LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Tivacoma
(icatibant acetate)

SE/H/2133/01/DC

This module reflects the scientific discussion for the approval of Tivacoma. The procedure was finalised on 2021-12-15. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, a marketing authorisation has been granted for Tivacoma, 30 mg, solution for injection in pre-filled syringe.

The active substance is icatibant acetate. A comprehensive description of the indication and posology is given in the SmPC.

For recommendations to the marketing authorisation not falling under Article 21a/22a/22 of Directive 2001/83/EC and conditions to the marketing authorisation pursuant to Article 21a/22a/ 22 of Directive 2001/83/EC to the marketing authorisation, please see section VI.

The application for Tivacoma, 30 mg, solution for injection in pre-filled syringe, is a generic application made according to Article 10(1) of Directive 2001/83/EC. The applicant, Day Zero ehf, applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and ES as concerned member state (CMS).

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Firazyr, 30 mg, solution for injection in pre-filled syringe authorised in the Union since 2008, with Shire Pharmaceuticals Ireland Limited as marketing authorisation holder.

Potential similarity with orphan medicinal products
Having considered the arguments presented by the applicant and with reference to Article 8 of Regulation (EC) No 141/2000, Tivacoma is considered not similar (as defined in Article 3 of Commission Regulation (EC) No. 847/2000) to Takhzyro. Therefore, with reference to Article 8 of Regulation (EC) No. 141/2000, the existence of any market exclusivity for Takhzyro in the *symptomatic treatment of acute attacks of hereditary angioedema (HAE) in adults, adolescents and children aged 2 years and older, with C1-esterase-inhibitor deficiency*, does not prevent the granting of the marketing authorisation of Tivacoma. This finding is without prejudice to the outcome of the scientific assessment of the marketing authorisation application.

II. QUALITY ASPECTS

II.1 Drug Substance

The structure of the drug substance has been adequately proven and its physico-chemical properties are sufficiently described.

The manufacture of the drug substance has been adequately described and satisfactory specifications have been provided for starting materials, reagents and solvents.

The drug substance specification includes relevant tests and the limits for impurities and degradation products have been justified. The analytical methods applied are suitably described and validated.

Stability studies confirm the retest period.

II.2 Medicinal Product

The medicinal product is formulated using excipients listed in section 6.1 in the Summary of Product Characteristics.

The manufacturing process has been sufficiently described and critical steps identified.

The tests and limits in the specification are considered appropriate to control the quality of the finished product in relation to its intended purpose.

Stability studies have been performed and data presented support the shelf life and special precautions for storage claimed in the Summary of Product Characteristics, sections 6.3 and 6.4.

III. NON-CLINICAL ASPECTS

Pharmacodynamic, pharmacokinetic and toxicological properties of Icatibant are well known. As Icatibant is a widely used, well-known active substance, no further studies are required, and the applicant provides none. Overview based on literature review is, thus, appropriate.

Environmental Risk Assessment (ERA)
Since Tecraveno is a generic product, it will not lead to an increased exposure to the environment. An environmental risk assessment is therefore not deemed necessary.

There are no objections to approval of Tivacoma from a non-clinical point of view.

IV. CLINICAL ASPECTS

Pharmacokinetics
The applied product is to be administered as a subcutaneous solution containing the same active substance in the same concentration as the currently authorised product. The applied product also contains the same excipients in similar amounts as the reference product. For this type of product, no bioequivalence studies are required according to the Guideline on the investigation of Bioequivalence (CPMP/EWP/QWP/1401/98 Rev. 1).

Pharmacodynamics/Clinical efficacy/Clinical safety
No new studies on pharmacodynamics, clinical efficacy or clinical safety have been submitted which is acceptable.

Risk Management Plan
The MAH has submitted a risk management plan, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to Tivacoma.

Safety specification
The Applicant has provided an updated version of the RMP (version 1.1; final sign off-date 2021-07-01). The Summary of safety concerns is presented in Table 1.

Table 1: Summary of safety concerns

Summary of safety concerns	
Important identified risks	Injection site reactions
Important potential risks	Deterioration of cardiac function under ischaemic conditions due to bradykinin antagonism Partial bardykinin agonism (excluding injection site reactions) Antigenicity manifesting as drug hypersensitivity and lack of efficacy Lack of efficacy Medication errors Effect on reproductive hormone levels in pubertal/post-pubertal children

Summary of safety concerns	
Missing information	Use in pregnant and lactating women Use in children less than 2 years of age

Pharmacovigilance Plan
Routine pharmacovigilance is suggested and no additional pharmacovigilance activities are proposed by the applicant, which is endorsed.

Risk minimisation measures
Routine risk minimisation is suggested and no additional risk minimisation activities are proposed by the applicant, which is endorsed.

Summary of the RMP
The MAH has satisfactorily responded to the questions raised and updated the RMP accordingly. **The submitted Risk Management Plan, version 1.1 signed 2021-07-01 is considered acceptable**

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing Authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:
- At the request of the RMS;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

If the dates for submission of a PSUR and the update of a RMP coincide, they can be submitted at the same time, but via different procedures.

V. USER CONSULTATION

The package leaflet has been evaluated via a user consultation study in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC. The language used for the purpose of user testing the PIL was English.
The results show that the package leaflet meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of the generic product, Tivacoma, is found adequate. There are no objections to approval of Tivacoma, from a non-clinical and clinical point of view. The product information is acceptable. The benefit/risk ratio is considered positive and the application is therefore recommended for approval.

List of recommendations not falling under Article 21a/22a/22 of Directive 2001/83/EC in case of a positive benefit risk assessment

N/A

List of conditions pursuant to Article 21a/22a or 22 of Directive 2001/83/EC

N/A

VII. APPROVAL

The decentralised procedure for Tivacoma, 30 mg, solution for injection in pre-filled syringe was positively finalised on 2021-12-15.

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Public Assessment Report – Update

Procedure number*	Scope	Product Information affected (Yes/No)	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse

*Only procedure qualifier, chronological number and grouping qualifier (when applicable)

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