Medicines & Healthcare products
Regulatory Agency

Public Assessment Report

National Procedure

Lansoprazole 15 mg oro-dispersible tablets
Lansoprazole 30 mg oro-dispersible tablets

lansoprazole

PL 14894/0802-0803

Sun Pharma UK Limited

LAY SUMMARY

Lansoprazole 15 & 30 mg oro-dispersible tablets
lansoprazole

This is a summary of the Public Assessment Report (PAR) for Lansoprazole 15 & 30 mg oro-dispersible tablets. It explains how these products were assessed and their authorisation recommended, as well as their conditions of use. It is not intended to provide practical advice on how to use these products.

These products will be referred to as Lansoprazole in this lay summary for ease of reading.

For practical information about using Lansoprazole, patients should read the Patient Information Leaflet (PIL) or contact their doctor or pharmacist.

What is Lansoprazole and what is it used for?
These products are generic medicines. This means that these medicines are the same as, and considered interchangeable with, reference medicines already authorised, called Zoton Fastab 15mg and Zoton Fastab 30mg (PL 00057/1296-1297).

Lansoprazole is used for the following indications:

- Treatment of duodenal and stomach ulcer
- Treatment of inflammation in the oesophagus (reflux oesophagitis)
- Prevention of reflux oesophagitis
- Treatment of heartburn and acid regurgitation
- Treatment of infections caused by the bacteria *Helicobacter pylori* when given in combination with antibiotic therapy
- Treatment or prevention of duodenal or stomach ulcer in patients requiring continued non-steroidal anti-inflammatory drugs (NSAID) treatment (NSAID treatment is used against pain or inflammation)
- Treatment of Zollinger-Ellison syndrome.

A doctor may have prescribed Lansoprazole for another indication or with a dose different from that which is written the PIL. The patient should take their medicine in consultation with their doctor.

The patient must talk to a doctor if they do not feel better or if they feel worse after 14 days.

How does Lansoprazole work?
The active ingredient in Lansoprazole is lansoprazole, which is a proton pump inhibitor. Proton pump inhibitors reduce the amount of acid that the stomach makes.

How is Lansoprazole used?
The pharmaceutical form of these medicines is an oro-dispersible tablet and the route of administration is oral (by mouth).

The patient should place the tablet on their tongue and suck gently. The tablet rapidly dissolves in the mouth, releasing microgranules which the patient should swallow without chewing. The patient can also swallow the tablet whole with a glass of water.

The patient's doctor might instruct them to take the tablet with a syringe, in case they have serious difficulties with swallowing.

The following instructions should be followed if administered via syringe:

It is important that the appropriateness of the selected syringe is carefully tested.
- Remove the plunger of the syringe (at least 5 mL syringe for the 15 mg tablet and 10 mL syringe for the 30 mg tablet)
- Put the tablet into the barrel
- Put the plunger back onto the syringe
- For the 15 mg tablet: Draw 4 mL tap water into the syringe
- For the 30 mg tablet: Draw 10 mL tap water into the syringe
- Invert the syringe and draw an additional 1 mL of air into it
- Shake the syringe gently for 10-20 seconds until the tablet is dispersed
- The contents can be emptied directly into the mouth
- Refill the syringe with 2-5 mL of tap water to flush the remnants out of the syringe into the mouth.

If the patient is taking Lansoprazole once a day, they should try to take it at the same time each day. The patient may get best results if they take Lansoprazole first thing in the morning.

If the patient is taking Lansoprazole twice a day, they should have the first dose in the morning and the second dose in the evening.

The packaging has been printed with the days of the week to help the patient keep track of the medicines they have already taken.

The dose of Lansoprazole depends on the patient's condition. The usual doses of Lansoprazole for adults are given below. The patient's doctor will sometimes prescribe them a different dose and will tell them how long their treatment will last.

Treatment of heartburn and acid regurgitation: one 15 mg or 30 mg oro-dispersible tablet every day for 4 weeks. If the patient's symptoms are not relieved within 4 weeks, they should contact their doctor.

Treatment of duodenal ulcer: one 30 mg oro-dispersible tablet every day for 2 weeks.

Treatment of stomach ulcer: one 30 mg oro-dispersible tablet every day for 4 weeks.

Treatment of inflammation in the oesophagus (reflux oesophagitis): one 30 mg oro-dispersible tablet every day for 4 weeks.

Long-term prevention of reflux oesophagitis: one 15 mg oro-dispersible tablet every day, the patient's doctor may adjust their dose to one 30 mg oro-dispersible tablet every day.

Treatment of infection of *Helicobacter pylori*: The usual dose is one 30 mg oro-dispersible tablet in combination with two different antibiotics in the morning and one 30 mg oro-dispersible tablet in combination with two different antibiotics in the evening. Treatment will usually be every day for 7 days.

The recommended combinations of antibiotics are:
- 30 mg Lansoprazole together with 250-500 mg clarithromycin and 1000 mg amoxicillin.
- 30 mg Lansoprazole together with 250 mg clarithromycin and 400-500 mg metronidazole.

If the patient is being treated for infection because they have an ulcer, it is unlikely that their ulcer will return if the infection is successfully treated. To give the medicine the best chance of working, the patient should take it at the right time and **should not miss a dose.**

Treatment of duodenal or stomach ulcer in patients requiring continued NSAID treatment: one 30 mg oro-dispersible tablet every day for 4 weeks.

Prevention of duodenal or stomach ulcer in patients requiring continued NSAID treatment: one 15 mg oro-dispersible tablet every day, the patient's doctor may adjust their dose to one 30 mg oro-dispersible tablet every day.

Zollinger-Ellison syndrome: The usual dose is two 30 mg oro-dispersible tablets every day to start with, then depending on how the patient responds to Lansoprazole the dose that their doctor decides is best for them.

Use in children
Lansoprazole should not be given to children.

For further information on how Lansoprazole is used, refer to the PIL and Summaries of Product Characteristics (SmPCs) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

These medicines can only be obtained with a prescription.

The patient should always take this medicine exactly as their doctor/pharmacist has told them. The patient should check with their doctor or pharmacist if they are not sure.

What benefits of Lansoprazole have been shown in studies?
Because Lansoprazole are generic medicines, studies in healthy volunteers have been limited to tests to determine that it is bioequivalent to the reference medicine. Two medicines are bioequivalent when they produce the same levels of the active substance in the body.

What are the possible side effects of Lansoprazole?
For the full list of all side effects reported with these medicines, see Section 4 of the PIL or the SmPCs available on the MHRA website.

If a patient gets any side effects, they should talk to their doctor, pharmacist or nurse. This includes any possible side effects not listed in the product information or the PIL that comes with the medicine. Patients can also report suspected side effects themselves, or a report can be made on their behalf by someone else who cares for them, directly via the Yellow Card scheme at https://yellowcard.mhra.gov.uk or search for 'MHRA Yellow Card' online. By reporting side effects, patients can help provide more information on the safety of this medicine.

Because Lansoprazole are generic medicines and are bioequivalent to the reference medicines, their benefits and possible side effects are considered to be the same as the reference medicines.

Why was Lansoprazole approved?
It was concluded that, Lansoprazole has been shown to be bioequivalent to the reference medicine. Therefore, the MHRA decided that, as for the reference medicine, the benefits are greater than the risks and recommended that it can be approved for use.

What measures are being taken to ensure the safe and effective use of Lansoprazole?
As for all newly-authorised medicines, a Risk Management Plan (RMP) has been developed for Lansoprazole. The RMP details the important risks of Lansoprazole, how these risks can be minimised, any uncertainties about Lansoprazole (missing information), and how more information will be obtained about the important risks and uncertainties.

The following safety concerns have been recognised for Lansoprazole:

Summary of safety concerns	
Important identified risks	Hip, wrist or spine fracture Hypomagnesaemia
Important potential risks	Pneumonia Decreased absorption of vitamin B12
Missing information	None

The information included in the SmPC and the PIL is compiled based on the available quality, non-clinical and clinical data, and includes appropriate precautions to be followed by healthcare professionals and patients. Side effects of Lansoprazole are continuously monitored and reviewed including all reports of suspected side-effects from patients, their carers, and healthcare professionals.

An RMP and a summary of the pharmacovigilance system have been provided with these applications and are satisfactory.

Other information about Lansoprazole
Marketing Authorisations for Lansoprazole were granted in the United Kingdom (UK) on 30 October 2024.

The full PAR for Lansoprazole follows this summary.

This summary was last updated in December 2024.

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I INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the applications for Lansoprazole 15 & 30 mg oro-dispersible tablets (PL 14894/0802-0803) could be approved.

The products are approved for the following indications:

- Treatment of duodenal and gastric ulcer
- Treatment of reflux oesophagitis
- Prophylaxis of reflux oesophagitis
- Eradication of *Helicobacter pylori* (*H. pylori*) concurrently given with appropriate antibiotic therapy for treatment of *H.pylori*-associated ulcers
- Treatment of non-steroidal anti-inflammatory drug (NSAID)-associated benign gastric and duodenal ulcers in patients requiring continued NSAID treatment
- Prophylaxis of NSAID-associated gastric ulcers and duodenal ulcers in patients at risk requiring continued therapy
- Symptomatic gastroesophageal reflux disease
- Zollinger-Ellison syndrome.

The active substance, lansoprazole, is a gastric proton pump inhibitor. It inhibits the final stage of gastric acid formation by inhibiting the activity of H^+/K^+ ATPase of the parietal cells in the stomach. The inhibition is dose-dependent and reversible, and the effect applies to both basal and stimulated secretion of gastric acid. Lansoprazole is concentrated in the parietal cells and becomes active in their acidic environment, whereupon it reacts with the sulphydryl group of H^+/K^+ATPase causing inhibition of the enzyme activity.

These applications were approved under Regulation 51B of The Human Medicines Regulation 2012, as amended (previously Article 10(1) of Directive 2001/83/EC, as amended), as generic medicines of suitable originator medicinal products, Zoton Fastab 15mg and Zoton Fastab 30mg (PL 00057/1296-1297) that has been licensed for suitable time, in line with the legal requirements.

No new non-clinical studies were conducted, which is acceptable given that the applications are for generic medicinal products of suitable reference products.

With the exception of the bioequivalence studies, no new clinical studies were conducted, which is acceptable given that the applications are for generic medicinal products of suitable reference products. The bioequivalence studies were conducted in-line with current Good Clinical Practice (GCP).

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for these products at all sites responsible for the manufacture, assembly and batch release of these products.

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with these applications and are satisfactory.

Marketing Authorisations for Lansoprazole were granted in the United Kingdom (UK) on 30 October 2024.

II QUALITY ASPECTS

II.1 Introduction

The active substance is lansoprazole.
Each oro-dispersible tablet contains either 15 mg or 30 mg of lansoprazole respectively.

The other ingredients are microcrystalline cellulose pellets, magnesium carbonate, low substituted hydroxypropylcellulose, hydroxypropylcellulose, hypromellose, talc, mannitol, maize starch, methacrylic acid – ethyl acrylate copolymer (1:1) dispersion 30 percent, macrogols 6000, glyceryl monostearate, polysorbate 80, triethyl citrate, citric acid anhydrous, crospovidone, magnesium stearate, aspartame (E951), strawberry flavour, iron oxide red (E172) iron oxide yellow (E172) and magnesium stearate.

Lansoprazole 15 mg Oro-Dispersible Tablets are packed in AL/HDPE/PE with Desiccant/HDPE blister, in cartons containing 14, 28, 56, 98 tablets Oro-Dispersible Tablets.

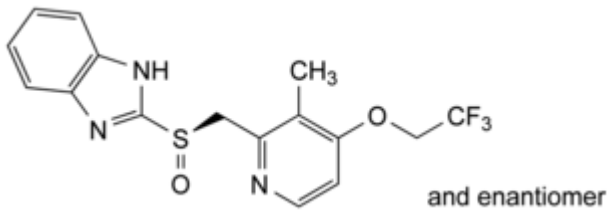
Lansoprazole 30 mg Oro-Dispersible Tablets are packed in AL/HDPE/PE with Desiccant/HDPE blister, in cartons containing 7,14, 28, 56, 98 tablets Oro-Dispersible Tablets.

Not all pack sizes may be marketed.

Satisfactory specifications and Certificates of Analysis have been provided for all packaging components. All primary packaging complies with the current regulations concerning materials in contact with food.

II.2 ACTIVE SUBSTANCE

rINN: lansoprazole
Chemical Name: 2-[(*RS*)-[[3-Methyl-4-(2,2,2-trifluoroethoxy)pyridin-2-yl]methyl]sulfinyl]-1*H*-benzimidazole.
Molecular Formula: $C_{16}H_{14}F_3N_3O_2S$



Chemical Structure:
Molecular Weight: 369.4
Appearance: White or brownish powder.
Solubility: Practically insoluble in water, soluble in anhydrous ethanol, very slightly soluble in acetonitrile.

Lansoprazole is the subject of a European Pharmacopoeia monograph.

All aspects of the manufacture and control of the active substance are covered by a European Directorate for the Quality of Medicines and Healthcare (EDQM) Certificate of Suitability.

II.3 DRUG PRODUCTS

Pharmaceutical development

A satisfactory account of the pharmaceutical development was provided.

Comparative *in vitro* dissolution and impurity profiles were provided for the proposed and reference products.

All excipients comply with either their respective European/national monographs, or suitable in-house specification. Satisfactory Certificates of Analysis were provided for all excipients.

No excipients of animal or human origin are used in the final products.

Confirmation has been given that the magnesium stearate used in the tablets is of vegetable origin.

These products do not contain or consist of genetically modified organisms (GMO).

Manufacture of the products

A description and flow-chart of the manufacturing method has been provided.

Satisfactory batch formulation data have been provided for the manufacture of the products, along with an appropriate account of the manufacturing process. The manufacturing process has been validated and has shown satisfactory results.

Finished Product Specifications

The finished product specifications at release and shelf-life are satisfactory. The test methods have been described and adequately validated. Batch data have been provided that comply with the release specifications. Certificates of Analysis have been provided for any working standards used.

Stability

Finished product stability studies have been conducted in accordance with current guidelines, using batches of the finished product stored in the packaging proposed for marketing. Based on the results, a shelf-life of 24 months, with the storage conditions ‘Do not store above 30°C’, is acceptable.

Suitable post approval stability commitments have been provided to continue stability testing on batches of finished product.

II.4 Discussion on chemical, pharmaceutical and biological aspects

The grant of marketing authorisations was recommended.

III NON-CLINICAL ASPECTS

III.1 Introduction

As the pharmacodynamic, pharmacokinetic and toxicological properties of lansoprazole are well-known, no new non-clinical studies are required, and none have been provided. An overview based on the literature review is, thus, appropriate.

III.2 Pharmacology

No new pharmacology data were provided, and none were required for these applications.

III.3 Pharmacokinetics
No new pharmacokinetic data were provided, and none were required for these applications.

III.4 Toxicology
No new toxicology data were provided, and none were required for these applications.

III.5 Ecotoxicity/Environmental Risk Assessment
Suitable justification was provided for non-submission of an Environmental Risk Assessment. As the applications are for generic versions of already authorised products, an increase in environmental exposure is not anticipated following approval of the marketing authorisations for the proposed products.

III.6 Discussion on the non-clinical aspects
The grant of marketing authorisations was recommended.

IV CLINICAL ASPECTS

IV.1 Introduction
The clinical pharmacology, efficacy and safety of lansoprazole are well-known. With the exception of data from two bioequivalence studies undertaken (LAN07022 and LAN07122), no new clinical data are provided or are required for this type of application. An overview based on a literature review and a review of these studies is, thus, satisfactory.

IV. 2 Pharmacokinetics
In support of the application, the applicant submitted the following:

Study 1: LAN07022
This study was a balanced, randomised, two-treatment, two-sequence, four-period, single dose fully replicate crossover, bioequivalence study comparing Lansoprazole Gastro-Resistant Oro-Dispersible Tablets 30mg (test product) with Zoton (lansoprazole) 30 mg Orodispersible Tablets (reference product) in healthy adult human subjects under fasting conditions.

A single dose of either the test or reference product was administered after an overnight fast of at least 10 hours, in each study period. Blood samples were taken pre-dose and up to 24 hours post dose, with a washout period of 5 days between the treatment periods.

A summary of the pharmacokinetic results is presented below:

Parameters (Units)	Test (T) vs Reference (R)
Lansoprazole	
C_{max} (ng/mL)	102.66% (96.68% - 109.02%)
AUC_{0-t} (ng.h/mL)	101.85% (97.39% - 106.51%)
$AUC_{0-\infty}$ (ng.h/mL)	101.81% (97.39% - 106.43%)

In accordance with the regulatory requirements, the Test/Reference ratios and their 90% confidence intervals were within the specified limits to show bioequivalence between the test product and the reference product.

Study 2: LAN07122

This study was a balanced, randomised, two-treatment, two-sequence, four-period, single dose fully replicate crossover, bioequivalence study comparing Lansoprazole Gastro-Resistant Oro-Dispersible Tablets 30mg (test product) with Zoton (lansoprazole) 30 mg Orodispersible Tablets (reference product) in healthy adult human subjects under fed conditions.

In each study period, subjects were administered a single dose of either the test or reference product after an overnight fast of at least 10 hours. Subjects consumed a high fat, high calorie breakfast within 30 minutes prior to drug administration. Blood samples were taken pre-dose and up to 24 hours post dose, with a washout period of 5 days between the treatment periods.

A summary of the pharmacokinetic results is presented below:

Parameters (Units)	Test (T) vs Reference (R)
Lansoprazole	
C_{max} (ng/mL)	100.22 % (92.75 % - 108.29 %)
AUC_{0-t} (ng.h/mL)	109.68 % (104.16 % - 115.49 %)
$AUC_{0-\infty}$ (ng.h/mL)	109.70 % (104.83 % - 114.79 %)

In accordance with the regulatory requirements, the Test/Reference ratios and their 90% confidence intervals were within the specified limits to show bioequivalence between the test product and the reference product.

As the additional (15 mg) strength of the product met the biowaiver criteria specified in the current bioequivalence guideline, the results and conclusions from the bioequivalence study on the product strength can be extrapolated to the other strengths.

IV.3 Pharmacodynamics

No new pharmacodynamic data were submitted for these applications and none were required.

IV.4 Clinical efficacy

No new efficacy data were submitted with these applications and none were required.

IV.5 Clinical safety

With the exception of the safety data submitted with the bioequivalence studies, no new safety data were submitted with these applications.

The safety data from the bioequivalence studies showed that the test and reference products were equally well tolerated. No new or unexpected safety issues were raised from the bioequivalence study.

IV.6 Risk Management Plan (RMP)

The applicant has submitted an RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulation 2012, as amended. The applicant proposes only routine pharmacovigilance and routine risk minimisation measures for all safety concerns. This is acceptable.

IV.7 Discussion on the clinical aspects

The grant of marketing authorisations was recommended for these applications.

V USER CONSULTATION

A full colour mock-up of the Patient Information Leaflet (PIL) was provided with the application in accordance with legal requirements, including user consultation.

VI OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of the products is acceptable, and no new non-clinical or clinical safety concerns have been identified. Extensive clinical experience with lansoprazole is considered to have demonstrated the therapeutic value of the compound. The benefit/risk is, therefore, considered to be positive.

The Summaries of Product Characteristics (SmPCs), Patient Information Leaflet (PIL) and labelling are satisfactory, in line with current guidelines and consistent with the reference products.

In accordance with legal requirements, the current approved UK versions of the SmPCs and PIL for these products are available on the MHRA website.

TABLE OF CONTENT OF THE PAR UPDATE

Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance).

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations where significant changes are made are recorded on the MHRA website or European Medicines Agency (EMA) website. Minor changes to the marketing authorisation are recorded in the current SmPC and/or PIL available on the MHRA website.

Application type	**Scope**	**Product information affected**	**Date of grant**	**Outcome**	**Assessment report attached Y/N**