LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Figozap
(dapagliflozin, dapagliflozin propanediol monohydrate)

SE/H/2410/01-02/DC

This module reflects the scientific discussion for the approval of Figozap. The procedure was finalised on 2025-02-26. For information on changes after this date please refer to the module 'Update'.

Postadress/Postal address: P.O. Box 26, SE-751 03 Uppsala, SWEDEN
Besöksadress/Visiting address: Dag Hammarskjölds väg 42, Uppsala
Telefon/Phone: +46 (0)18 17 46 00 Fax: +46 (0)18 54 85 66
Internet: www.lakemedelsverket.se E-mail: registrator@lakemedelsverket.se

I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, a marketing authorisation has been granted for Figozap, 5 mg, 10 mg, Film-coated tablet.

The active substance is dapagliflozin, dapagliflozin propanediol monohydrate. 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 Figozap, 5 mg, 10 mg, film-coated tablet, is a Generic Art. 10(1) application submitted according to Directive 2001/83/EC. The applicant applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and DE, DK, ES, FI, FR, IT, NL, NO, PL, RO as concerned member states (CMS).

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Forxiga, 5 mg, film-coated tablet authorised in Union since 2012, with AstraZeneca AB as marketing authorisation holder.

The reference product used in the bioequivalence study is Forxiga, 10 mg, film-coated tablet from the German market with AstraZeneca AB as marketing authorisation holder.

Potential similarity with orphan medicinal products

N/A

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

Pharmacology/Pharmacokinetics/Toxicology
Pharmacodynamic, pharmacokinetic and toxicological properties of dapagliflozin are well known. As dapagliflozin is a widely used, well-known active substance, no further studies are required, nor does the applicant provide any. Overview based on literature review is, thus, appropriate.

Environmental Risk Assessment (ERA)
Since Figozap is a generic product, it will not lead to an increased exposure to the environment. This justification for not providing ERA data is acceptable given that this application was submitted before the new ERA guideline came into force (September 2024).

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

IV. CLINICAL ASPECTS

Pharmacokinetics
To support the marketing authorisation application the applicant has conducted one bioequivalence study comparing Dapagliflozin, 10 mg, tablets, with the reference product Forxiga, 10 mg, tablets, in the fasted state.

Pharmacokinetic properties of the active substance
Absorption: Dapagliflozin has an oral bioavailability of 78 %. Following an oral dose of dapagliflozin maximal plasma concentrations occur at approximately 2 hours.

Administration with a high-fat meal decreased dapagliflozin C_{max} by up to 50% and prolonged t_{max} by approximately 1 hour but did not alter AUC as compared with the fasted state. These changes are not considered to be clinically meaningful. Hence, dapagliflozin can be administered with or without food.

Linearity: The pharmacokinetics of dapagliflozin is linear within the dose range 0.1-500 mg.

Elimination: The terminal half-life is 12.9 hours.

Study DAPAG-02-23
Methods
This was a single-dose, two-way crossover study conducted in 48 healthy volunteers, comparing Dapagliflozin, 10 mg, tablets, with Forxiga, 10 mg, tablets, under fasting conditions. Blood samples for concentration analysis were collected pre-dose and up to 48 hours post-dose. Plasma concentrations of dapagliflozin were determined with an LC-MS/MS method. Analysis of variance (ANOVA) was performed on the ln-transformed data for AUC_{0-t} and C_{max}. The study was conducted between 2023-11-24 and 2023-12-27.

Results

The results from the pharmacokinetic and statistical analysis are presented in Table 1 below.

Table 1. Pharmacokinetic parameters (non-transformed values; arithmetic mean ± SD, t_{max} median, range) for dapagliflozin, n=47 (test), n=46 (reference).

Treatment	AUC_{0-t} ng*h/ml	C_{max} ng/ml	t_{max} h
Test	**551.9736 (±116.511)**	**97.191 (±36.947)**	**1.500 (0.500 - 4.017)**
Reference	**551.5864 (±116.778)**	**96.279 (±23.969)**	**1.750 (0.667 - 4.000)**
***Ratio (90% CI)**	**100.39 (98.16 - 102.67)**	**99.21 (91.57 - 107.48)**	**-**

AUC_{0-t} area under the plasma concentration-time curve from time zero to t hours
C_{max} maximum plasma concentration
t_{max} time for maximum plasma concentration

**calculated based on ln-transformed data*

For AUC_{0-t} and C_{max} the 90% confidence interval for the ratio of the test and reference products fell within the conventional acceptance range of 80.00-125.00%.

A biowaiver was sought for the additional strength of 5 mg.

Discussion and overall conclusion
The bioequivalence study and its statistical evaluation were in accordance with accepted standards for bioequivalence testing, as stated in the Guideline on the investigation of Bioequivalence (CPMP/EWP/QWP/1401/98 Rev. 1/Corr). The bioanalytical methods were adequately validated.

Absence of studies with the additional strength of 5 mg is acceptable, provided that all conditions for biowaiver for additional strength, as described in the Guideline on the investigation of bioequivalence (CPMP/EWP/QWP/1401/98 Rev. 1/Corr) are fulfilled.

Based on the submitted bioequivalence study, Dapagliflozin, 10 mg, tablets, is considered bioequivalent with Forxiga, 10 mg, tablets.

Pharmacodynamics/Clinical efficacy/Clinical safety
No new studies on pharmacodynamics, clinical efficacy or clinical safety have been submitted. Provided that bioequivalence with the originator product is demonstrated, additional data is not necessary.

V. USER CONSULTATION

A user consultation with target patient groups on the package information leaflet (PL) has been performed on the basis of a bridging report making reference to Forxiga 5 mg and 10 mg film-coated tablets, EMA/689976/2012, and Morphine 1 mg/ml solution for infusion in pre-filled syringe, DE/H/6814/001-002/DC.

The bridging report submitted by the applicant has been found acceptable.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of the generic product, Figozap, is found adequate. There are no objections to approval of Figozap, from a non-clinical and clinical point of view. Bioequivalence between the test and reference product has been adequately demonstrated. The product information is acceptable. The benefit/risk 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 Figozap, 5 mg, 10 mg, Film-coated tablet was positively finalised on 2025-02-26.

LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

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)

Postadress/Postal address: P.O. Box 26, SE-751 03 Uppsala, SWEDEN
Besöksadress/Visiting address: Dag Hammarskjölds väg 42, Uppsala
Telefon/Phone: +46 (0)18 17 46 00 Fax: +46 (0)18 54 85 66
Internet: www.lakemedelsverket.se E-mail: registrator@lakemedelsverket.se