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Committee for Medicinal Products for Human Use (CHMP)

# Scientific conclusions and grounds for the variation to the terms of the marketing authorisation(s)

Active substance(s): icatibant

Procedure No. EMEA/H/C/PSUSA/00001714/201707

Period covered by the PSUR: 12 July 2016 to 11 July 2017

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## Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR(s) for icatibant, the scientific conclusions of CHMP are as follows:

In total 16 cases of urticaria have been reported from health care professionals or consumers related to the use of icatibant during the interval of this Periodic Safety Update Report (PSUR)

In one female patient with previous drug hypersensitivity to penicillin developed hives after injection. The physician confirmed an allergy with a positive skin test. Causality was considered as definite. Firazyr was discontinued.

In another patient the urticarial occurred following both the first and the second injection.

Among the rest of cases, although there was limited information in some cases from Patient supporting program, there was a close temporal relationship between the Firazyr injection and the occurrence of urticarial in a number of cases.

In addition, there seems to be biological plausibility, as both Partial Bradykinin Agonism (including hypersensitivity/drug hypersensitivity) and Antigenicity are labelled as potential risks. In clinical trials of the approved dose of icatibant, the most frequent adverse reactions were injection site reactions (skin irritation, swelling, pain, itchiness, erythema, burning sensation). Based on the data from preclinical studies, it is presumed that these are related to mast cell activation, and partial bradykinin agonism.

Based on available data, it is proposed that *Urticaria* is included under SOC *Skin and subcutaneous tissue disorders* with frequency "Unknown" in table 2, section 4.8 of the SmPC.

The CHMP agrees with the scientific conclusions made by the PRAC.

## Grounds for the variation to the terms of the marketing authorisation(s)

On the basis of the scientific conclusions for icatibant the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing icatibant is unchanged subject to the proposed changes to the product information

The CHMP recommends that the terms of the marketing authorisation(s) should be varied.