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 12 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 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 12 years and older. TAKHZYRO is a solution for subcutaneous injection into the abdomen, thigh, or upper arm. The recommended starting dose is 300 mg every 2 weeks. A dosing interval of 300 mg every 4 weeks is also effective and may be considered if a patient is well-controlled (e.g., attack free) for more than 6 months.[1]

The efficacy of TAKHZYRO for the prevention of angioedema attacks in patients 12 years of age and older with Type I or II HAE was demonstrated in a multicenter, randomized, double-blind, placebo-controlled parallel-group study (Trial 1). The study included 125 adult and adolescent patients who experienced at least one investigator-confirmed attack per 4 weeks during the run-in period. Patients were randomized into 1 of 4 treatment arms, stratified by baseline attack rate (placebo, TAKHZYRO 150 mg q4wks, TAKHZYRO 300 mg q4wks, or TAKHZYRO 300 mg q2wks), for the 26-week treatment period. Patients ≥18 years of age were required to discontinue 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 65% of patients and 56% were on prior long-term prophylaxis. During the study run-in period, attack rates of ≥3 attacks/month were observed in 52% of patients overall.[1]

All TAKHZYRO treatment arms produced clinically meaningful and statistically significant reductions in the mean HAE attack rate compared to placebo across all primary and secondary endpoints in the Intent-to-Treat population (ITT). TAKHZYRO 300 mg q2wks demonstrated significant reductions vs placebo in the primary endpoint of mean monthly attack rate at 26 weeks (87%) (0.26, n=27; 1.97, n=41) and in secondary endpoints of mean monthly rates of moderate or severe attacks (83%) and attacks requiring acute treatment (87%) (adjusted *P*<0.001 for all).* TAKHZYRO 300 mg q4wks demonstrated significant reductions vs placebo in the primary endpoint of mean monthly attack rate at 26 weeks (73%) (0.53, n=29; 1.97, n=41) and in secondary endpoints of mean monthly rates of moderate or severe attacks (73%) and attacks requiring acute treatment (74%) (Adjusted *P*<0.001 vs placebo for all).[1]*

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.[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 26-week treatment period was 44% in the TAKHZYRO 300 mg q2wks group and 31% in the 300 mg q4wks groups, compared to 2% in the placebo group.[1]

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; 2018. **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>