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Pharmacotherapeutic report on icatibant (Firazyr®) for the treatment of hereditary angio-oedema (HAE)

English Summary

The Medicinal Products Reimbursement Committee (CFH) has reviewed the pharmacotherapeutic report on icatibant (Firazyr®) for the treatment of hereditary angio-oedema (HAE). The committee has reached the following conclusions:

Medicine

Active substance and composition: icatibant (as acetate). Solution for subcutaneous injection (10 mg/ml) in pre-filled injection syringe (3 ml).

Registered indication: symptomatic treatment of acute attacks of hereditary angio-oedema (HAE) in adults (with C1-esterase inhibitor deficiency).

Dose: a single (30-mg) injection is administered for the treatment of an attack of oedema. If necessary, a second injection can be given after six hours, and a third injection after a further six hours. No more than three injections may be administered per 24 hours.

Mode of action: the symptoms of HAE are probably brought about by a local accumulation of bradykinin, which leads to vasodilation, stimulation of sensory nerve-endings (nociceptors), and an increase in vascular permeability. As a selective, competitive bradykinin-receptor type-2 antagonist, icatibant counteracts these processes. Icatibant has a similar structure to bradykinin, but contains five non-proteinogenic amino acids.

Summary of therapeutic value

Favourable effects/efficacy: as a singular treatment of patients with moderately severe to extremely severe swelling of the skin and stomach complaints, icatibant is more effective than treatment with placebo or tranexaminic acid. Unclear is whether tranexaminic acid was used optimally. Clinically relevant improvement in symptoms occurs about one hour after administration. Most of the symptoms have largely disappeared after about 10 hours. In spite of large differences in methods and the limited availability of data, based on an indirect comparison, the efficacy of icatibant is deemed equal to that of purified human C1-esterase inhibitor (INH) concentrate.

Unfavourable effects/side effects: the most frequently seen side effects of icatibant are skin reactions at the injection site. The use of C1-INH concentrate causes a more limited amount of reactions at the injection site and fever. As with all blood products, incidental allergic or anaphylactic reactions can develop. Tranexaminic acid mainly causes nausea, vomiting, diarrhoea and skin reactions.

Experience: experience with icatibant is limited. A lot of experience has been obtained with C1-INH concentrate and tranexaminic acid.

Applicability: icatibant, C1-INH concentrate and tranexaminic acid have a wide therapeutic range. Icatibant has not been studied for use in children and young adults (< 18 years). Patients with allergic reactions should be treated with an antihistamine and/or a corticosteroid before administering C1-INH concentrate. As it is a medicine prepared from human blood, the use of C1-INH concentrate can lead to viral infections of other infectious disorders. However, up till now, such infections have not occurred when using the product that is available in the Netherlands. The greatest possible caution is required when using tranexaminic acid in patients with thrombo-embolic disorders and/or (recent) haemorrhages.

Ease of use: as icatibant is administered subcutaneously, the ease of use is greater than when using the intravenously administered C1-INH concentrate. Other than with C1-INH concentrate, patients may not administer icatibant to themselves after receiving suitable instructions.

Final conclusion: The therapeutic value of icatibant is equal to that of C1-INH concentrate for the treatment of adults suffering from moderate to severe acute attacks of HAE. For this indication it has a therapeutic added value in comparison with tranexaminic acid.

*The original text of the summary of this **CFH-report** was in Dutch. Although great care was taken in translating the text from Dutch to English, the translation may nevertheless have resulted in discrepancies. Rights may only be derived on the basis of the Dutch version of the summary of the CFH-report.*
Furthermore, CVZ points out that only the summary of this report was translated. A proper understanding of all relevant considerations and facts would require familiarity with the Dutch version of this report, including all appendices.

Economic Evaluation

Comparator

Important Clinical Assumptions

Effects

Costs

Cost-effectiveness

Conclusion