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IN BRIEF

Icatibant (*Firazyr*) for Hereditary Angioedema

The FDA has approved icatibant (*Firazyr*—Shire), a selective bradykinin B2 receptor antagonist, for treatment of acute attacks of hereditary angioedema (HAE). HAE is a rare autosomal dominant disorder (estimated prevalence 1:10,000-50,000) in which patients experience recurrent and frequently unpredictable attacks of angioedema lasting 2-5 days, typically involving the extremities, gastrointestinal tract, genitalia, face, oropharynx or larynx. Laryngeal edema may be life-threatening. HAE is usually caused by a mutation of the C1-inhibitor (C1-INH) gene. C1-INH is a serine proteinase inhibitor that suppresses production of plasma kallikrein, which generates bradykinin. Bradykinin is a vasoactive substance that increases vascular permeability. Suppressing production of either kallikrein or bradykinin prevents uncontrolled vascular permeability and angioedema.

Icatibant is the third drug in the past 3 years approved for treatment of HAE. The other two are *Berinert*, a human plasma-derived C1 esterase inhibitor given intravenously (IV), and *Kalbitor*, a recombinant plasma protein kallikrein inhibitor given subcutaneously.¹ Icatibant is the only one of the three that can be administered subcutaneously by the patient. A fourth drug, *Cinryze*, a C1 esterase inhibitor is approved for prophylaxis; it is given IV every 3 or 4 days.

In a double-blind randomized trial, clinically significant relief of acute HAE symptoms occurred earlier with icatibant than with tranexamic acid (2 hours vs. 12 hours). In another trial, icatibant was found to have a nonsignificant benefit (2.5 hours vs. 4.6 hours) compared to placebo.² How it compares to the other 2 drugs approved for treatment of HAE remains to be determined.³ A single dose of icatibant costs \$2427.86⁴; patients who do not

respond to the first dose can receive a second dose and, if necessary, a third, at 6-hours intervals.

1. Three new drugs for hereditary angioedema. *Med Lett Drugs Ther* 2010; 52:66.
2. M Cicardi et al. Icatibant, a new bradykinin-receptor antagonist, in hereditary angioedema. *N Engl J Med* 2010; 363:532.
3. BP Morgan. Hereditary angioedema — therapies old and new. *N Engl J Med* 2010; 363:581.
4. Cost of a single dose according to most recent data (October 2011) from retail pharmacies nationwide available from Wolters Kluwer Health.

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