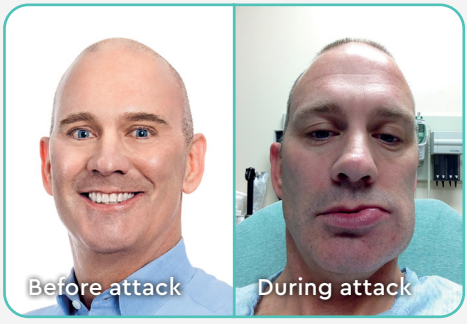
UNDERSTANDING HAE

What is HAE?[1-3]

Hereditary angioedema (HAE) is a rare genetic disease that causes recurrent, unpredictable, and potentially life-threatening attacks of angioedema in the body. HAE affects about 1 in 50,000 people of all ages. HAE attacks have been reported in patients as young as 3 years of age.

Where can attacks, or "swells," occur?[1,4]

- Face, hands, and feet
- Abdomen and genitals
- Larynx, where attacks can be life-threatening



Bob
Real patient

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. This adds to the unpredictable nature of the disease.[5]

Therefore, long-term prevention should be individualized and considered in all patients with HAE.[6]

CLICK TO GET STARTED

TAKHZYRO CLINICAL TRIALS SUMMARY

PIVOTAL TRIAL: HELP STUDY[7,8]

Number of patients studied	125
Study duration	26 weeks
Primary endpoint	HAE attack reduction in patients ≥12 years of age taking TAKHZYRO

HELP OPEN-LABEL EXTENSION STUDY[7,9]

Number of patients studied	212 (109 rollover patients from HELP)
Study duration	Up to 2.5 years (up to 132 weeks)
Primary endpoint	Long-term safety of TAKHZYRO in patients ≥12 years of age

PEDIATRIC TRIAL: OPEN-LABEL SPRING STUDY[7,10]

Number of patients studied	21
Study duration	52 weeks
Co-primary endpoints	Safety and pharmacokinetics of TAKHZYRO in patients 2 to <12 years of age

For the pediatric indication, 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.[7]

REAL-WORLD STUDY SUMMARY

EMPOWER PHASE 4 STUDY[7,11]

Number of patients enrolled	164*
Study duration	Up to 3 years
Primary endpoints	Real-world effectiveness of TAKHZYRO as measured by HAE attack rate before and after TAKHZYRO initiation in patients aged 12 years and older

*164 patients were enrolled in EMPOWER: 109 patients were evaluated in the Full Analysis Set, including 18 new TAKHZYRO users and 91 established TAKHZYRO users.

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.

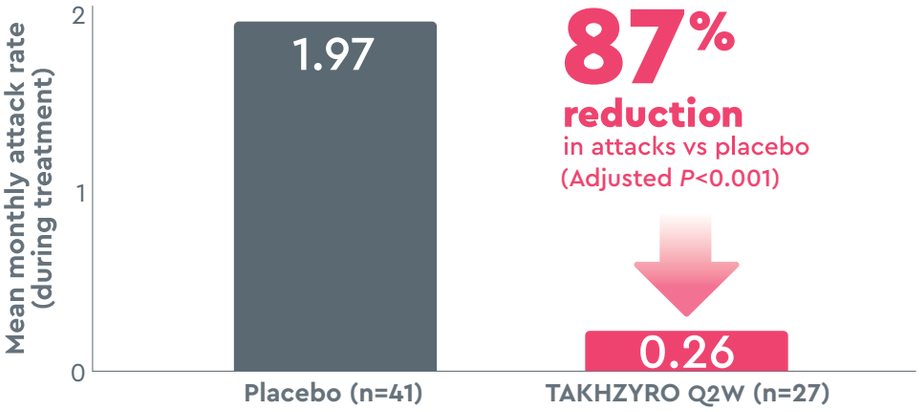
TAKHZYRO®
(lanadelumab-flyo) injection 300 mg·150 mg

HELP primary endpoints

REDISCOVER EFFECTIVE PREVENTION

Significant reduction in mean attack rate* vs placebo at 6.5 months in the HELP study[7,8]

TAKHZYRO vs placebo



87%
reduction
in attacks vs placebo
(Adjusted *P*<0.001)

- **TAKHZYRO 300 mg every 4 weeks resulted in a 73% reduction in attacks vs placebo (Adjusted *P*<0.001)[7†]**

Mean monthly attack rate during the run-in period[8]:

3.52	3.71	4.02
for Q2W arm (n=27)	for Q4W arm (n=29)	for placebo arm (n=41)

Mean monthly attack rate during the treatment period[7]:

0.26	0.53	1.97
for Q2W arm	for Q4W arm	for placebo arm

Secondary endpoints: Patients taking TAKHZYRO (n=27) had 83% fewer moderate or severe attacks and 87% fewer attacks that needed acute treatment vs placebo (n=41; Adjusted *P*<0.001).[7†]

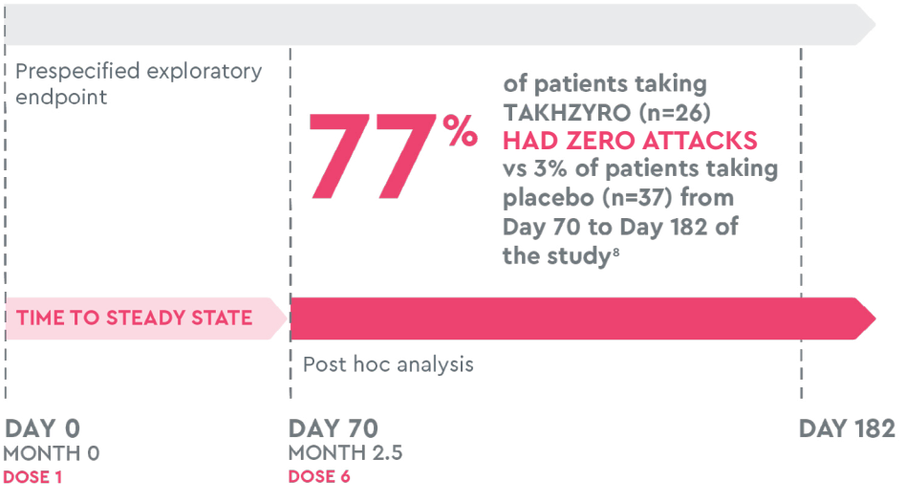
All data presented are for TAKHZYRO 300 mg every 2 weeks unless otherwise indicated.
*Mean monthly attack rate: number of attacks/4 weeks.[7]
†Adjusted *P*-values for multiple testing.[7]
Q2W=every 2 weeks; Q4W=every 4 weeks.

HELP secondary and exploratory endpoints

FREEDOM FROM HAE ATTACKS IN THE HELP STUDY

Many patients taking TAKHZYRO in the study had zero attacks[7,8]

44% of patients taking TAKHZYRO (n=27) **HAD ZERO ATTACKS** vs 2% of patients taking placebo (n=41) during the entire 6.5-month study[7,8]



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.

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TAKHZYRO®
(lanadelumab-flyo) injection 300 mg·150 mg

HELP safety results

SAFETY PROFILE ESTABLISHED IN ONE OF THE LARGEST PREVENTION STUDIES IN HAE[7,9,12-14]

Most common ARs (≥10%) observed in the pivotal trial[7,8*]	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[¶]	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.[7]

No incidence of anaphylaxis in the pivotal trial.[7]

Injection site reactions were the most common adverse reactions (ARs).[7]

The efficacy and safety of TAKHZYRO were evaluated in 3 clinical studies: a 6.5-month study and a 2.5-year open-label extension study in adolescents and adults, and a 12-month pediatric study.[7,9,10]

*≥10% in any TAKHZYRO group that also occurred at a higher rate than placebo group.[7]
†Additional injection site reactions included hematoma, hemorrhage, pruritus, swelling, induration, paresthesia, reaction, warmth, edema, and rash.[7]
‡Includes upper respiratory infection, viral upper respiratory infection.[7]
§Includes headache, tension headache, sinus headache.[7]
¶Includes rash, rash maculopapular, rash erythematous.[7]

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.

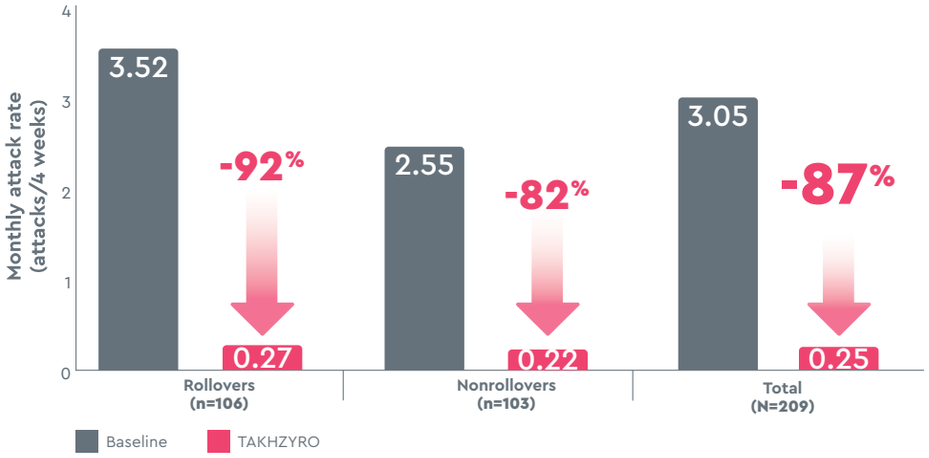
No data are available on TAKHZYRO in pregnant women. No data are available on the presence of lanadelumab in human milk or its effects on breastfed infants or milk production.

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 OLE secondary endpoints

IN A 2.5-YEAR STUDY WITH OVER 200 PATIENTS, EFFECTIVE PREVENTION SHOWN IN THE LONG TERM[9]

Patients taking TAKHZYRO for an average of 30 months experienced attack reduction vs baseline[9]



Patients who experienced a reduction in frequency and severity of attacks in the HELP study (rollover patients) were more likely to choose to continue treatment with TAKHZYRO in HELP OLE, which may affect the interpretation of these data.

- 0.25 mean monthly attack rate (N=209; baseline: 3.05)[9]
- 0.05 median monthly attack rate (range: 0.0-4.7; baseline: 2.00)[15]
- 84% reduction in moderate or severe attacks (N=209)[9]
- 93% reduction in attacks requiring acute treatment (n=106)[9]

The long-term safety of TAKHZYRO was the primary endpoint in the open-label extension study.[9]

All data presented are for TAKHZYRO 300 mg every 2 weeks unless otherwise indicated.
OLE=open-label extension.

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

TAKHZYRO®
(lanadelumab-flyo) injection 300 mg·150 mg

HELP OLE prespecified exploratory endpoints

Freedom from attacks for extended periods of time when taking TAKHZYRO for an average of 30 months (N=209)[9]

ZERO ATTACKS FOR

14.8

MONTHS
ON AVERAGE

Mean duration of attack-free period: 415 days (SD=12.4 months)[9]

98%

OF DAYS ON AVERAGE
DURING TREATMENT PERIOD*

(N=209, SD=6%)[9]

8 OUT OF 10

PATIENTS (82%)
WERE ATTACK FREE FOR AT LEAST A 6-MONTH PERIOD

Mean study duration: 29.6 (SD=8.2) months[9]

NEARLY 7 OUT OF 10

PATIENTS (69%)
WERE ATTACK FREE FOR AT LEAST A 1-YEAR PERIOD

Mean study duration: 29.6 (SD=8.2) months[9]

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.[15]

OLE=open-label extension; SD=standard deviation.

IMPORTANT SAFETY INFORMATION (cont'd)

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.

HELP OLE safety results

CONSISTENT SAFETY PROFILE SEEN IN 212 PATIENTS IN THE OPEN-LABEL EXTENSION STUDY[7]

Safety data of patients taking TAKHZYRO for an average of 30 months[9]

Most common ARs (≥10%) observed in the HELP open-label study[9]	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.[9†]

Six patients discontinued due to treatment-emergent adverse events (TEAEs).[9]

- Three patients discontinued due to hypersensitivity reactions[9]
- One hypersensitivity event was considered related to the study drug and led to discontinuation[9]

No treatment-related serious adverse events or anaphylaxis were observed.[9]

Mean study duration: 29.6 (SD=8.2) months.[9]

†Related, treatment-emergent hypersensitivity reactions.[9]

AR=adverse reaction; OLE=open-label extension; SD=standard deviation.

TAKHZYRO® (lanadelumab-flyo) injection 300 mg·150 mg

EMPOWER REAL-WORLD PHASE 4 STUDY[11]

Mean patient time on TAKHZYRO[11]

- 32 months (SD=17) in established TAKHZYRO patients (n=91)*
- 26 months (SD=13) in new TAKHZYRO patients (n=18)†

Limitations of EMPOWER

- This was an observational, self-controlled, real-world study lacking a standardized treatment protocol or control arm
- Small sample size due to the rarity of HAE
- Potential selection bias due to including established patients
- Possible misclassification of effectiveness and safety data due to patient HAE attack diary data capture and recall bias
- Follow-up duration was truncated in some patients due to the sponsor ending the study earlier than planned, which may have resulted in conservative estimates of patients persisting with long-term treatment
- 1 new patient received 1 dose of TAKHZYRO before study enrollment; another new patient had 3 doses of TAKHZYRO before study enrollment

Statistical analysis for EMPOWER[11]:

To assess the effectiveness of TAKHZYRO in new patients, mean attack rate (attacks/month), incidence rate ratios (IRRs), and 95% confidence intervals (CIs) were calculated by a generalized linear model for pre-TAKHZYRO, early, and steady-state periods. To assess the effectiveness of TAKHZYRO in established patients, mean attack rate and 95% CIs were calculated for the overall study period.

The recommended starting dose in patients 12 years of age and older is 300 mg subcutaneously every 2 weeks. A dosing interval of 300 mg every 4 weeks may be considered if the patient is well-controlled (eg, attack free) for more than 6 months.[7]

*Established patients were defined as those who had received ≥4 doses of TAKHZYRO before enrollment and were either receiving TAKHZYRO at enrollment or received their most recent dose <70 days before enrollment.[11]

†New patients were defined as those who had not started TAKHZYRO at enrollment or started TAKHZYRO before enrollment but received <4 doses.[11]

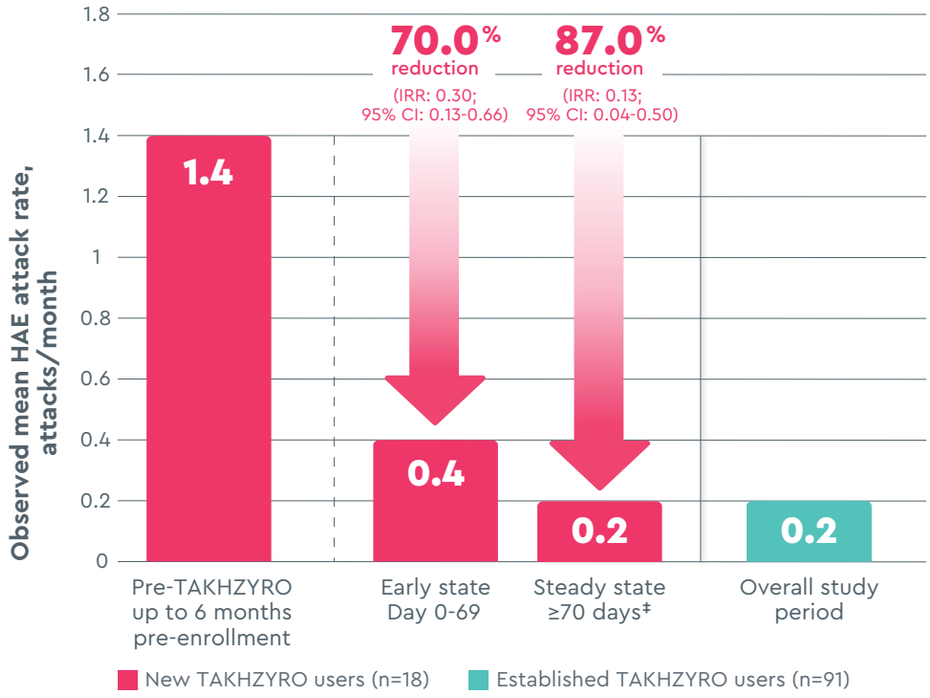
IMPORTANT SAFETY INFORMATION (cont'd)

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.

EMPOWER primary endpoints

HAE ATTACK REDUCTION SEEN IN REAL-WORLD EVIDENCE FOR UP TO 30 MONTHS[11,15]

Reductions in mean monthly HAE attack rates[11,15]



The limitations of this noninterventional study include lack of a standardized treatment protocol and a control arm, with most safety and effectiveness parameters based on participants' recall or self-reported information.

Some patients in the study reported concomitant use of other medications for STP or for LTP while transitioning to TAKHZYRO.

Definition of incidence rate ratio (IRR): a measure to compare the pre-TAKHZYRO attack rate and the on-TAKHZYRO attack rate over a specific period of time. Percent reduction was calculated by: (1-IRR) x 100.

‡Early state was from TAKHZYRO initiation to Day 69 and steady state was from Day 70 after TAKHZYRO initiation.[11]

CI=confidence interval; IRR=incidence rate ratio; LTP=long-term prophylaxis; STP=short-term prophylaxis.

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

TAKHZYRO® (lanadelumab-flyo) injection 300 mg·150 mg

EMPOWER primary endpoints

REDUCED HAE ATTACK RATES OBSERVED IN DOSING SUBGROUPS[11]

Mean attack rates per month in new and established TAKHZYRO patients in the full analysis set[11]*

	Q2W (n=77)	Q4W (n=13)	Q2W to Q4W (n=18)
New patients (n=18)	(n=14) Pre-TAKHZYRO: **1.72** Steady state ≥70 days†: **0.25**	(n=0)	(n=4) Pre-TAKHZYRO: **0.37** Q2W period: **0.04** Q4W period: **0.00** Steady state ≥70 days†: **0.03**
Established patients (n=86)	(n=60) Steady state ≥70 days†: **0.25**	(n=12) Steady state ≥70 days†: **0.09**	(n=14) Q2W period: **0.01** Q4W period: **0.02** Steady state ≥70 days†: **0.04**

The recommended starting dose in patients 12 years of age and older is 300 mg administered subcutaneously every 2 weeks. A dosing interval of 300 mg every 4 weeks may be considered if the patient is well controlled (eg, attack free) for more than 6 months.[7]

*Attack rates were calculated based on patients with available data in the FAS.[11]

†Early state was from TAKHZYRO initiation to Day 69 and steady state was from Day 70 after TAKHZYRO initiation.[11]

FAS=full analysis set; Q2W=every 2 weeks; Q4W=every 4 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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EMPOWER safety results

EMPOWER 3-YEAR SAFETY FINDINGS WERE CONSISTENT WITH THE OVERALL TAKHZYRO SAFETY PROFILE[11]

Six (4.3%) TEAEs in 2 (3.8%) patients were determined to be related to TAKHZYRO[11]

In total, 58 of 112 patients in the safety analysis set reported 154 TEAEs. Of these 154 TEAEs, 6 (in 2 patients) were classified as related to TAKHZYRO[11]

- Fatigue (3), tachycardia (2), and papular rash (1)[11]
- One new and 1 established patient discontinued TAKHZYRO due to TEAEs related to TAKHZYRO (papular rash and fatigue, respectively)[11]
- Among patients in the overall safety set[11]:
  - Infections and infestations were the most frequent (43 events in 34 patients) TEAE Class, followed by
  - Gastrointestinal disorders (14 events in 10 patients), and
  - General disorders and administration site conditions (11 events in 6 patients)
- There were no reports of injection site reactions related to TAKHZYRO in EMPOWER. Injection site reactions were the most commonly observed adverse reactions in ≥10% of patients in the phase 3 HELP clinical trial[7,11]
  - TEAEs were mostly mild (66/154) or moderate (79/154) in severity with 7 classified as severe
  - Most TEAEs were nonserious (146/154), with 8 considered serious
- Two patient deaths, which were unrelated to TAKHZYRO, occurred during the study (COVID-19 infection [n=1]; traumatic brain injury [n=1])[11]

TEAE=treatment-emergent adverse event.

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

TAKHZYRO® (lanadelumab-flyo) injection 300 mg·150 mg

TOGETHER
WITH TAKHZYRO

"TAKHZYRO is approved for use in the **broadest range of patients aged 2 years and older.**"

— Dr Cristina Ramos

"I recommend [patients] consider a preventive medication like TAKHZYRO."

— Dr Michael Manning

Want to watch what HAE experts have to say about TAKHZYRO visit TAKHZYRO.com/hcp/support-and-resources.

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TAKHZYRO® (lanadelumab-flyo) injection 300 mg·150 mg

References: 1. Busse PJ, Christiansen SC, Riedl MA, et al. *J Allergy Clin Immunol Pract*. 2021;9(1):132-150.e3. doi:10.1016/j.jaip.2020.08.046 **2.** Banerji A. *Ann Allergy Asthma Immunol*. 2013;111(5):329-336. doi:10.1016/j.anai.2013.08.019 **3.** Farkas H. *Allergy Asthma Clin Immunol*. Published online July 28, 2010. doi:10.1186/1710-1492-6-18 **4.** Zuraw BL. *N Engl J Med*. 2008;359(10):1027-1036. doi:10.1056/NEJMcp0803977 **5.** Bork K, Davis-Lorton M. *Eur Ann Allergy Clin Immunol*. 2013;45(1):7-16. **6.** Maurer M, Magerl M, Betschel S, et al. *Allergy*. 2022;77(7):1961-1990. doi:10.1111/all.15214 **7.** Takhzyro. Prescribing information. Dyax Corp; 2025. **8.** Banerji A, Riedl MA, Bernstein JA, et al. *JAMA*. 2018;320(20):2108-2121. doi:10.1001/jama.2018.16773 **9.** Banerji A, Bernstein JA, Johnston DT, et al; HELP OLE Investigators. *Allergy*. 2022;77(3):979-990. doi:10.1111/all.15011 **10.** Maurer M, Lumry WR, Li HH, et al; SPRING Investigators. *J Allergy Clin Immunol Pract*. 2024;12(1):201-211.e6. doi:10.1016/j.jaip.2023.09.009 **11.** Bernstein JA, Betschel SD, Busse PJ, et al. *Adv Ther*. Published online June 12, 2025. doi:10.1007/s12325-025-03226-3 **12.** Cinryze. Prescribing information. Takeda Pharmaceuticals USA, Inc; 2023. **13.** Haegarda. Prescribing information. CSL Behring LLC; 2022. **14.** Orladeyo. Prescribing information. BioCryst Pharmaceuticals, Inc; 2022. **15.** Data on File. Takeda Pharmaceuticals.

THE *#1 PRESCRIBED* HAE PREVENTIVE TREATMENT*

See what the TAKHZYRO experience can mean for patients aged 2 years and older[7]

The 6.5-month HELP clinical trial of 125 patients led to the 2018 FDA approval of TAKHZYRO[7,8]

Studied for

11

YEARS IN US CLINICAL AND REAL-WORLD STUDIES[15]

Studied in over

800

PATIENTS GLOBALLY ACROSS 15 STUDIES[15†]

Prescribed to over

4000

US PATIENTS SINCE 2018[12‡]

*Based on total patients on HAE preventive treatment according to US third-party industry healthcare data.
†Includes clinical and real-world evidence studies.[9]
‡Based on third-party US specialty pharmacy data.

INDICATION

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

IMPORTANT SAFETY INFORMATION

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