Table 1: Clinical Experience

<table>
<thead>
<tr>
<th>Drug</th>
<th>Comparator</th>
<th>Placebo</th>
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<tbody>
<tr>
<td>A</td>
<td>B</td>
<td>C</td>
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Adverse reactions for icatibant were similar in nature and frequency to those reported in Table 1.

6.1 Clinical Trials Experience

None.

2.1 Recommended Dosing

Under the guidance of a healthcare professional or if symptoms recur. No more than 3 doses may be administered in any 24 hour period.

13.2 Animal Toxicology and/or Pharmacology

In rats and premature birth, abortion, fetal death, and pre-implantation loss in rabbits. Delayed parturition occurred in rats at 0.5-fold times the MRHD and premature birth and abortion in rabbits. Icatibant should be used in rats, rabbits, and in animals when possible. Icatibant is not degraded by oxidative metabolism.

7 DRUG INTERACTIONS

Icatibant did not influence the pharmacokinetics of antifibrinolytic agents, or C1 inhibitors. Response to therapy was primarily assessed using visual analog scores (VAS). Response was defined as at least a 50% reduction in the pretreatment VAS.

Icatibant injection is provided as a sterile, isotonic, and buffered solution of icatibant acetate in a single-dose, prefilled glass syringe. Each glass syringe has a bromobutyl rubber seal of 3 mL of a sterile solution of icatibant 30 mg (as icatibant acetate). Each glass syringe is filled with a prefilled needle for subcutaneous injection.

The primary endpoint was assessed using a 3-item composite visual analog score (VAS), comprised of the primary item and 2 secondary items, at 0.5, 1, 2, 4, 6, 8, and 24 hours. The primary item was pain, and the secondary items were skin swelling and skin pain.

In all three controlled trials, patients were eligible for treatment of subsequent attacks in an open-label extension. Patients in the controlled trials received a total of 570 doses with exposure to icatibant in 545 patients. The median times to a 50% reduction from the pretreatment composite VAS were 0.75 hours for icatibant, 2.0 hours for placebo, and 0.5 hours for comparator.

Across repeated treatment in the controlled trials, 4 patients tested positive for anti-icatibant antibodies. Three of these patients were receiving the comparator, and one patient was receiving placebo. No association between anti-icatibant antibodies and efficacy was observed.

In adults 18 years and older. It is not known if icatibant is safe or effective for other age groups. Icatibant is a medicine used to treat acute attacks of hereditary angioedema (HAE).

Elderly patients may have decreased body weight, which may decrease clearance of icatibant. Clearance of icatibant is correlated with body weight; therefore, it is not necessary for patients with impairment of hepatic function to use ICATIBANT INJECTION safely and under the guidance of a healthcare professional.
Step 1. Preparing your dose of Icatibant Injection
• Wash your hands with soap and water.
• You will need the following supplies:
  o Your Icatibant Injection carton that includes 1 single-dose Icatibant Injection prefilled syringe and 1 needle.
  o An alcohol wipe
  o The medicine inside your Icatibant Injection prefilled syringe should be clear and colorless. Do not use your Icatibant Injection prefilled syringe if the solution contains particles, is cloudy, or an unusual color.

Step 2. Remove the prefilled syringe and needle from the carton. See Figure B.

Step 3. Remove the seal from the needle cap (the needle should remain inside the protective needle cap until ready to use). See Figure C.

Step 4. Remove the protective cap from the end of the pre-filled syringe by unscrewing the cap. Hold the syringe firmly. Carefully attach the needle to the prefilled syringe containing the colorless icatibant solution. See Figure D.

Step 5. Firmly screw the needle on the prefilled syringe. Be careful not to remove the needle from the needle cap. See Figure E.

Step 6. Choose the injection site. The injection site should be a fold of skin on your stomach, about 2 to 4 inches (5 to 10 cm) below your belly button on either side. See Figure F.

Step 7. Clean your Icatibant Injection site with an alcohol wipe and allow it to dry. See Figure G.

Step 8. Remove the needle from the needle cap by holding the needle cap and carefully pulling the syringe. Do not pull up on the plunger. See Figure H.

Step 9. Hold the Icatibant Injection prefilled syringe in 1 hand, between your fingers and thumb. See Figure I.

Step 10. Use your other hand to gently pinch the fold of skin you cleaned with the alcohol wipe between your thumb and fingers for your injection. See Figure J.

Step 11. Hold the syringe between a 45 to 90 degree angle to your skin with the needle facing the fold of skin you are holding. See Figure K.

Step 12. Hold the fold of skin. Bring the syringe to the skin and quickly insert the needle into the skin. See Figure L.

Step 13. Push the plunger of the top of the syringe, very fast, until no icatibant is in the syringe. See Figure M.

Step 14. Release the skin fold and gently pull the needle out. See Figure N.

Disposal of your used Icatibant Injection prefilled syringe
Step 15. Place the used Icatibant Injection syringe, with the needle attached, in a sharps container (such as a red biohazard container), a hard plastic container, (such as a detergent bottle), or a metal container (such as an empty coffee can). Seal the container and throw it away the right way. There may be state and local laws about the right way to throw away used syringes and needles. Ask your healthcare provider or pharmacist how to throw away used syringes and needles. See Figure O.