TAKHZYRO
(lanadelumab-flyo) injection

TAKHZYRO is a plasma kallikrein inhibitor (monoclonal antibody) indicated for prophylaxis to prevent attacks of hereditary angioedema (HAE) in patients 12 years and older, with a recommended starting dose of every 2 weeks to help prevent attacks.

WHAT IS HEREDITARY ANGIOEDEMA?

HAE is a rare, genetic disorder that results in recurring attacks of edema (swelling) in various parts of the body, including the abdomen, face, feet, genitals, hands and throat.[1,2,3]

Common Triggers

Stress

Trauma

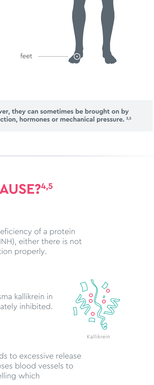
Dental Procedure

Hormones

Surgery

Infection

Laryngeal attacks that obstruct the airways are potentially life-threatening due to the risk of asphyxiation.[1,2]



HAE attacks often happen without a known trigger; however, they can sometimes be brought on by stress, physical trauma, surgery, or a dental procedure, infection, hormones or mechanical pressure.[1,3]

WHAT IS THE CAUSE?[4,5]

Prekallikrein

Most people with HAE have a deficiency of a protein called C1 esterase inhibitor (C1-INH), either there is not enough of it or it does not function properly.

Without sufficient or functional C1-INH, plasma kallikrein in the body is not appropriately inhibited.

Kallikrein

Edema

Overactive plasma kallikrein leads to excessive release of bradykinin which directly causes blood vessels to release fluid, leading to the swelling which characterizes an HAE attack.

TAKHZYRO HELPS PREVENT HAE ATTACKS IN A WHOLE NEW WAY[6]

EVERY 2 WEEKS

TAKHZYRO directly inhibits plasma kallikrein, which is chronically uncontrolled in people with HAE, to help prevent HAE attacks.

TAKHZYRO has a half-life of approximately 2 weeks.

TAKHZYRO is administered every 2 weeks as one subcutaneous self-injection at the recommended starting dose. In clinical trials, the majority of patients took one minute or less to complete the injection.

The recommended starting dose of TAKHZYRO is 300 mg every two weeks. A dosing interval of 300 mg every four weeks is also effective and may be considered if the patient is well-controlled (e.g., attack free) for more than six months.

SELECT IMPORTANT SAFETY INFORMATION

TAKHZYRO may cause serious side effects including allergic reactions.

Allergic reactions may happen with TAKHZYRO. Call your healthcare provider or get emergency help right away if you have any of the following symptoms:

- wheezing
- difficulty breathing
- chest tightness
- fast heartbeat
- faintness
- rash
- hives

Please see complete Important Safety Information at the end of the fact sheet and visit TAKHZYRO.com for full Prescribing Information.

HELP™ STUDY DESIGN

The HELP™ study was a randomized, parallel group, double-blind, placebo-controlled study evaluating the efficacy and safety of TAKHZYRO in patients ≥12 years of age (n=125) with type I or II HAE for 26 weeks.

Patients were randomized to receive TAKHZYRO 150 mg every 4 weeks (n=28), TAKHZYRO 300 mg every 4 weeks (n=29), TAKHZYRO 300 mg every 2 weeks (n=27), or placebo (n=41) for 26 weeks. Prior to randomization, patients completed a two-week long-term prophylaxis wash out period before entering a four-week run-in period to determine baseline attack rate.

Patients with ≥1 investigator confirmed HAE attack during the run-in period were eligible for study enrollment. The primary endpoint was the number of investigator-confirmed HAE attacks over the entire 26-week study duration.

IN THE LARGEST PREVENTION STUDY CONDUCTED TO DATE IN HAE, TREATMENT WITH TAKHZYRO RESULTED IN: [6]

87%

REDUCTION IN ATTACKS VS PLACEBO (ADJUSTED P<0.001)

Patients who took TAKHZYRO 300 mg every 2 weeks (n=27) had an 87% reduction in mean monthly attack rate vs placebo (n=41). The reduction was 73% for patients who took TAKHZYRO 300 mg every 4 weeks.

Patients taking TAKHZYRO 300 mg every 2 weeks also had 83% fewer moderate to severe attacks and 87% fewer attacks that needed on-demand treatment. Patients taking TAKHZYRO 300 mg every 4 weeks had 73% fewer moderate or severe attacks and 74% fewer attacks that needed on-demand treatment.

IN A POST HOC, EXPLORATORY ANALYSIS, AFTER 6 DOSES OF TAKHZYRO (300 MG EVERY 2 WEEKS):

NEARLY **8** OUT OF **10**

PATIENTS HAD ZERO ATTACKS FOR THE NEXT 4 MONTHS OF TREATMENT

77% of patients taking TAKHZYRO 300 mg every 2 weeks (n=26) had zero attacks vs 3% of patients taking placebo (n=37) [Day 70 to 182].

Based on an exploratory analysis over the entire 6.5-month study duration, 44% of patients taking TAKHZYRO 300 mg every 2 weeks (n=27) had zero attacks vs 2% of patients taking placebo (n=41) [Day 0 to Day 182].

Most Common Side Effects

The most commonly observed adverse reactions (≥10% and higher than placebo) associated with TAKHZYRO were injection site reactions consisting mainly of pain, erythema, and bruising at the injection site; upper respiratory infection; headache; rash; myalgia; dizziness; and diarrhea.

INDICATION

TAKHZYRO (lanadelumab-flyo) is indicated for prophylaxis to prevent attacks of hereditary angioedema (HAE) in patients ≥12 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.

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

Use in Specific Populations: The safety and efficacy of TAKHZYRO in pediatric patients <12 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 wholly-owned, indirect subsidiary of Shire plc) at 1-800-828-2088, or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

For additional Important Safety Information, please see full **Prescribing Information**.

TAKHZYRO
(lanadelumab-flyo) injection

References:

1. Banerji A. The burden of illness in patients with hereditary angioedema. Ann Allergy Asthma Immunol. 2013;111(5):329-336.
2. Cicardi M, Bork K, Caballero T, et al, on behalf of HAWK (hereditary angioedema working knowledge). Evidence-based, consensus recommendations for the therapeutic management of angioedema owing to hereditary C1 inhibitor deficiency: consensus report of an International Working Group. Allergy. 2012;67(2):147-157.
3. Zuraw BL. Hereditary angioedema. N Engl J Med. 2008;359(10):1027-1036.
4. Banerji et al. Inhibiting plasma kallikrein for hereditary angioedema prophylaxis. N Engl J Med. 2017; 376(8):717-728.
5. Longhurst HJ, Bork K. Hereditary angioedema: causes, manifestations, and treatment. Br J Hosp Med. 2006;67(11):614-617.
6. TAKHZYRO Prescribing Information, 2018.

06/18
336110