CMDh/223/2005
February 2014

Public Assessment Report

Scientific discussion

Almotriptan Qualix 12.5 mg orodispersible tablets (almotriptan malate)

ES/H/0924/001/DC

Date: 28 July 2025

This module reflects the scientific discussion for the approval of Almotriptan Qualix 12.5 mg orodispersible tablets. The procedure was finalised at 28 July 2025. For information on changes after this date please refer to the module 'Update'.

I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, the Member States have granted a marketing authorisation for Almotriptan Qualix 12.5 mg orodispersible tablets, from Qualix Pharma S.L.

The product is indicated for the acute treatment of the headache phase of migraine attacks with or without aura.

A comprehensive description of the indications and posology is given in the SmPC."

The marketing authorisation has been granted pursuant to Article Article 10.1 of Directive 2001/83/EC."

II. QUALITY ASPECTS

II.1 Introduction

The product Almotriptan Qualix 12.5 mg orodispersible tablets consists on white, round and 7.0 mm diameter orodispersible tablets containing almotriptan malate as drug substance, at the doses of 12.5 mg.
The maximum daily dose is 25 mg of Almotrioptan malate.
Benzydamine hydrochloride 3 mg honey-orange flavoured lozenges are packaged in Aluminium/Aluminium blisters.

II.2 Drug Substance

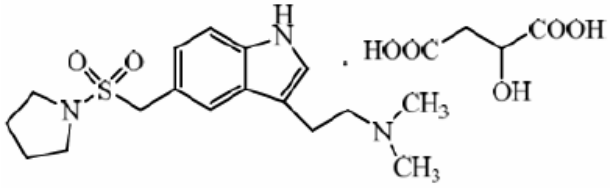
The CEP procedure is used to support the quality of the drug substance.

General Information

Nomenclature:

INN: Almotriptan Malate
Chemical name: N,N-Dimethyl-2-[5-[(pyrrolidine-l sulfonyl)methyl]-1 H-indol-3yl]ethan-1-amine (RS)-2-hydroxybutanedioate
CAS: 181183-52-8

Chemical structure:



Empirical Formula: $C_{21}H_{31}N_3O_7S$
Molecular weight: 469.6

General Properties:

Appearance: White to slightly yellow crystalline powder.
Solubility: Soluble in water, slightly soluble in methanol, practically insoluble in anhydrous ethanol and in heptane.
Potential Isomerism: Almotriptan does not exhibit optical isomerism.
Hygroscopicity: Non-hygroscopic.
Polymorphism: There are no reported polymorphs available in the literature of almotriptan malate.

Manufacture, process controls and characterisation

As CEP procedure is used, information on manufacture, process controls and characterisation of the active substance has been assessed by EDQM.

Specification, analytical procedures, batch analysis

Active substance specifications are in accordance with Ph. Eur. monograph and additional relevant tests are included.

Container closure system

As CEP procedure is used, information on packaging material of active substance has been assessed by EDQM.

Stability

Re-test period is included in the CEP. Stability studies have been assessed by EDQM.

II.3 Medicinal Product

Description of the product

The drug product is a white, round and 7.0 mm diameter orodispersible tablet containing almotriptan malate as drug substance, at the dose of 12.5 mg.
The qualitative composition of the finished product is as follows:
Almotriptan malate
Mannitol
Cellulose microcrystalline
Sodium croscarmellose
Aspartame
Sodium stearyl fumarate
Silica colloidal anhydrous
Spearmint flavour

The packaging material intended for the commercial use consists in Aluminium/Aluminium blisters.

Pharmaceutical Development

The development of the product has been described, the choice of excipients is justified and their functions explained.
The physicochemical characteristics of the active substance that may affect the pharmaceutical form are identified and their control strategy is justified.

Manufacture of the product

The manufacturing process is fully described and in-process controls are appropriate considering the nature of the product and the manufacturing process. The industrial batch size is well-defined.
Sufficient validation data are provided.

Excipients

Excipients used are well known and of appropriate quality.
None of the excipients is of animal origin.

Product specification, analytical procedures, batch analysis

The finished product specifications are adequate to control the finished product. Provided description and validation data for the analytical methods are adequate. Batch analysis data have been submitted and the results show that the finished product meets the proposed release specification.

Container closure system

The finished product is packaged in Aluminium/Aluminium blisters.. The choice of the container closure system is justified considering the nature of the finished product. Compliance with the relevant requirements and/or regulations is confirmed.

Stability

Stability studies have been performed in accordance with current guidelines. The proposed protocol is considered adequate. The packaging material is the same as that intended for marketing. Proposed shelf-life and storage conditions are properly established.

Shelf-life: 2 years.

Storage conditions: This medicinal product does not require any special storage conditions.

III. NON-CLINICAL ASPECTS

Pharmacodynamic, pharmacokinetic and toxicological properties of almotriptan malate are well known. As almotriptan malate is a widely used, well-known active substance, the applicant has not provided additional studies and further studies are not required.

Environmental Risk Assessment (ERA)
Since Almotriptan Qualix 12.5 mg orodispersible tablet is a generic product, it will not lead to an increased exposure to the environment. Additional ERA studies are therefore not deemed necessary.

IV. CLINICAL ASPECTS

IV.1 Introduction

Almotriptan malate is a well-known active substance with established efficacy and safety. A clinical overview has been provided, which is based on scientific literature. The clinical overview justifies that there no need to generate additional clinical data.

For this generic application of an immediate release formulation, the MAH has submitted a bioequivalence study which is discussed below.

IV.2 Pharmacokinetics

Biowaiver
N/A.

Bioequivalence studies

Study code UECHUP-ALM/23-6

GCP compliance
The studies were conducted in accordance with Good Clinical Practice (GCP) standards. Monitoring reports and certificates of audits carried out by the Quality Assurance Unit are presented. The sites have been previously inspected by EU regulatory authorities.

Clinical and analytical facilities
The clinical part of the study was performed at Clinical Trial Unit, Hospital Universitario de La Princesa, located at C/ Diego de León, nº62, Madrid, Spain. The analytical part of the study was performed at Laboratorios Anapharm Europe S.LU, located at C/ Encuny 22, Barcelona, Spain.

Design
A randomised, single-dose, two-treatment, two-period, two sequence, crossover bioequivalence study was carried out under fasted conditions in 28 healthy male and female subjects, aged 19–52 years. The medication was administered as a single dose by oral route with 240 mL of water for reference film coated tablets and 20 mL of water to wet the mouth before the administration of the test orodispersible tablets on the tongue after an overnight fast of at least ten hours. There were two dosing periods, separated by a washout period of 7 days.

Analytical and statistical methods
The analytical method has been adequately validated and is considered acceptable for analysis of the plasma samples.
The 90% confidence interval (90% CI) of the ratio of the test formulation to the reference formulation for the log-transformed values of Cmax and AUC was calculated using an ANOVA model. This model included the covariates sequence, period, formulation and subject nested to sequence. Bioequivalence was defined when the 90% CI of the ratios (test/reference) for Cmax and AUC was in the range 80.00 -125.00%.
The methods used in this study for the pharmacokinetic calculations and statistical evaluation are considered acceptable.

Results
28 subjects were included in the study. 28 subjects were treated; 27 subjects completed the study and 27 were used in the statistical analysis according to the protocol.
The inclusion and exclusion criteria are considered acceptable for a bioequivalence study.

Descriptive statistics

Pharmacokinetic parameter	Arithmetic Means (±SD)	
	Test product	Reference Product
$AUC_{(0-t)}$ (ng·h/mL)	314.39 (85.33)	307.01 (85.42)
$AUC_{(0-\infty)}$ (ng·h/mL)	323.44 (87.73)	316.13 (87.51)
Cmax (ng/mL)	50.62 (20.21)	49.54 (16.90)
Tmax[1] (hours)	1.75 (0.25 – 3.50)	1.50 (0.75 – 4.00)

[1]Median (Min, Max)

Bioequivalence evaluation

Pharmacokinetic parameter	Geometric Mean Ratio Test/Ref	Confidence Intervals	CV%[1]
$AUC_{(0-t)}$	102.88	99.15 - 106.75	7.95
Cmax	101.44	94.95 - 108.37	14.28

[1]Estimated from the Residual Mean Squares.

Based on the submitted bioequivalence study, Almotriptan Qualix 12.5 mg orodispersible tablets, when compared with the Reference Product in fasting conditions seems to meet the bioequivalence criteria with respect to the Cmax and AUC.

Conclusion on bioequivalence studies:
Based on the submitted bioequivalence study, Almotriptan Qualix 12.5 mg orodispersible tablets is considered bioequivalent with the Reference Product.

IV.3 Pharmacodynamics/Clinical efficacy/ Clinical safety

No new clinical data have been provided and none is required for this type of generic application.

The submitted clinical documentation based on scientific literature is sufficient and acceptable regarding clinical information.

IV.4 Risk Management Plan

The MAH has submitted a risk management plan (version 01, 12 June 2024), 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 Almotriptan Qualix 12.5 mg orodispersible tablets.

There are neither proposed additional pharmacovigilance activities nor proposed additional risk minimisation measures planned for Almotriptan Qualix 12.5 mg orodispersible tablets.

IV.5 Discussion on the clinical aspects

For generic applications please refer to section IV.2.

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.

The test consisted of a preliminary round with 4 participants followed by two rounds with 10 participants each. The questions covered the following areas sufficiently: traceability, comprehensibility and applicability.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of the generic product Almotriptan Qualix 12.5 mg orodispersible tablets is found adequate. There are no objections to the approval of Almotriptan Qualix 12.5 mg orodispersible tablets 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.