Summary of the Risk Management Plan for Firazyr

Firazyr (Icitabant acetate)
Marketing Authorisation Holder: Shire Switzerland GmbH, Zug
EU RMP Version 7.0
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Disclaimer

The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimise them.

The RMP summary of FIRAZYR is a concise document and does not claim to be exhaustive. As the RMP is an international document, the summary might differ from the "Arzneimittelinformation / Information sur le médicament" approved and published in Switzerland, e.g. by mentioning risks occurring in populations or indications not included in the Swiss authorization.

Please note that the reference document which is valid and relevant for the effective and safe use of FIRAZYR in Switzerland is the "Arzneimittelinformation / Information sur le médicament" (see www.swissmedic.ch) approved and authorized by Swissmedic. Shire Switzerland GmbH is fully responsible for the accuracy and correctness of the content of the published summary RMP of FIRAZYR.

I. The medicine and what it is used for

FIRAZYR is indicated for symptomatic treatment of acute attacks of hereditary angioedema (HAE) in adults, adolescents and children aged 2 years and older with C1-esterase-inhibitor deficiency. It contains icatibant acetate as the active substance and it is given by subcutaneous injection.

Further information about the evaluation of FIRAZYR's benefits can be found in FIRAZYR's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage link to the EPAR summary landing page. https://www.ema.europa.eu/en/medicines/human/EPAR/firazyr link to product's EPAR summary landing page on the EMA webpage.

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of Firazyr, together with measures to minimise such risks and the proposed studies for learning more about its risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorised pack size the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.

Together, these measures constitute routine risk minimisation measures.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed so that immediate action can be taken as necessary. These measures constitute routine pharmacovigilance activities.

If important information that may affect the safe use of Firazyr is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Firazyr are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Firazyr. Potential risks are concerns for which an association with the use of this medicine is possible based on available data,

but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine);

Table 1. List of Important Risks and Missing Information

Important identified risks	Injection site reactions
Important potential risks	Deterioration of cardiac function under ischaemic conditions due to bradykinin antagonism Partial bradykinin agonism (excluding injection site reactions) Antigenicity manifesting as drug hypersensitivity and lack of efficacy Lack of efficacy Medication errors
Missing information	Use in pregnant and lactating women Use in children below 2 years of age

II.B Summary of important risks

Table 2. Important Identified Risk: Injection site Reaction

Risk minimisation measures	**Routine risk minimisation measures:** Injection site reactions are described in the SmPC Section 4.8 Undesirable effects. **Additional risk minimisation measures:** None.
Additional pharmacovigilance activities	Icatibant Outcome Survey (IOS)

Table 3. Important Potential Risk: Deterioration of cardiac function under ischaemic conditions due to bradykinin antagonism

Risk minimisation measures	**Routine risk minimisation measures:** Ischaemic heart disease addressed in Section 4.4 of the SmPC. **Additional risk minimisation measures:** None.
Additional pharmacovigilance activities	Icatibant Outcome Survey (IOS)

Table 4. Important Potential Risk: Partial bradykinin agonism (excluding injection site reactions)

Risk minimisation measures	**Routine risk minimisation measures:** None Proposed **Additional risk minimisation measures:** None.
Additional pharmacovigilance activities	Icatibant Outcome Survey (IOS)

Table 5. Important Potential Risk: Antigenicity manifesting as drug hypersensitivity and lack of efficacy

Risk minimisation measures	**Routine risk minimisation measures:** Instructions in case of lack of efficacy described in Section 4.2 of the SmPC Immunogenicity described in Section 4.8 of the SmPC **Additional risk minimisation measures:** None.
Additional pharmacovigilance activities	Icatibant Outcome Survey (IOS)

Table 6. Important Potential Risk: Lack of efficacy

Risk minimisation measures	**Routine risk minimisation measures:** Sections 4.2, 4.4 in the EU SmPC **Additional risk minimisation measures:** None.
Additional pharmacovigilance activities	Icatibant Outcome Survey (IOS)

Table 7. Important Potential Risk: Medication Errors

Risk minimisation measures	**Routine risk minimisation measures:** Sections 4.1, 4.2 in the EU SmPC **Additional risk minimisation measures:** None
Additional pharmacovigilance activities	Icatibant Outcome Survey (IOS)

Table 8. Important Missing Information: Use during pregnancy and lactation

Risk minimisation measures	**Routine risk minimisation measures:** Text in the SmPC: • Section 4.6 Fertility, pregnancy and lactation **Additional risk minimisation measures:** None
Additional pharmacovigilance activities	Icatibant Outcome Survey (IOS)

Table 10. Important Missing Information: Use in children less than 2 years of age

Risk minimisation measures	**Routine risk minimisation measures:** Text in the SmPC: Indication in Section 4.1. Section 4.2 (Posology and method of administration) **Additional risk minimisation measures:** None
Additional pharmacovigilance activities	Icatibant Outcome Survey (IOS)

II.C Post-authorisation development plan

II.C.1 Studies which are conditions of the marketing authorization

There are no studies which are conditions of the marketing authorisation or specific obligation of Firazyr.

II.C.2 Other studies in the post-authorisation development plan

Study	Objective
Icatibant Outcome Survey (IOS)	**Primary Objective:** The objectives of the IOS are to monitor the safety of icatibant during long-term use by patients, with a focus on the frequency of cardiac ischaemic events, generalised reactions that might be indicative of B2 receptor agonism (eg, hypotension, mucosal swelling, bronchoconstriction, and aggravation of pain), use in children and adolescents (particularly effects on sexual maturation in pubertal adolescents), monitoring the safety and response to treatment in patients with laryngeal oedema, and hypersensitivity reactions.