LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Abiraterone Vocate
(abiraterone acetate)

SE/H/2408/01/DC

This module reflects the scientific discussion for the approval of Abiraterone Vocate. The procedure was finalised on 2025-03-13. 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 Abiraterone Vocate, 500 mg, Film-coated tablet.

The active substance is abiraterone 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 Abiraterone Vocate, 500 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 EL as the sole concerned member state (CMS).

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Zytiga, 250 mg, Film-coated tablet authorised in the European Union since 2011, with Janssen-Cilag International N.V. as marketing authorisation holder.

The reference product used in the bioequivalence study is Zytiga, 500 mg, Film-coated tablet from Germany with Janssen-Cilag International N.V. 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 abiraterone acetate are well known. As abiraterone acetate 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 Abiraterone Vocate is a generic product, it will not lead to an increased exposure to the environment. An environmental risk assessment is therefore not deemed necessary.

IV. CLINICAL ASPECTS

Pharmacokinetics
To support the marketing authorisation application the applicant has conducted one bioequivalence study comparing Abiraterone Vocate (Abiraterone acetate) with the reference product Zytiga.

Pharmacokinetic properties of the active substance
Absorption: Following oral administration of abiraterone acetate in the fasting state, the time to reach maximum plasma abiraterone concentration is approximately 2 hours.

Administration of abiraterone acetate with food, compared with administration in a fasted state, results in up to a 10-fold (AUC) and up to a 17-fold (C_{max}) increase in mean systemic exposure of abiraterone, depending on the fat content of the meal. Given the normal variation in the content and composition of meals, taking abiraterone acetate with meals has the potential to result in highly variable exposures. Therefore, abiraterone acetate must not be taken with food.

Biotransformation: Abiraterone acetate is rapidly converted *in vivo* to abiraterone.

Elimination: The mean half-life of abiraterone in plasma is approximately 15 hours based on data from healthy subjects.

Study AZ/BE/03/20/06
Methods
This was a single-dose, four-period, fully replicate crossover study conducted in 48 healthy volunteers (45 subjects completed all four periods), comparing Abiraterone acetate, 500 mg, film-coated tablet with Zytiga, 500 mg, film-coated tablet under fasting conditions. Blood samples for concentration analysis were collected pre-dose and up to 48 hours post-dose. Plasma concentrations of abiraterone were determined with a LC-MS/MS method. Analysis of variance (ANOVA) was performed on the log-transformed data for AUC_{0-t} and C_{max}. The study was conducted between 22-Oct-2020 and 04-Dec-2020.

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 abiraterone, n=90.

Treatment	AUC_{0-t} ng*h/ml	C_{max} ng/ml	t_{max} h
Pooled Test	**304.29 ± 187.84**	**60.59 ± 45.36**	**2.00 (1.00 - 5.00)**
Pooled Reference	**301.76 ± 155.56**	**60.21 ± 32.77**	**2.00 (1.00 - 5.00)**
***Ratio (90% CI)**	**99.70 (92.64-107.29)**	**98.89 (90.40-108.18)**	**-**

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%.

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 **) and the EMA Abiraterone acetate tablets 250 mg and 500 mg product-specific bioequivalence guidance (EMA/CHMP/474712/2016 Rev. 1* Corr. 1**). The product-specific bioequivalence guidance for abiraterone recommends one single dose cross-over study in fasting state with the highest strength 500 mg in healthy male subjects. The parent compound, abiraterone acetate, is almost immediately metabolised after administration and therefore it is not reliably measurable in plasma. Bioequivalence should be based on the metabolite, abiraterone. The bioanalytical method was adequately validated.

Based on the submitted bioequivalence study, Abiraterone Vocate is considered bioequivalent with Zytiga.

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.

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 Abiraterone Vocate.

Part II Safety specification

Table SVIII.1: Summary of safety concerns

Summary of safety concerns	
Important identified risks	• None
Important potential risks	• None
Missing information	• None

The summary of safety concerns is identical to the reference product.

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

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

Part VI Summary of the RMP
The Summary of the RMP is endorsed.

Conclusion RMP assessment
The submitted Risk Management Plan, version 0.1 signed 08/12/2023 is considered acceptable.

It is consistent with the RMP v 15.1 for the originator Zytiga published on the EMA website https://www.ema.europa.eu/en/medicines/human/EPAR/zytiga

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

Bridging
A user consultation with target patient groups on the package information leaflet (PL) has been performed on the basis of a bridging report.

The Parent PL in the content analysis, ZYTIGA 500 mg tablets, was approved in the procedure EMEA/H/C/002321. The EPAR proving that the Parent PL was authorized has been submitted in the applicant's response Day 106.

The Parent PL in the visual comparison, Levetiracetam Hetero 750 mg Film-Coated Tablets, was approved in the procedure PT/H/515/01-04/DC. The PAR proving that the Parent PL was authorized has been submitted as in the applicant's response Day 106.
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, Abiraterone Vocate, is found adequate. There are no objections to approval of Abiraterone Vocate, 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 Abiraterone Vocate, 500 mg, Film-coated tablet was positively finalised on 2025-03-13.

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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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