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 FIRAZYR® (icatibant injection)

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 FIRAZYR® (icatibant injection). FIRAZYR is indicated for the treatment of acute attacks of hereditary angioedema (HAE) in adults 18 years of age 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 can lead to elevated plasma levels of bradykinin, which is thought to be responsible for characteristic HAE symptoms of localized swelling and pain.[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).[3,4] Swelling attacks can be disabling. Abdominal attacks may be extremely painful.[5,6] Laryngeal attacks are potentially life-threatening due to the risk of suffocation.[7,8] Signs and symptoms of HAE may be mistaken for those of allergic angioedema and the patient may not respond to standard treatment for allergic angioedema.[9]

FIRAZYR

FIRAZYR is a bradykinin B2 receptor antagonist indicated for treatment of acute attacks of HAE in adults 18 years of age and older. FIRAZYR is a solution for subcutaneous injection into the abdominal area. The recommended dose is 30 mg injection upon recognition of an HAE attack. If response is inadequate or symptoms recur, additional FIRAZYR injections of 30 mg may be administered at intervals of at least 6 hours. No more than 3 (three) 30 mg injections may be administered in a 24 hour period.[1]

The efficacy and safety of FIRAZYR for the treatment of acute attacks of HAE in adults were studied in three controlled clinical trials that included 223 patients who received FIRAZYR 30 mg (n=113), placebo (n=75) or comparator (n=38). Response to therapy was primarily assessed using visual analog scores on a 100 mm scale and patient- and physician-reported symptom scores for abdominal and cutaneous pain and swelling. Trial 1 was a randomized, placebo-controlled, double-blind, parallel-group study of 98 adult patients with a median age of 36 years. Patients who developed moderate to severe cutaneous or abdominal or mild to moderate laryngeal attacks of HAE were randomized to receive either FIRAZYR 30 mg or placebo by subcutaneous injection. Patients with severe laryngeal attacks of HAE received open-label FIRAZYR 30 mg. The primary endpoint was assessed using a 3-item composite visual analog score (VAS), comprised of averaged assessments of skin swelling, skin pain, and abdominal pain. Response was defined as at least a 50% reduction from the pretreatment composite 3-item VAS score. The median time to 50% reduction in symptoms for patients with cutaneous or abdominal attacks treated with FIRAZYR (n=43) compared to placebo (n=45) was 2.0 hours [95% CI 1.5, 3.0] versus 19.8 hours [95% CI 6.1, 26.3], respectively ($p<0.001$). Other evaluated endpoints included time to almost complete symptom relief (VAS<10 mm) and rescue medication use. In Trial 1, the median times to almost complete symptom relief were 8.0 versus 36.0 hours for FIRAZYR and placebo, respectively. In terms of rescue medication use, 3/43 (7%) patients treated with FIRAZYR used additional rescue medication in comparison to 18/45 (40%) patients treated with placebo.[1]

In a second placebo-controlled trial and an active-controlled trial, a total of 26 and 35 patients respectively received FIRAZYR 30 mg for treatment of an acute HAE attack. Across the three trials, FIRAZYR had a median time to 50% reduction from baseline symptoms ranging from 2.0 to 2.3 hours. In all three controlled trials, patients were eligible for treatment of subsequent attacks in an open-label extension. Patients were treated with FIRAZYR 30 mg and could receive up to 3 doses of FIRAZYR 30 mg administered at least 6 hours apart for each attack in a 24 hour period. Response was consistent across repeated attacks during the open label extension trials. A total of 225 patients were treated with 1,076 doses of 30 mg FIRAZYR for 987 attacks of acute HAE in these trials. In an assessment of the first 5 FIRAZYR-treated attacks (621 doses for 582 attacks) the median times to a 50% reduction from pretreatment composite 3-item VAS score were similar across attacks (2.0, 2.0, 2.4, 2.0, 1.5 hours). The majority (93%) of these attacks of HAE were treated with a single dose of FIRAZYR.[1]

A total of 60 patients with laryngeal attacks were treated with FIRAZYR in the controlled trials. Efficacy results were similar to those observed for non-laryngeal (cutaneous and abdominal) sites of attack.[1] Self-administration of FIRAZYR by 56 patients was assessed in an open label trial. Patients who administered FIRAZYR during an acute attack of HAE had a median time to onset of symptom relief of 2.6 hours.[1]

Treatment Plan

My intended use and dosing of FIRAZYR 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 FIRAZYR and send verification of <Patient Name>'s coverage for FIRAZYR 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>

References: 1. FIRAZYR® (icatibant injection) Prescribing Information. Shire. 2. Kaplan AP, Greaves MW. Angioedema. *J Am Acad Dermatol*. 2005;53:373-388. 3. Longhurst HJ, Bork K. Hereditary angioedema: causes, manifestations, and treatment. *Br J Hosp Med.* 2006;67(12):654-657. 4. Zuraw BL. Hereditary angioedema. *N Engl J Med.* 2008;359(10):1027-1036. 5. Craig T, Aygören-Pürsün E, Bork K, et al. WAO guideline for the management of hereditary angioedema. *World Allergy Organ J.* 2012;5(12):182-199 6. Longhurst HJ, Farkas H, Craig T. HAE international home therapy consensus documenr. *Allerfy Asthma Clim Immunol*. 2010;6(1):1-7. 7. 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. 8. Lumry WR, Castaldo AJ, Vernon MK, et al. The humanistic burden of hereditary angioedema: impact on health-related quality of life, productivity, and depression. *Allergy Asthma Proc.* 2010;31(5):407-414. 9. 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>