ON OFFICE LETTERHEAD INCLUDING PROVIDER NAME AND ADDRESS

SAMPLE LETTER OF INTENT TO TREAT

<Date>
<Payer Name>
<Payer Address>

Patient Name: <Patient Name>
Policy ID: <Policy ID> **Group #:** <Group #>
Subject: Intent to Treat with TAKHZYRO® (lanadelumab-flyo)

To Whom It May Concern:
I am writing on behalf of my patient <Patient Name>, who has been diagnosed with hereditary angioedema (HAE). I am planning to treat <Patient Name> with TAKHZYRO® (lanadelumab-flyo). TAKHZYRO is indicated for prophylaxis to prevent attacks of hereditary angioedema (HAE) in patients 2 years and older.[1]

Hereditary Angioedema
Hereditary angioedema (HAE) is a chronic rare genetic disease caused by low levels or a dysfunction of C1 esterase inhibitor (C1-INH).[2] Reduced C1-INH activity leads to uncontrolled increases in plasma kallikrein activity, causing elevated plasma levels of bradykinin, which is a potent vasodilator that increases vascular permeability resulting in swelling and pain associated with HAE.[1] HAE is characterized by recurrent unpredictable attacks of edema of the skin (hands, arms, feet, legs, thighs, face, genitals) or the mucous membranes (gastrointestinal tract, larynx).[3] Swelling attacks can be disabling. Abdominal attacks may be extremely painful.[2,4] Laryngeal attacks, while rare, are potentially life-threatening due to the risk of suffocation.[5] Signs and symptoms of HAE may be mistaken for those of allergic angioedema and a patient experiencing an HAE attack will not respond to standard treatment for allergic angioedema.[6]

TAKHZYRO
TAKHZYRO is a plasma kallikrein inhibitor (monoclonal antibody) indicated for prophylaxis to prevent attacks of HAE in patients 2 years and older. TAKHZYRO is administered as a solution for subcutaneous injection into the abdomen, thigh, or upper arm.

The recommended starting dosage in adult and pediatric patients 12 years of age and older is 300 mg administered subcutaneously every 2 weeks (q2wks). A dosing interval of 300 mg every 4 weeks (q4wks) is also effective and may be considered if the patient is well-controlled (e.g., attack free) for more than 6 months. The recommended starting dosage in pediatric patients 6 to less than 12 years of age is 150 mg administered subcutaneously q2wks. A dosing interval of 150 mg q4wks may be considered if the patient is well-controlled (e.g., attack free) for more than 6 months. The recommended dosage in pediatric patients 2 to less than 6 years of age is 150 mg administered subcutaneously q4wks.[1]

The TAKHZYRO pivotal trial was a multicenter, double-blind, parallel group, placebo-controlled, dose-ranging study, which assessed the safety and efficacy of TAKHZYRO in 125 patients with HAE type I or II (≥12 years of age) 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. All patients entered a 4-week run-in period to determine baseline HAE attack rate. Patients with ≥1 investigator-confirmed HAE attack during the run-in period were eligible for study enrollment and randomization. The primary efficacy endpoint was the rate of investigator–confirmed attacks during the treatment period.

All TAKHZYRO treatment arms showed significant reductions in the mean HAE attack rate compared to placebo across all primary and secondary endpoints. The mean reduction in HAE attack rate was consistently higher across the TAKHZYRO treatment arms compared to placebo regardless of the baseline history of prior long-term prophylaxis, laryngeal attacks, or attack rate during the run-in period. In the pivotal trial, patients receiving 300 mg every 2 weeks experienced an overall 87% reduction in HAE attacks versus placebo, an 87% reduction in attacks requiring acute treatment, and an 83% reduction in moderate or severe attacks during the 26-week treatment period (N=125).[1]

Additional pre-defined exploratory endpoints included the percentage of patients who were attack free for the entire 26-week treatment period. The percentage of attack-free patients for the entire treatment period was 44% in the TAKHZYRO 300 mg q2wks group compared to 2% of placebo patients.[1]

The most common adverse reactions with TAKHZYRO (≥10%) are injection site reactions, upper respiratory infections, headache, rash, dizziness, diarrhea, and myalgia.[1] Hypersensitivity reactions have been observed. In case of a severe hypersensitivity reaction, discontinue TAKHZYRO administration and institute appropriate treatment.

There was no incidence of anaphylaxis in the pivotal trial.

Treatment Plan
My intended use and dosing of TAKHZYRO for <Patient Name> will be <insert treatment plan>. I have enclosed <Patient Name>'s <statement of medical necessity, clinical history, and diagnosis of HAE disease> to support my treatment plan.

Please review the information I have provided promptly for authorization for treatment with TAKHZYRO and send verification of <Patient Name>'s coverage for TAKHZYRO as soon as possible. I can be reached at <Phone> if you have any questions regarding <Patient Name>'s clinical history and/or my treatment plan. Thank you in advance for your immediate attention to this request.

Sincerely,
<Physician Name>

*Adjusted *P*-values for multiple testing.

References: 1. TAKHZYRO (lanadelumab-flyo) [prescribing information]. Lexington, MA: Shire LLC; 2023. **2.** Busse PJ, Christiansen SC, Riedl MA, et al. US HAEA Medical Advisory Board 2020 guidelines for the management of hereditary angioedema [published online September 6, 2020]. J Allergy Clin Immunol Pract. doi:10.1016/j.jaip.2020.08.046. **3.** Zuraw BL. Hereditary angioedema. *N Engl J Med*. 2008;359(10):1027-1036. **4.** Longhurst HJ, Farkas H, Craig T. HAE international home therapy consensus document. *Allergy Asthma Clin Immunol*. 2010;6(1):1-7. **5.** Agostoni A, Aygören-Pürsün E, Binkley KE, et al. Hereditary and acquired angioedema: problems and progress: proceedings of the third C1 esterase inhibitor deficiency workshop and beyond. *J Allergy Clin Immunol*. 2004;114(3 Suppl):S51-S131. **6.** Parish LC. Hereditary angioedema: diagnosis and management—a perspective for the dermatologist. *J Am Acad Dermatol*. 2011;65(4):843-850.

<Enclosures: formulary exception form (if required, available on the payer's website), original claim form and subsequent denial/EOB (if relevant), patient medical history, full Prescribing Information, additional supporting documents>