

National Horizon Scanning Centre

Icatibant (Firazyr) for acute hereditary angioedema

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Icatibant (Firazyr) for acute hereditary angioedema

Target group

- Hereditary angioedema (HAE) - acute attacks.

Background

HAE is a rare genetic disease characterised by spontaneous and recurrent attacks of oedema in various parts of the body including: the upper airway, hands, feet, face and abdomen. Precipitants of attacks of angioedema include:

- Stress (both physical and mental)
- Trauma (including minor and major surgery)
- Infection
- Menstruation
- Pregnancy
- Oestrogen containing medications including: oral contraceptives and hormone replacement therapy
- ACE inhibitors

HAE is caused by an autosomal dominant mutation of the gene that inhibits the activation of the C1 component of complement. The associated C1-INH protein is also an inhibitor of the release of bradykinin. Bradykinin increases vascular permeability, dilates blood vessels and contracts non-vascular smooth muscle cells. When produced in excess, bradykinin causes typical symptoms of inflammation including: swelling, reddening, warmth and pain, which are mediated through the bradykinin B2 receptors.

Technology description

Icatibant (Firazyr) is a peptidomimetic consisting of ten amino acids that acts as a competitive bradykinin B2 receptor antagonist. Icatibant is administered as a SC injection and will be supplied in a pre-filled syringe (30mg in 3ml solution). In the majority of cases (90% of attacks) a single injection of icatibant is sufficient to treat an attack. In case of insufficient relief or recurrence of symptoms, further injections of icatibant can be administered every 6 hours. No more than 3 injections of icatibant should be administered in a 24 hour period. Icatibant is intended as a substitute for current treatments.

Innovation and/or advantages

Icatibant is the first in a new drug class (bradykinin B2 receptor inhibitor) for this indication. Use of icatibant may avoid concerns over the microbiological safety of using blood derived C1 inhibitor concentrates. Icatibant is the first drug for this indication which can be administered subcutaneously.

Developer

Jerini AG.

Availability, launch or marketing dates, and licensing plans:

Icatibant is a designated orphan drug in the EU and a marketing application was filed in August 2007. The Committee for Medicinal Products for Human Use (CHMP) of the EMEA has given the product a positive opinion.

Relevant guidance

- Clinical Knowledge Summaries (formerly PRODIGY). Angio-oedema and anaphylaxis. 2007¹.

- Clinical and Experimental Immunology. C1 inhibitor deficiency. 2005².

Clinical need and burden of disease

HAE attacks affecting the face, hands and feet are extremely uncomfortable and abdominal attacks are marked by severe abdominal pain, nausea, vomiting and/or diarrhoea. Attacks affecting the throat can be life-threatening, as swelling can constrict the larynx and enlarge the tongue.

The prevalence of HAE has been estimated as between 1 in 10,000 and 1 in 50,000 of the population². This equates to between 1,075 and 5,373 people in England and Wales with the condition. On average, patients suffer 12 attacks per year each lasting 2-5 days if left untreated. In 2006/7 there were 546 hospital admissions where the primary diagnosis was defects in the complement system and one death was recorded for 2005³.

Existing comparators and treatments

- Prophylaxis for frequent and troublesome attacks - synthetic androgens (danazol and stanozolol); tranexamic acid.
- Acute attacks - C₁ esterase inhibitor in fresh frozen plasma or in partially purified form.

Efficacy and safety

Trial code or name	NCT00097695; phase III ⁴ .	NCT00500656; icatibant vs. oral tranexamic acid; phase III ⁵ .
Sponsor	Jerini AG	Jerini AG
Status	Ongoing	Ongoing
Location	USA	Europe
Design	Randomised, double-blind, placebo controlled.	Randomised, double-blind.
Participants	n=56 (planned); adults; HAE type I or II; moderate-to-severe oedema in the cutaneous, abdominal and/or laryngeal areas. Randomised to 30mg icatibant SC or placebo. Open label extension with 30mg icatibant SC. Repeat dosing in open-label extension was permitted up to three injections per attack. If symptoms worsened more than 48 hours after the initial treatment this was considered a new attack.	n=80; adults; HAE type I or II; moderate-to-severe oedema in the cutaneous, abdominal and/or laryngeal areas. Randomised to 30mg icatibant SC with oral placebo, or placebo SC and oral tranexamic acid. Open label extension with 30mg icatibant. Repeat dosing in open-label extension was permitted.
Follow-Up	Contact every 3 months.	Contact every 6 months.
Outcomes	Safety and tolerability; efficacy; pharmacoeconomics.	Safety and tolerability; efficacy; pharmacoeconomics.
Expected reporting date	Q4 2008.	Q4 2008.

Estimated cost and cost impact

The cost of icatibant is yet to be determined.

Potential or intended impact – speculative

Patients

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| <input checked="" type="checkbox"/> Reduced morbidity | <input type="checkbox"/> Reduced mortality or increased survival | <input checked="" type="checkbox"/> Improved quality of life for patients and/or carers |
| <input type="checkbox"/> Quicker, earlier or more accurate | <input type="checkbox"/> Other: | <input type="checkbox"/> None identified |

