduction in moderate to severe attacks and attacks requiring acute treatment vs placebo at 6.5 months^{1,12}

Attack reduction vs placebo (Adjusted <i>P</i> <0.001) ^{1,12‡}	Reduction in moderate or severe attacks	Reduction in attacks requiring acute treatment
TAKHZYRO 300 mg every 2 weeks (n=27)	83%	87%
TAKHZYRO 300 mg every 4 weeks (n=29)	73%	74%



Since starting TAKHZYRO, the frequency and severity of my attacks have decreased. I was accustomed to multiple attacks per week. I've even gone a month or 2 without an attack."

— Jack

Real TAKHZYRO patient since 2018

Individuals featured are TAKHZYRO patients as of 2023 and are sharing their own experiences. Individual experiences may vary. *Adjusted P-values for multiple testing.1

Please see additional Important Safety Information throughout and full Prescribing Information.



^{*}Mean monthly attack rate: number of attacks/4 weeks.1

[†]Adjusted P-values for multiple testing.¹

HELP prespecified exploratory endpoints

SUBGROUP RESULTS FROM THE 300 mg Q4W ARM OF THE HELP STUDY

Attack History

- 80% reduction in attacks on average vs placebo for patients who had 1 to <2 HAE attacks per month at baseline (n=9)^{16*}
- 77% reduction in attacks on average vs placebo for patients that had 2 to <3 attacks per month (n=5)¹⁶
- 71% reduction in attacks on average vs placebo for patients that had ≥3 attacks per month (n=15)¹⁶

Body Mass Index (BMI)

- 86% reduction in attacks on average vs placebo for patients with a normal BMI (n=6)^{16†‡}
- 70% reduction in attacks on average vs placebo for patients with an overweight BMI (n=5)^{16§}
- 74% reduction in attacks on average vs placebo for patients with an obese BMI (n=8)^{16¶}

These studies were prespecified exploratory analyses in the pivotal HELP study to evaluate the efficacy and safety of TAKHZYRO compared to placebo in patients of varying BMIs and in patients with different baseline run-in attack rates.

Your patient may be considered for less frequent dosing with TAKHZYRO if they are well controlled (eg. attack free) for more than 6 months.¹



My HAE was so bad [that] I had a hard time making plans with my family... I decided I wanted a medication that would help prevent attacks before they happened."

— Soraya

Real TAKHZYRO patient since 2018

*In the HELP study, TAKHZYRO provided reductions in monthly attack rates relative to placebo in patients with HAE, regardless of baseline attack rate.16

†In the HELP study, TAKHZYRO reduced the HAE attack rate compared with placebo, regardless of patients' BMI.16

 ‡ A normal BMI was defined as 18.5 to <25 kg/m² (n=35). 16

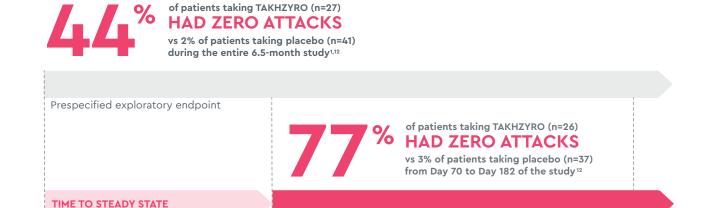
 $^{\rm s}\!$ An overweight BMI was defined as 25 to <30 kg/m² (n=43).16

[¶]An obese BMI was defined as ≥30 kg/m² (n=36).¹⁶

HELP exploratory endpoints

FREEDOM FROM HAE ATTACKS IN THE HELP STUDY

Many patients taking TAKHZYRO in the study had zero attacks^{1,12}



DAY 0

DOSE 1

DAY 70 MONTH 2.5 DOSE 6

Post hoc analysis

DAY 182

Learn how your patients may experience freedom from HAE attacks for periods of time with TAKHZYRO at TAKHZYRO.com/hcp.

All data presented are for TAKHZYRO 300 mg every 2 weeks unless otherwise indicated.

IMPORTANT SAFETY INFORMATION (cont'd)

Use in Specific Populations: The safety and efficacy of TAKHZYRO in pediatric patients <2 years of age have not been established.

No data are available on TAKHZYRO in pregnant women. No data are available on the presence of lanadelumab in human milk or its effects on breastfed infants or milk production.

To report SUSPECTED ADVERSE REACTIONS, contact Dyax Corp., a Takeda company, at 1-877-TAKEDA-7 (1-877-825-3327), or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see additional <u>Important Safety Information</u> throughout and full <u>Prescribing Information</u>.



HELP OLE secondary endpoints

EFFECTIVE PREVENTION IN THE LONG TERM

Patients taking TAKHZYRO for an average of 30 months experienced attack reduction vs baseline²

87%
REDUCTION IN ATTACKS

vs baseline (N=209)²

- 0.25 mean monthly attack rate (N=209; baseline: 3.05)²
- 0.05 median monthly attack rate (range: 0.0-4.7; baseline: 2.00)¹⁷
- 84% reduction in moderate or severe attacks (N=209)²
- 93% reduction in attacks requiring acute treatment (n=106)²

Long-term, open-label extension data were consistent with the safety profile and efficacy in the pivotal trial.^{1,2}

All data presented are for TAKHZYRO 300 mg every 2 weeks unless otherwise indicated.

IMPORTANT SAFETY INFORMATION

Hypersensitivity reactions have been observed. In case of a severe hypersensitivity reaction, discontinue TAKHZYRO administration and institute appropriate treatment.

Please see additional <u>Important Safety Information</u> throughout and full <u>Prescribing Information</u>.

HELP OLE prespecified exploratory endpoints

Freedom from attacks for extended periods of time when taking TAKHZYRO for an average of 30 months (N=209)²

ZERO ATTACKS FOR

14.8 MONTHS

ON AVERAGE

Mean duration of attack-free period: 415 days (SD=12.4 months)²

8 OUT OF 1 O

PATIENTS (81.8%)
FOR AT LEAST A 6-MONTH PERIOD

Mean study duration: 29.6 (SD=8.2) months²

98%
OF DAYS ON AVERAGE DURING TREATMENT PERIOD*

(N=209, SD=6%)²

All data presented are for TAKHZYRO 300 mg every 2 weeks unless otherwise indicated.

*The percentage of days with zero attacks was calculated by counting the number of days in the treatment period without an HAE attack and dividing by the number of days the patient spent in the treatment period.¹⁷



ESTABLISHED EFFECTIVENESS AND SAFETY PROFILE IN PEDIATRIC PATIENTS 2 TO <12 YEARS OF AGE¹

Use of TAKHZYRO for patients 2 to <12 years of age was supported by extrapolation of efficacy data from the HELP study, with additional pharmacokinetic analyses showing similar drug exposures between adults and pediatric patients, and safety and pharmacodynamic data from the SPRING study.1

Lanadelumab-flyo exposures in pediatric patients 2 to <12 years of age receiving TAKHZYRO 150 mg every 2 weeks or every 4 weeks were comparable to those in adult patients receiving TAKHZYRO 300 mg every 2 weeks¹⁵

• Pharmacokinetics (Co-primary Endpoint): Patients aged 2 to <12 years taking TAKHZYRO in the 52-week open-label study experienced systemic exposure to TAKHZYRO¹⁵

> The safety and pharmacokinetics of TAKHZYRO were the co-primary endpoints in the SPRING study.¹⁵

IMPORTANT SAFETY INFORMATION (cont'd)

Adverse Reactions: The most commonly observed adverse reactions (≥10%) associated with TAKHZYRO were injection site reactions consisting mainly of pain, erythema, and bruising at the injection site; upper respiratory infection; headache; rash; dizziness; diarrhea; and myalgia. Less common adverse reactions observed included elevated levels of transaminases; one patient discontinued the trial for elevated transaminases.

Please see additional **Important Safety Information** throughout and full **Prescribing Information**.

Limitations

Because this was a noncontrolled, open-label study that enrolled 21 pediatric patients and lacked statistical hypothesis testing, these data have less evidentiary value than a double-blind, placebo-controlled study. Further confirmatory studies are required to draw any conclusions from these data.

Patients aged 2 to <12 years taking TAKHZYRO in the 52-week open-label study experienced attack reduction vs baseline^{1,15}

Secondary Endpoints

- 95% reduction in attacks on average vs baseline (N=21)¹⁵
 - Mean monthly attack rate at baseline (during observation period): 1.84 (N=21)¹⁵
 - Mean monthly attack rate on treatment: 0.08 (N=21)15
- 76% of patients experienced freedom from attacks for the entire 52-week study (n=16)15
- 99.5% of days on average with zero attacks during the entire treatment period (N=21)¹⁵



Efficacy

TAKHZYRO

(lanadelumab-flyo) injection

HELP safety results

SAFETY PROFILE ESTABLISHED IN ONE OF THE LARGEST PREVENTION STUDIES IN HAE^{1,2,9-11}

Most common ARs (≥10%) observed in the pivotal trial ^{1,12*}	TAKHZYRO every 2 weeks (n=27)	TAKHZYRO every 4 weeks (n=29)	Placebo (n=41)
Injection site reactions†	56%	45%	34%
• Pain	52%	31%	29%
Erythema	7%	7%	2%
Bruising	4%	7%	0%
Upper respiratory infection‡	44%	31%	32%
Headache [§]	33%	21%	22%
Rash ⁹	4%	10%	5%
Dizziness	4%	10%	0%
Diarrhea	4%	0%	5%
Myalgia	11%	0%	0%

Hypersensitivity reactions have been observed. In case of a severe hypersensitivity reaction, discontinue TAKHZYRO administration and institute appropriate treatment.¹

No incidence of anaphylaxis in the pivotal trial.¹

Injection site reactions were the most common adverse reactions (ARs).1

To report SUSPECTED ADVERSE REACTIONS, contact Dyax Corp., a Takeda company, at 1-877-TAKEDA-7 (1-877-825-3327), or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see additional <u>Important Safety Information</u> throughout and full **Prescribing Information**.

HELP OLE safety results

CONSISTENT SAFETY PROFILE SEEN IN 212 PATIENTS IN THE OPEN-LABEL **EXTENSION STUDY**¹

Safety data of patients taking TAKHZYRO for an average of 30 months²

Most common ARs (≥10%) observed in the HELP open-label study²	TAKHZYRO every 2 weeks (N=212)
Injection site pain	47%
Viral upper respiratory tract infection	42%
Upper respiratory tract infection	26%
Headache	25%
Injection site erythema	17%
Arthralgia	13%
Injection site bruising	12%
Back pain	12%
Diarrhea	11%
Sinusitis	11%
Influenza	10%
Nausea	10%
Urinary tract infection	10%

Hypersensitivity reactions (2%, n=4) were reported in the study.^{2#} Six patients discontinued due to treatment-emergent adverse events (TEAEs).²

- Three patients discontinued due to hypersensitivity reactions²
- One hypersensitivity event was considered related to the study drug and led to discontinuation²

No treatment-related serious adverse events or anaphylaxis were observed.²



^{*≥10%} in any TAKHZYRO group that also occurred at a higher rate than placebo group.¹

[†]Additional injection site reactions included hematoma, hemorrhage, pruritus, swelling, induration, paresthesia, reaction, warmth,

^{*}Includes upper respiratory infection, viral upper respiratory infection.1

[§]Includes headache, tension headache, sinus headache.

[&]quot;Includes rash, rash maculopapular, rash erythematous."

SAFETY PROFILE SEEN IN PATIENTS AS YOUNG AS 2 YEARS OF AGE

Safety data of 21 pediatric patients taking TAKHZYRO for 52 weeks^{1,15}

Most common related TEAEs ^{15*}	TAKHZYRO 150 mg every 2 or 4 weeks (N=21)
Injection site pain	29%
Injection site erythema	14%
Injection site swelling	5%
Administration site pain	5%
Injection site reaction	5%

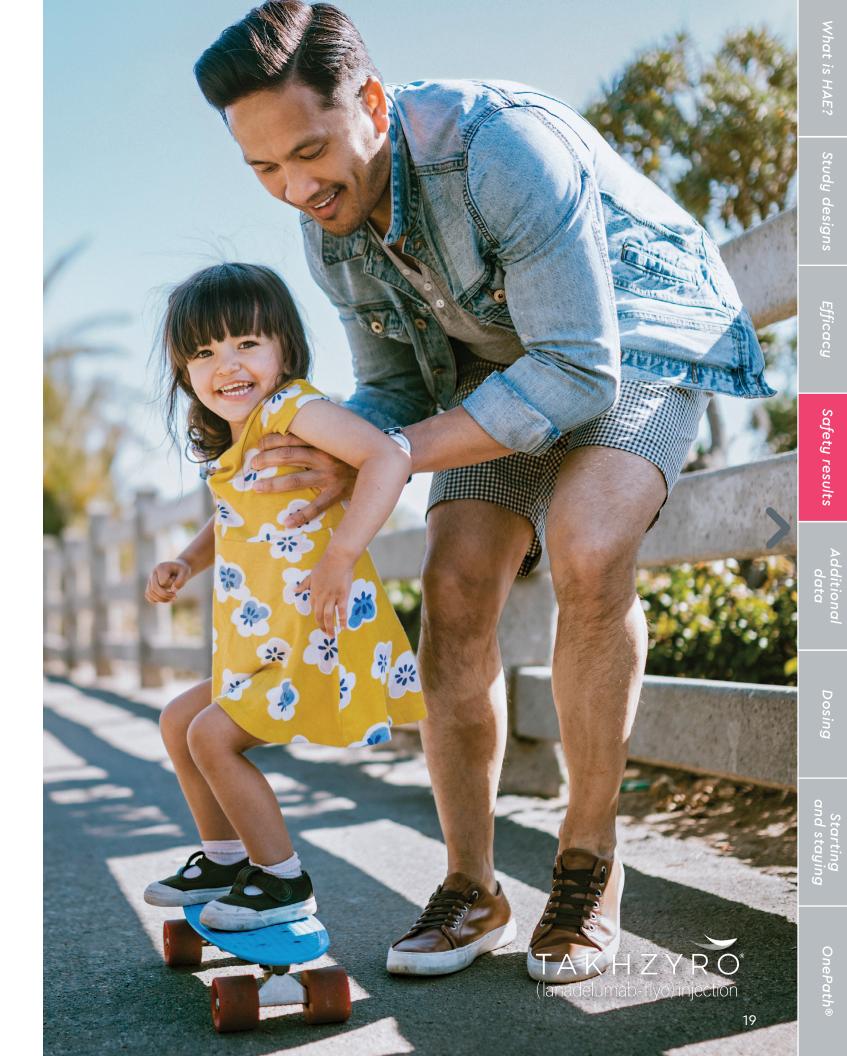
The profile of related TEAEs was similar between the every-2-weeks and every-4-weeks dosing treatment groups.¹⁵

No deaths, serious TEAEs, hospitalizations, or discontinuations due to TEAEs were observed.¹⁵

No new safety signals were observed in these patients. Overall, the safety was similar between adult patients and pediatric patients (2 to <18 years of age).¹

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^{*}TEAEs reported by \geq 3 patients are presented. 15

HR-QoL prespecified exploratory endpoint

THE BURDEN OF HAE GOES BEYOND THE ATTACK

The unpredictable nature of HAE can affect various facets of a patient's life.³

In the HELP study, quality of life (QoL) measures were evaluated using the AE-QoL and EQ-5D-5L questionnaires¹⁸

Limitations: These results should be interpreted with caution as they are based on patient recall and are observational/descriptive in nature. These data were also from an exploratory objective and had less evidentiary value than the primary and secondary objectives. The AE-QoL was administered to 10 adolescent patients in the study, an age group for which the instrument was not validated.¹⁸

For the EQ-5D-5L questionnaire, an instrument used to measure health status on a given day, no differences were observed. The nondisease-specific EQ-5D-5L questionnaire was administered on days 0, 98, and 182.¹⁸



- 81% of patients receiving TAKHZYRO 300 mg Q2W (95% CI, 61-93; n=26)
 experienced improvement in AE-QoL total score vs 37% of patients taking placebo
 (P<0.05; 95% CI, 22-54; n=38)¹⁸
- Patients receiving TAKHZYRO 300 mg Q2W were 7.2 times more likely to achieve improvement in AE-QoL total score vs patients taking placebo (P<0.01)¹⁸

Definitions: The AE-QoL is a validated, angioedema-specific questionnaire in adults that was administered monthly, consisting of **4 domains (functioning, fatigue/mood, fears/shame, nutrition)** and total scores. The minimal clinically important difference (MCID) is the minimum change in score that is meaningful to patients. For the AE-QoL total score, the predefined MCID is a reduction of 6 points.¹⁸⁻²⁰

AE-QoL=Angioedema Quality of Life Questionnaire; EQ-5D-5L=5-level EuroQol 5-dimensional; HR-QoL=health-related quality of life; Q2W=every 2 weeks.

IMPORTANT SAFETY INFORMATION (cont'd)

Use in Specific Populations: The safety and efficacy of TAKHZYRO in pediatric patients <2 years of age have not been established.

No data are available on TAKHZYRO in pregnant women. No data are available on the presence of lanadelumab in human milk or its effects on breastfed infants or milk production.

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Please see additional <u>Important Safety Information</u> throughout and full <u>Prescribing Information</u>.





For adult and adolescent patients ≥12 years of age

FREEDOM FROM DAILY DOSING

Self-injection that requires no reconstitution¹



The TAKHZYRO subcutaneous prefilled syringe. Not actual size.

- TAKHZYRO has a half-life of ~14 days; therefore, it takes ~10 weeks (ie, 6 doses) to reach **steady state** and ~2 weeks until 50% of TAKHZYRO leaves the body^{1,21}
- The recommended starting dosage in adult and pediatric patients 12 years of age and older is 300 mg every 2 weeks. TAKHZYRO 300 mg every 4 weeks is also effective and may be considered if the patient is well-controlled (eg, attack free) for more than 6 months¹

All data presented are for TAKHZYRO 300 mg every 2 weeks unless otherwise indicated.

IMPORTANT SAFETY INFORMATION

Hypersensitivity reactions have been observed. In case of a severe hypersensitivity reaction, discontinue TAKHZYRO administration and institute appropriate treatment.

Please see additional <u>Important Safety Information</u> throughout and full <u>Prescribing Information</u>.

For pediatric patients 2 to <12 years of age

A LOWER DOSE FOR YOUNGER PATIENTS

Age-based dosing interval of every 2 or 4 weeks¹

AGES	NUMBER OF DOSES PER MONTH		
2 TO <6 YEARS	150 mg/1 mL SUBCUTANEOUS INJECTION (1 INJECTION EVERY 4 WEEKS) ¹		
6 TO <12 YEARS	150 mg/1 mL SUBCUTANEOUS INJECTIONS (1 INJECTION EVERY 2 WEEKS) ¹ A dosing interval of 150 mg every 4 weeks may be considered if the patient is well-controlled (eg, attack free) for more than 6 months. ¹		

Remind your patients and their caregivers to always have acute treatment on hand and periodically check the date to ensure it hasn't expired.

One month is defined as 28 days.





^{*}In clinical studies, the majority of patients self-administered TAKHZYRO within 10 to 60 seconds.

These injection times are based on vial administration.

TWO DOSING OPTIONS PROVIDE FLEXIBILITY TO HELP MEET PATIENTS' CHANGING HAE NEEDS

Total doses per month for adult and adolescent patients ≥12 years of age

Q2W DOSING
TAKHZYRO1*

OR IF WELL
CONTROLLED

SUBCUTANEOUS INJECTIONS
VIA PREFILLED SYRINGE
(one 300 mg/2 mL
injection every 2 weeks)

Q4W DOSING
TAKHZYRO1*

SUBCUTANEOUS INJECTION
VIA PREFILLED SYRINGE
(one 300 mg/2 mL injection every
4 weeks if attack free for 6 months)

C1 ESTERASE INHIBITOR (HUMAN)

7

OR

INTRAVENOUS INFUSIONS (1000 units every 3 or 4 days) SUBCUTANEOUS INJECTIONS (one injection twice weekly; every 3 or 4 days) ORAL PLASMA
KALLIKREIN INHIBITOR

28

CAPSULES (one 150 mg capsule daily)

This presentation is not intended to compare the relative safety or efficacy of these treatments. Please refer to each product's full Prescribing Information.

One month is defined as 28 days.

IMPORTANT SAFETY INFORMATION (cont'd)

Adverse Reactions: The most commonly observed adverse reactions (≥10%) associated with TAKHZYRO were injection site reactions consisting mainly of pain, erythema, and bruising at the injection site; upper respiratory infection; headache; rash; dizziness; diarrhea; and myalgia. Less common adverse reactions observed included elevated levels of transaminases; one patient discontinued the trial for elevated transaminases.

Please see additional <u>Important Safety Information</u> throughout and full <u>Prescribing Information</u>.

Total doses per month for pediatric patients

AGES	TAKHZYRO ¹	C1 ESTERASE INHIBITOR (HUMAN)	ORAL PLASMA KALLIKREIN INHIBITOR
2 TO <6 YEARS	SUBCUTANEOUS INJECTION (one 150 mg/1 mL injection every 4 weeks) ^{1†}	No approved options	No approved options
6 TO <12	SUBCUTANEOUS INJECTIONS (one 150 mg/1 mL injection every 2 weeks)¹‡ OR IF WELL CONTROLLED	INTRAVENOUS INFUSIONS (1000 units every 3 or 4 days) OR	No approved options
YEARS	SUBCUTANEOUS INJECTION (one 150 mg/1 mL injection every 4 weeks if attack free for 6 months)1‡	SUBCUTANEOUS INJECTIONS (one injection twice weekly; every 3 or 4 days)	Options

This presentation is not intended to compare the relative safety or efficacy of these treatments. Please refer to each product's full Prescribing Information.

TAKHZYRO is the only approved HAE preventive treatment indicated for pediatric patients 2 to <6 years of age.

One month is defined as 28 days.

'The recommended dosage in pediatric patients 2 to less than 6 years of age is 150 mg administered subcutaneously every 4 weeks.'

*The recommended starting dosage in pediatric patients 6 to less than 12 years of age is 150 mg administered subcutaneously every 2 weeks. A dosing interval of 150 mg every 4 weeks may be considered if the patient is well-controlled (eg, attack free) for more than 6 months.



^{*}The recommended starting dosage in adult and pediatric patients 12 years of age and older is 300 mg every 2 weeks.

TAKHZYRO 300 mg every 4 weeks is also effective and may be considered if the patient is well-controlled (eg, attack free) for more than 6 months.¹

LONG-TERM PREVENTION. LONG-TERM SUPPORT.

Helping your patients stay on track with treatment

Whether you currently treat patients with HAE or have prescribed TAKHZYRO recently, it's important to help you and your patients plan for the long term.

In addition to the established safety profile and clinically proven efficacy of TAKHZYRO, evaluated across 2 studies of adult and adolescent patients ≥12 years of age, Takeda has:



in treating and providing access and product support for patients with HAE^{1,2}

Think of a patient taking TAKHZYRO—where are they on their treatment journey?

IMPORTANT SAFETY INFORMATION (cont'd)

Use in Specific Populations: The safety and efficacy of TAKHZYRO in pediatric patients <2 years of age have not been established.

No data are available on TAKHZYRO in pregnant women. No data are available on the presence of lanadelumab in human milk or its effects on breastfed infants or milk production.

To report SUSPECTED ADVERSE REACTIONS, contact Dyax Corp., a Takeda company, at 1-877-TAKEDA-7 (1-877-825-3327), or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

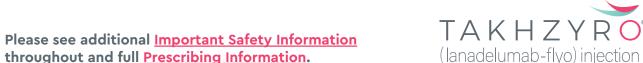
STARTING OFF RIGHT WITH TAKHZYRO

Establishing treatment expectations and goals



- HAE is a genetic, unpredictable, and lifelong condition, and it's important to set specific goals for therapy³
- Choosing effective prevention with TAKHZYRO means working together with your patients to help prevent and reduce the severity of their HAE attacks—which may align with their treatment goals³

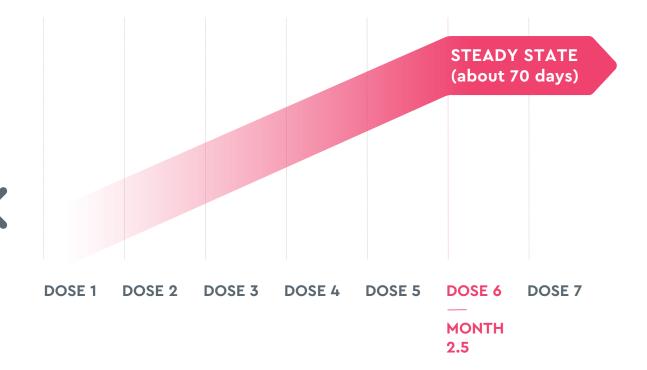
Create a regular check-in schedule to review progress and treatment goals—as routine monitoring is recommended by the 2020 US HAEA guidelines.³



CHECKING IN WITH PATIENTS AS THEY BEGIN TREATMENT

Help adult and adolescent patients ≥12 years of age stay focused on taking TAKHZYRO as prescribed

TAKHZYRO has a half-life of ~14 days and dosing is every 2 weeks. Because of this, it takes ~10 weeks (ie, 6 doses) to reach steady state and ~2 weeks until 50% of TAKHZYRO leaves the body.^{1,21} This provides patients with freedom from daily dosing.



Remind your patients that the most common side effects are injection site reactions. It is also normal to experience breakthrough attacks.¹

STAYING ON LONG-TERM PREVENTION

Living with periods of freedom from HAE attacks

- Continue to check in with your patients even if they have been taking TAKHZYRO for 6 months or longer
 - TAKHZYRO has the option for less frequent dosing if a patient is attack free for more than 6 months¹
- Remind patients of the impact effective prevention has had on their lives and their progress since starting TAKHZYRO
- Patients taking TAKHZYRO in a 6.5-month study and a 2.5-year open-label extension study had HAE attacks less often. Some patients in the studies had zero attacks for periods of time^{1,2}



To help your patients learn what to expect from treatment with TAKHZYRO, hear from a healthcare professional as well as 2 patients taking TAKHZYRO. Visit <u>TAKHZYRO.com/events</u>.

IMPORTANT SAFETY INFORMATION

Hypersensitivity reactions have been observed. In case of a severe hypersensitivity reaction, discontinue TAKHZYRO administration and institute appropriate treatment.

Please see additional <u>Important Safety Information</u> throughout and full <u>Prescribing Information</u>.



At OnePath®, WE TAILOR OUR SUPPORT TO YOUR PATIENT

Providing product support to patients with HAE for over 12 years

When you prescribe TAKHZYRO® (lanadelumab-flyo) for your patient, OnePath is here to provide them with dedicated product support. We'll connect your patient with a OnePath specialist who acts as their go-to person. They will:



Work with your patient's insurance provider to help them receive their prescribed Takeda treatment



Provide information about financial assistance options



Arrange for a trained nursing professional to teach your patient how to self-administer TAKHZYRO at home, once requested by your office



Help your patient access the OnePath Mobile App to connect with OnePath and track their health in a personal eDiary

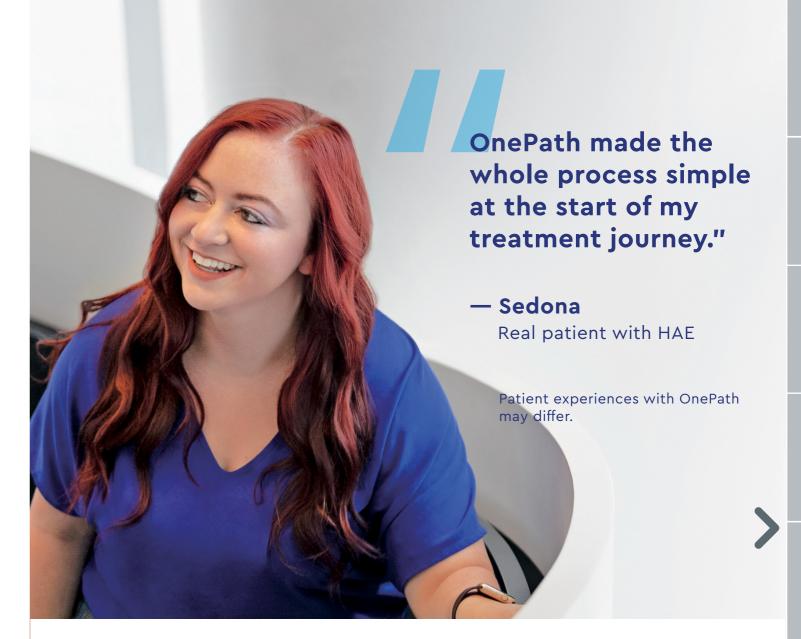
Get patients started today through the Quick Start Program!* Visit <u>TAKHZYRO.com/hcp/quick-start</u>.

If you have questions, call OnePath at **1-866-888-0660**, Monday through Friday, **8:30** AM to **8:00** PM ET.



*Timing is dependent upon when the forms are received by OnePath. The Quick Start Program is available to all commercially insured patients ≥2 years of age who are US residents with a confirmed diagnosis of HAE. To enroll patients, a commercial insurance investigation must be initiated by filling out both the TAKHZYRO Start Form and Quick Start Program: Enrollment Form. Takeda and its affiliates reserve the right to change or discontinue this program at any time, without notice. Void where prohibited by law. This program does not constitute a financial assistance program.

Please see Important Safety Information throughout and full Prescribing Information.



References: 1. Takhzyro. Prescribing information. Dyax Corp; 2023. 2. Banerji A, Bernstein JA, Johnston DT, et al; HELP OLE Investigators. Long-term prevention of hereditary angioedema attacks with lanadelumab: the HELP OLE study. Allergy. 2022;77(3):979-990. doi:10.1111/all.15011 3. Busse PJ, Christiansen SC, Riedl MA, et al. US HAEA Medical Advisory Board 2020 guidelines for the management of hereditary angioedema. J Allergy Clin Immunol Pract. 2021;9(1):132-150.e3. doi:10.1016/j.jaip.2020.08.046 4. Banerji A. The burden of illness in patients with hereditary angioedema. Ann Allergy Asthma Immunol. 2013;111(5):329-336. doi:10.1016/j.anai.2013.08.019 5. Bork K, Davis-Lorton M. Overview of hereditary angioedema caused by C1-inhibitor deficiency: assessment and clinical management. Eur Ann Allergy Clin Immunol. 2013;45(1):7-16. 6. Zuraw BL. Clinical practice. Hereditary angioedema. N Engl J Med. 2008;359(10):1027-1036. doi:10.1056/NEJMcp0803977 7. Johnston DT, Smith RC. Hereditary angioedema: special considerations in children. Allergy Asthma Proc. 2020;41(6)(suppl 1):S43-S46. doi:10.2500/aap.2020.41.200042 8. Maurer M. Magerl M, Betschel S, et al. The international WAO/EAACI guideline for the management of hereditary angioedema—the 2021 revision and update. Allergy. 2022;77(7):1961-1990. doi:10.1111/all.15214 9. Cinryze. Prescribing information. Takeda Pharmaceuticals USA, Inc; 2023. 10. Haegarda. Prescribing information. CSL Behring LLC; 2022. 11. Orladeyo. Prescribing information. BioCryst Pharmaceuticals, Inc; 2022. 12. Banerji A, Riedl MA, Bernstein JA, et al. Effect of lanadelumab compared with placebo on prevention of hereditary angioedema attacks: a randomized clinical trial. JAMA. 2018;320(20):2108-2121. doi:10.1001/jama.2018.16773 13. Data on file, SHP643-066, Shire Inc. 14. Riedl MA, Bernstein JA, Craig T, et al. An open-label study to evaluate the long-term safety and efficacy of lanadelumab for prevention of attacks in hereditary angioedema: design of the HELP study extension. Clin Transl Allergy. 2017;7:36. doi:10.1186/s13601-017-0172-9 15. Data on file, TAK743-301, Takeda Pharmaceuticals USA, Inc. 16. Data on file, TAK743-303, Takeda Pharmaceuticals USA, Inc. 17. Data on file, TAK743-098, Takeda Pharmaceuticals USA, Inc. 18. Lumry WR, Weller K, Magerl M, et al; HELP Study Investigators. Impact of lanadelumab on health-related guality of life in patients with hereditary angioedema in the HELP study. Allergy. 2021;76(4):1188-1198. doi:10.1111/all.14680 19. Weller K, Groffik A, Magerl M, et al. Development and construct validation of the angioedema quality of life questionnaire. Allergy. 2012;67(10):1289-1298. doi:10.1111/all.12007 20. Weller K, Magerl M, Peveling-Oberhag A, Martus P, Staubach P, Maurer M. The Angioedema Quality of Life Questionnaire (AE-QoL) – assessment of sensitivity to change and minimal clinically important difference. Allergy. 2016;71(8):1203-1209. doi:10.1111/all.12900 21. Wang Y, Marier JF, Kassir N, Chang C, Martin P. Pharmacokinetics, pharmacodynamics, and exposure-response of lanadelumab for hereditary angioedema. Clin Transl Sci. 2020;13(6):1208-1216. doi:10.1111/cts.12806

THE #1 PRESCRIBED HAE PREVENTIVE TREATMENT*

Imagine what the TAKHZYRO experience can mean for all of your patients aged 2 years and older¹

- Studied in the broadest range of patients aged 2 years and older^{1,9-11}
- Long-term freedom from attacks for an average of 14.8 months for adult and adolescent patients^{2†}
- Freedom from daily dosing with every-2-weeks or every-4-weeks administration based on age¹
 - See full Prescribing Information for additional details

Studied in over

200

ADULT AND ADOLESCENT PATIENTS ACROSS 2 STUDIES^{1,2} Studied for up to

2.5

YEARS IN THE HELP OPEN-LABEL EXTENSION STUDY² Prescribed to over

3250

PATIENTS SINCE 2018‡



*Based on total patients on HAE preventive treatments according to US third-party industry healthcare data.

[†]Mean duration of the attack-free period in the open-label extension study was 14.8 (SD=12.4) months (N=209).² [‡]Based on third-party US specialty pharmacy data.

Enroll your patients today and find other useful resources online at TAKHZYRO.com/hcp/quick-start.

INDICATION

TAKHZYRO is indicated for prophylaxis to prevent attacks of hereditary angioedema (HAE) in patients ≥2 years of age.

IMPORTANT SAFETY INFORMATION

Hypersensitivity reactions have been observed. In case of a severe hypersensitivity reaction, discontinue TAKHZYRO administration and institute appropriate treatment.

Please see additional Important Safety Information throughout and full Prescribing Information.



