CLINICAL UPDATE

Brand Name	Sajazir™
Generic Name	icatibant
Drug Manufacturer	Cycle Pharmaceuticals Ltd.

Clinical Update

TYPE OF CLINICAL UPDATE

New Brand

FDA APPROVAL DATE

June 3, 2021

LAUNCH DATE

N/A

REVIEW DESIGNATION

Standard

TYPE OF REVIEW

Abbreviated New Drug Application (ANDA): 212446

DISPENSING RESTRICTIONS

N/A

Overview

INDICATION(S) FOR USE

Sajazir™ (icatibant) injection is a bradykinin B2 receptor antagonist indicated for treatment of acute attacks of hereditary angioedema (HAE) in adults 18 years of age and older.

MECHANISMS OF ACTION

Icatibant is a competitive antagonist selective for the bradykinin B2 receptor, with an affinity similar to bradykinin. Hereditary angioedema is caused by an absence or dysfunction of C1-esterase-inhibitor, a key regulator of the Factor XII/kallikrein proteolytic cascade that leads to bradykinin production. Bradykinin is a vasodilator which is thought to be responsible for the characteristic HAE symptoms of localized swelling, inflammation, and pain. icatibant inhibits bradykinin from binding the B2 receptor and thereby treats the clinical symptoms of an acute, episodic attack of HAE.

DOSAGE FORM(S) AND STRENGTH(S)

Injection: 10 mg per mL

DOSE & ADMINISTRATION

- 30 mg injected subcutaneously in the abdominal area.
- If response is inadequate or symptoms recur, additional injections of 30 mg may be administered at intervals of at least 6 hours.

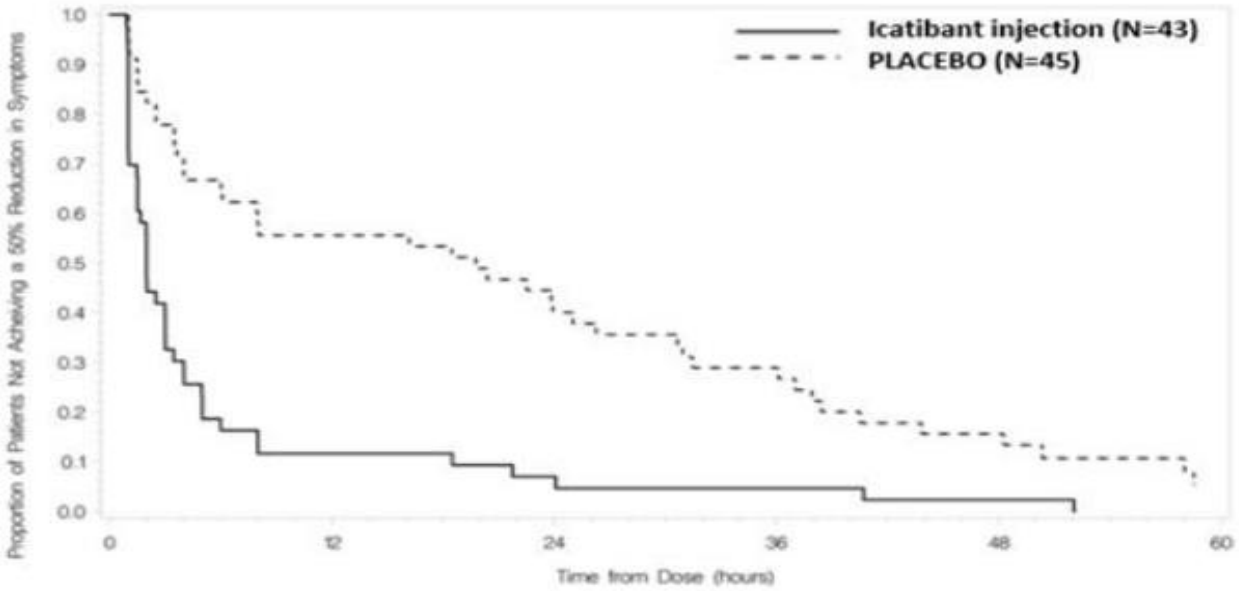
- Do not administer more than 3 injections in 24 hours.
- Patients may self-administer upon recognition of an HAE attack.

EFFICACY

The efficacy and safety of icatibant injection for the treatment of acute attacks of HAE in adults were studied in three controlled clinical trials. Among the 223 patients (mean age was 38 years) was 38 years, 64% were female, and 95% were white. Approximately 57% of patients reported use of attenuated androgens, antifibrinolytic agents, or C1 inhibitors. 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 had developed moderate to severe cutaneous or abdominal or mild to moderate laryngeal attacks of HAE were randomized to receive either icatibant injection 30 mg or placebo by subcutaneous injection. Patients with severe laryngeal attacks of HAE received open label icatibant injection 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 icatibant injection (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).

Figure: Time to 50% reduction from baseline in 3-item VAS score.



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 icatibant injection and placebo, respectively. In terms of rescue medication use, 3/43 (7%) patients treated with icatibant injection used additional rescue medication in comparison to 18/45 (40%) patients treated with placebo.

In a second placebo-controlled trial and an active-controlled trial, a total of 26 and 35 patients, respectively, received icatibant injection 30 mg for the treatment of an acute HAE attack. Across the three trials, icatibant injection had a median time to 50% reduction from baseline symptoms ranging from 2.0 to 2.3 hours.

Recurrent attacks

In all three controlled trials, patients were eligible for treatment of subsequent attacks in an open-label extension. Patients were treated with icatibant injection 30 mg and could receive up to 3 doses of icatibant injection 30 mg administered at least 6 hours apart for each attack. A total of 225 patients were treated with 1,076 doses of 30 mg icatibant injection for 987 attacks of acute HAE in these trials. In an assessment of the first 5 icatibant injection-treated attacks (621 doses for 582 attacks), the median times to a 50% reduction from the pretreatment composite 3-itemVAS 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 icatibant injection.

Laryngeal attacks

A total of 60 patients with laryngeal attacks were treated with icatibant injection in the controlled trials. Efficacy results were similar to those observed for non-laryngeal (cutaneous and abdominal) sites of attack.

Self-administration

Self-administration of icatibant injection by 56 patients was assessed in an open label trial. Patients who administered icatibant injection during an acute attack of HAE had a median time to 50% reduction from the pretreatment composite 3-itemVAS score of 2.6 hours.