Medicines Evaluation Board

Public Assessment Report

Scientific discussion

Telauburite 40 mg and 80 mg, film-coated tablets (enzalutamide)

NL/H/6300/001-002/DC

Date: 21 July 2026

This module reflects the scientific discussion for the approval of Telauburite 40 mg and 80 mg, film-coated tablets. The procedure was finalised on 23 October 2025. For information on changes after this date please refer to the 'steps taken after finalisation' at the end of this PAR.

List of abbreviations

ASMF	Active Substance Master File
CEP	Certificate of Suitability to the monographs of the European Pharmacopoeia
CHMP	Committee for Medicinal Products for Human Use
CMD(h)	Coordination group for Mutual recognition and Decentralised procedure for human medicinal products
CMS	Concerned Member State
EDMF	European Drug Master File
EDQM	European Directorate for the Quality of Medicines
EEA	European Economic Area
EMA	European Medicines Agency
ERA	Environmental Risk Assessment
ICH	International Conference of Harmonisation
MAH	Marketing Authorisation Holder
Ph.Eur.	European Pharmacopoeia
PL	Package Leaflet
RH	Relative Humidity
RMP	Risk Management Plan
RMS	Reference Member State
SmPC	Summary of Product Characteristics
TSE	Transmissible Spongiform Encephalopathy

I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, the Member States have granted a marketing authorisation for Telauburite 40 mg and 80 mg, film-coated tablets, from Day Zero ehf.

The product is indicated:

- as monotherapy or in combination with androgen deprivation therapy for the treatment of adult men with high-risk biochemical recurrent (BCR) non-metastatic hormone-sensitive prostate cancer (nmHSPC) who are unsuitable for salvage-radiotherapy
- in combination with androgen deprivation therapy for the treatment of adult men with metastatic hormone-sensitive prostate cancer (mHSPC)
- for the treatment of adult men with high-risk non-metastatic castration-resistant prostate cancer (CRPC)
- for the treatment of adult men with metastatic CRPC who are asymptomatic or mildly symptomatic after failure of androgen deprivation therapy in whom chemotherapy is not yet clinically indicated
- for the treatment of adult men with metastatic CRPC whose disease has progressed on or after docetaxel therapy

A comprehensive description of the up-to-date indications and posology is given in the SmPC.

The marketing authorisation has been granted pursuant to Article 10(1) of Directive 2001/83/EC, which concerns a generic application.

In this decentralised procedure, essential similarity is proven between the new product and the innovator product Xtandi 40 mg and 80 mg film-coated tablets from Astellas Pharma Europe B.V., which has been registered in the EEA via a centralised procedure (EU/1/13/846) since 21 September 2017.

The concerned member state (CMS) involved in this procedure was Germany.

II. QUALITY ASPECTS

II.1 Introduction

Telauburite is a film-coated product. Each tablet contains as active substance 40 mg or 80 mg enzalutamide, depending on the strength. The two strengths are distinguishable by their form, seize and debossing, as follows:

<u>40 mg strength</u>
The tablets are yellow to light yellow, round and film-coated, approximately 11 mm, debossed with “3415” on one side and “TV” on the other side.

<u>80 mg strength</u>
The tablets are yellow to light yellow, oval and film-coated, approximately 17 mm x 9 mm, debossed with “3416” on one side and “TV” on the other side.

The excipients are:
Tablet core - cellulose, microcrystalline, croscarmellose sodium, hypromellose phthalate, sodium laurilsulfate, hydroxypropyl cellulose, low substituted, silica colloidal and magnesium stearate.
Tablet coating - hypromellose (E464), titanium dioxide (E171), macrogol (E1521) and iron oxide yellow (E172).

The two tablet strengths are dose proportional.

The film-coated tablets are packed in blisters consisting of polyvinyl chloride (PVC), polychlorotrifluoroethylene (PCTFE) and aluminium (Alu): PVC/PCTFE/PVC//Alu, or in blisters with polyethylene (PE) instead of PCTFE: PVC/PE/PVDC//Alu.

II.2 Drug Substance

The active substance is enzalutamide, an established active substance not described in the European, British or US Pharmacopoeia. The active substance is a white to off-white solid. Different crystalline forms exist according to the publicly available literature. Form A was selected for the development of the drug product. During the finished product manufacturing process, the active substance is dissolved, so initial form and particle size distribution are not relevant.
Enzalutamide is freely soluble in acetone and practically insoluble in water (BCS Class 2, low solubility). Enzalutamide does not contain any chiral centre. Polymorphic form A is consistently produced.

The Active Substance Master File (ASMF) procedure is used for the active substance. The main objective of the ASMF procedure, commonly known as the European Drug Master File (EDMF) procedure, is to allow valuable confidential intellectual property or 'know-how' of the manufacturer of the active substance (ASM) to be protected, while at the same time allowing the applicant or marketing authorisation holder (MAH) to take full responsibility for the medicinal product, the quality and quality control of the active substance. Competent Authorities/EMA thus have access to the complete information that is necessary to evaluate the suitability of the use of the active substance in the medicinal product.

Manufacturing process
The manufacturing process consists of three stages of synthesis. Adequate specifications have been adopted for starting materials, solvents and reagents. The active substance has been adequately characterised and the manufacturing process is described in sufficient detail.

Quality control of drug substance
The in-house methods for assay, related substances and residual solvent have been adequately validated. Tests and requirements are acceptable in view of the route of synthesis and the various European guidelines. Batch analytical data demonstrating compliance with this specification have been provided for six process validation batches.

Stability of drug substance
Stability data on the active substance have been provided for three production scale batches in accordance with applicable European guidelines. Based on the data submitted, a retest period could be granted of five years when stored under the stated conditions.

II.3 Medicinal Product

Pharmaceutical development
The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines. The choice of excipients is justified, and their functions are explained. Enzalutamide has a poor aqueous solubility.

Therefore, the drug substance was converted to an amorphous, granulated form first. The granules were mixed with extra-granular material and compressed into tablets.
During development, the conversion to the amorphous form as well as the percentage drug release was evaluated. Extra-granular excipients were used to aid tablet performance.

Manufacturing process
The manufacturing process has been validated according to relevant European/ICH guidelines. The manufacturing process is a non-standard manufacturing process, as it includes the manufacture of an amorphous solid dispersion of enzalutamide. The granules are prepared and coated with the amorphous solid dispersion in multiple steps. This is followed by conventional manufacturing steps, which involves mixing, slugging, milling, mixing, lubrication, compression, coating, and packaging. Process validation data on the product have been presented for three batches for both strengths in accordance with the relevant European guidelines.

Control of excipients
Except for iron oxide yellow, the excipients used are of Ph.Eur. quality. Iron oxide yellow complies with its national formulary monograph and Regulation EU 231/2012. The control of functionality related characteristics tests listed in corresponding Ph.Eur. monographs have adequately been discussed and appropriate tests and limits are adopted in the excipient specifications as applied by the finished product manufacturer. A premix is used for the film-coating. Suitable specifications for this material have been adopted. All specifications are acceptable.

Quality control of drug product
The finished product specifications are adequate to control the relevant parameters for the dosage form. The specification includes tests for description, identification, water content, dissolution, uniformity of dosage units, assay active substance, related substances, acetone content of enzalutamide, and microbial quality. Limits in the specification have been justified and are considered appropriate for adequate quality control of the product. An adequate nitrosamines risk evaluation report has been provided. No risk for presence of nitrosamines in the drug product was identified.

Satisfactory validation data for the analytical methods have been provided.

Batch analytical data from three batches per strength from the proposed production site have been provided, demonstrating compliance with the specification.

Stability of drug product
Stability data on the product have been provided for three batches per strength stored at 25°C/ 60% RH (24 months) and 40°C/75% RH (6 months). Samples of each batch are packed in both blister configurations. The stability was tested in accordance with applicable European guidelines. All parameters remained well within specification limits and no clear trends are observed, except for the dissolution for one 80 mg batch packed in PVC/PE/PVdC blisters. Photostability studies have been performed, demonstrating that the product is not sensitive to light. On basis of the data submitted, a shelf life was granted of three years, without storage conditions for both strengths packed in PVC/PCTFE/PVC//Alu blisters and for the 40 mg packed in PVC/PE/PVDC//Alu blisters. For the 80 mg strength packed in PVC/PE/PVDC//Alu blisters, a shelf life was granted of two years, with labeled storage condition "*Do not store above 25°C*".

Specific measures concerning the prevention of the transmission of animal spongiform encephalopathies
There are no substances of ruminant animal origin present in the product nor have any been used in the manufacturing of this product, so a theoretical risk of transmitting TSE can be excluded.

II.4 Discussion on chemical, pharmaceutical and biological aspects

Based on the submitted dossier, the member states consider that Telauburite has a proven chemical-pharmaceutical quality. Sufficient controls have been laid down for the active substance and finished product.

No post-approval commitments were made.

III. NON-CLINICAL ASPECTS

III.1 Ecotoxicity/environmental risk assessment (ERA)

At the time of submission of this application, before 1st of September 2024, the revised ERA guideline (EMEA/CHMP/SWP/4447/00 Rev. 1- Corr.*) was not yet applicable. At the time of approval the conclusion for this medicinal product was: since Telauburite is intended for generic substitution, this will not lead to an increased exposure to the environment. An environmental risk assessment was therefore not deemed necessary.

III.2 Discussion on the non-clinical aspects

This product is a generic formulation of Xtandi which is available on the European market. Reference was made to the preclinical data obtained with the innovator product. A non-clinical overview on the pharmacology, pharmacokinetics and toxicology has been provided, which was based on up-to-date and adequate scientific literature. The overview justifies why there is no need to generate additional non-clinical pharmacology, pharmacokinetics and toxicology data. Therefore, the member states agreed that no further non-clinical studies are required.

IV. CLINICAL ASPECTS

IV.1 Introduction

Enzalutamide is a well-known active substance with established efficacy and tolerability. A clinical overview has been provided, which is based on scientific literature. The member states agreed that no further clinical studies are required, besides two bioequivalence studies, which are discussed below. In addition, a biowaiver of strengths is requested for the 40 mg formulation.

IV.2 Pharmacokinetics

The MAH conducted two pivotal bioequivalence studies, in which the pharmacokinetic profile of the test product Telauburite 80 mg, film-coated tablets (Teva Nederland B.V., the Netherlands) was compared with the pharmacokinetic profile of the reference product Xtandi 2x40 mg film-coated tablets (Astellas Pharma Europe B.V., the Netherlands).

According to the SmPC, enzalutamide may be taken without reference to food intake. However, the specific formulation of enzalutamide film-coated tablets is known to impact the performance of the tablets in fed conditions. Therefore, both fasting and fed studies should be performed with the highest strength for film-coated tablets. Both bioequivalence studies, under fasting or fed conditions, are in accordance with CPMP/EWP/QWP/1401/98 Note for Guidance on the investigation of bioavailability and bioequivalence.

Dissolution studies were conducted in different pH conditions (QC-medium, pH 1.2, pH 4.5 and pH 6.8). The choice of the reference product in the bioequivalence study has been justified by comparison of dissolution study results and composition. The formula and preparation of the bioequivalence batch was identical to the formula proposed for marketing.

Biowaiver

The following general requirements were met for a waiver for the additional 40 mg strength, according to the EMA Bioequivalence guideline:

a. both strengths are manufactured by the same manufacturing process,
b. the qualitative composition of the different strengths is the same,
c. the composition of the strengths are quantitatively proportional, i.e. the ratio between the amount of each excipient to the amount of active substance(s) is the same for all strengths
d. appropriate *in vitro* dissolution data confirm the adequacy of waiving additional *in vivo* bioequivalence testing.

The dissolution was investigated according to the EMA Bioequivalence guideline. The calculated f_2 similarity factor values were within criteria (>50%) for the dissolution profiles in pH 1.2 and 4.5. An f_2 value between 50 and 100% suggests that the two dissolution profiles are similar. In pH 6.8, sink conditions for the 40 mg strength were not achieved. To prove that the difference between 40 mg and 80 mg is drug substance related, the dissolution profiles were studied at the same dose between test products: two tablets of 40 mg versus one tablet of 80 mg. The results at same dose between 40 mg (test) and 80 mg (BE test) indicated the similarity of profiles with f_2 = >50% between the test product strengths.
In QC media, more than 85% of drug was dissolved at 15 minutes time point. Dissolution profiles can therefore be accepted as similar; hence calculation of f_2 is unnecessary.

As all of the above conditions for a biowaiver for the additional strength are met, a biowaiver for the 40 mg strength is justified.

Bioequivalence studies

Design pivotal study BE-2291-23: 80 mg under fasting conditions

A single-dose, open label, randomised, two way crossover bioequivalence study was carried out under fasted conditions in 40 healthy male subjects, aged 22-43 years. Each subject received a single dose (80 mg) of one of the two enzalutamide formulations (80 mg test product or 2x40 mg reference product). The tablet(s) was/were orally administered with 240 mL water after an overnight fast of at least 10 hours. There were two dosing periods, separated by a washout period of 46 days.

Blood samples were collected pre-dose and at 0.25, 0.5, 0.75, 1, 1.33, 1.67, 2, 2.33, 2.67, 3, 3.33, 3.67, 4, 4.50, 5, 6, 8, 12, 16, 24, 48 and 72 hours after administration of the products.

The design of the study is acceptable. According to the SmPC, enzalutamide may be taken without reference to food intake.

Analytical/statistical methods

The analytical method has been adequately validated and is considered acceptable for analysis of the plasma samples. The methods used in this study for the pharmacokinetic calculations and statistical evaluation are considered acceptable.

Results

40 Subjects enrolled in the study, of which 34 completed both periods of the study. Four subjects discontinued from the study before Period II, due to not reporting to the test facility (2), a positive drug test (1) and protocol non-compliance (1, tobacco). Two subjects

discontinued after dosing in Period II due to adverse events (1 swelling over right wrist and 1 sore throat). Overall, 36 subjects were eligible for pharmacokinetic analysis.

Table 1. Pharmacokinetic parameters (non-transformed values; arithmetic mean ± SD, t_{max} (median, range)) of enzalutamide, 80 mg under fasted conditions.

Treatment N=36	**AUC_{0-t} (ng.h/mL)**	**C_{max} (ng/mL)**	**t_{max} (h)**
Test	73484.9 ± 15975.9	2648.5 ± 502.1	2.30 (1.00 - 4.50)
Reference	75674.2 ± 16428.3	2687.5 ± 559.0	2.50 (1.00 - 4.50)
***Ratio (90% CI)**	97.7 (95.9 - 99.5)	98.8 (94.2 - 103.5)	--

$AUC_{0-\infty}$	Area under the plasma concentration-time curve from time zero to infinity
AUC_{0-t}	Area under the plasma concentration-time curve from time zero to t = 72 hours
C_{max}	Maximum plasma concentration
t_{max}	Time after administration when maximum plasma concentration occurs
CI	Confidence interval

**ln-transformed values*

Design pivotal study BE-2292-23: 80 mg under fed conditions
A single-dose, open label, randomised, two way crossover bioequivalence study was carried out under fed conditions in 54 healthy male subjects, aged 19-44 years. Each subject received a single dose (80 mg) of one of the two enzalutamide formulations (80 mg test product or 2x40 mg reference product). The tablet(s) was/were orally administered with 240 mL water 30 minutes after the start of standardised high calorie, high fat breakfast administered after an overnight fast of at least 10 hours. There were two dosing periods, separated by a washout period of 46 days.

Blood samples were collected pre-dose and at 0.33, 0.67, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5, 6, 6.5, 7, 8, 12, 16, 24, 48 and 72 hours after administration of the products.

The design of the study is acceptable.

Analytical/statistical methods
The analytical method has been adequately validated and is considered acceptable for analysis of the plasma samples. The methods used in this study for the pharmacokinetic calculations and statistical evaluation are considered acceptable.

Results
54 Subjects enrolled in the study, of which 45 completed both study periods. Four subjects were withdrawn after dosing in Period I due to adverse events (1 x fever, 2 x upper respiratory tract infection and 1 x abrasion on left forearm). Four subjects were withdrawn before Period II, due to not reporting to the test facility (1) and protocol non-compliance (3 x positive drug or alcohol test). One subject was withdrawn after dosing in period II due to an adverse event (high levels of the enzyme serum glutamic-oxaloacetic transaminase in blood (SGOT)). In total, 45 subjects were eligible for pharmacokinetic analysis.

Table 2. Pharmacokinetic parameters (non-transformed values; arithmetic mean ± SD, t_{max} (median, range)) of enzalutamide, 80 mg under fed conditions.

Treatment N=45	AUC_{0-t} (ng.h/mL)	C_{max} (ng/mL)	t_{max} (h)
Test	72523.3 ± 15415.0	2149.6 ± 478.2	5.50 (4.00-7.00)
Reference	75628.4 ± 17740.8	2349.9 ± 480.6	4.00 (1.50-6.00)
***Ratio (90% CI)**	96.30 (94.59 - 98.04)	90.9 (86.3 – 95.7)	--

$AUC_{0-\infty}$	Area under the plasma concentration-time curve from time zero to infinity
AUC_{0-t}	Area under the plasma concentration-time curve from time zero to t = 72 hours
C_{max}	Maximum plasma concentration
t_{max}	Time after administration when maximum plasma concentration occurs
CI	Confidence interval

**ln-transformed values*

Conclusion on bioequivalence studies:
The 90% confidence intervals calculated for AUC_{0-t} and C_{max} are within the bioequivalence acceptance range of 0.80 – 1.25. Based on the submitted bioequivalence studies Telauburite 80 mg is considered bioequivalent with Xtandi 2x40 mg, under fasting and fed conditions.

The results of studies BE-2291-23 and BE-2292-23 with 80 mg formulation can be extrapolated to the 40 mg strength, according to conditions in Guideline on the Investigation of Bioequivalence CPMP/EWP/QWP/1401/98 Rev. 1/Corr*, section 4.1.6.

The MEB has been assured that the bioequivalence studies have been conducted in accordance with acceptable standards of Good Clinical Practice (GCP, see Directive 2005/28/EC) and Good Laboratory Practice (GLP, see Directives 2004/9/EC and 2004/10/EC).

IV.3 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 Telauburite. At the time of approval, the most recent version of the RMP was version 1.1, dated 7 January 2025.

Table 3. Summary table of safety concerns as approved in RMP

Important identified risks	• Seizure • Fall • Non-pathological fracture • Ischemic heart disease
Important potential risks	None
Missing information	None

The member states agreed that routine pharmacovigilance activities and routine risk minimisation measures (in line with the reference product) are sufficient for the risks and areas of missing information.

IV.4 Discussion on the clinical aspects

For this authorisation, reference is made to the clinical studies and experience with the innovator product Xtandi. No new clinical studies were conducted. The MAH demonstrated

through two bioequivalence studies that the pharmacokinetic profile of the product is similar to the pharmacokinetic profile of this reference product. Risk management is adequately addressed. This generic medicinal product can be used instead of the reference product.

V. USER CONSULTATION

The package leaflet (PL) 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.

A user consultation with target patient groups on the package leaflet (PL) has been performed on the basis of a bridging report making reference to Xtandi 80 mg, film-coated tablets, EMEA/H/C/002639 for the content and to Paracetamol 500 mg, film-coated tablets, DE/H/6476/001/DC, for the layout. The bridging report submitted by the MAH has been found acceptable; bridging is justified for both content and layout of the leaflet.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

Telauburite 40 mg and 80 mg, film-coated tablets have a proven chemical-pharmaceutical quality and are generic forms of Xtandi 40 mg and 80 mg film-coated tablets. Xtandi is a well-known medicinal product with an established favourable efficacy and safety profile.

Bioequivalence has been shown to be in compliance with the requirements of European guidance documents.

The Board followed the advice of the assessors.

There was no discussion in the CMD(h). Agreement between member states was reached during a written procedure. The member states, on the basis of the data submitted, considered that essential similarity has been demonstrated for Telauburite with the reference product, and have therefore granted a marketing authorisation. The decentralised procedure was finalised with a positive outcome on 23 October 2025.

STEPS TAKEN AFTER THE FINALISATION OF THE INITIAL PROCEDURE - SUMMARY

Procedure number	Scope	Product Information affected	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse
N.A.	N.A.	N.A.	N.A.	N.A.	N.A.