Medicines & Healthcare products
Regulatory Agency

Public Assessment Report

National Procedure

Benzydamine Hydrochloride 0.15 % w/v Oromucosal Spray

benzydamine hydrochloride

PL 17780/1251

Zentiva Pharma UK Limited

LAY SUMMARY

Benzydamine Hydrochloride 0.15 % w/v Oromucosal Spray

benzydamine hydrochloride

This is a summary of the Public Assessment Report (PAR) for Benzydamine Hydrochloride 0.15 % w/v Oromucosal Spray. It explains how this product was assessed and its authorisation recommended, as well as its conditions of use. It is not intended to provide practical advice on how to use this product products.

This product will be referred to as Benzydamine Hydrochloride Spray in this lay summary for ease of reading.

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

What is Benzydamine Hydrochloride Spray and what is it used for?

This application is the same as Benzydamine Hydrochloride 0.15 % w/v Oromucosal Spray (PL 39360/0012), which is already authorised.

The Company responsible for Benzydamine Hydrochloride 0.15 % w/v Oromucosal Spray, has agreed that its scientific data can be used as the basis for the grant of an identical licence for Benzydamine Hydrochloride Spray.

Benzydamine Hydrochloride Spray is used to treat many painful conditions of the mouth or throat, including:

- Mouth ulcers
- Sore throat
- Sore tongue or gums
- Discomfort associated with dentures or dental work.

How does Benzydamine Hydrochloride Spray work?

Benzydamine Hydrochloride Spray contains the active substance benzydamine hydrochloride, which belongs to a group of medicines called non-steroidal anti-inflammatory drugs or NSAIDS. Benzydamine Hydrochloride Spray works by stopping pain and swelling (inflammation).

How is Benzydamine Hydrochloride Spray used?

This medicine's pharmaceutical form is a mouth spray (oromucosal spray), and its route of administration is by spraying into the mouth (oromucosal use).

Benzydamine Hydrochloride Spray should not be used in or near the patient's eyes. If any spray does get into the eyes, the eyes should be rinsed immediately with cold water.

Benzydamine Hydrochloride Spray should not be used for more than 7 days except under medical supervision.

The product should be sprayed directly onto the affected area of the mouth or throat as follows:

Adults, adolescents and elderly:

spray 4 - 8 puffs to the sore area every 1.5 – 3 hours.

Children 6 to 12 years of age:
spray 4 puffs to the sore area every 1.5 – 3 hours.

Children less than 6 years of age:
spray 1 puff for every 4 kilograms of body weight, up to a maximum of 4 puffs, to the sore area every 1.5 – 3 hours.

For further information on how Benzydamine Hydrochloride spray is used, refer to the PIL and Summary of Product Characteristics (SmPC) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

This medicine can be obtained without a prescription.

What benefits of Benzydamine Hydrochloride Spray have been shown in studies?
Benzydamine Hydrochloride Spray is considered identical to the previously authorised product with the same benefits and risks. No new studies have been provided for Benzydamine Hydrochloride Spray; however, reference is made to the studies for Benzydamine Hydrochloride 0.15 % w/v Oromucosal Spray PL 39360/0012.

What are the possible side effects of Benzydamine Hydrochloride Spray?
For the full list of all side effects reported with this medicine/these medicines, see Section 4 of the PIL or the SmPC 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.

Benzydamine Hydrochloride Spray is considered to be identical to the previously authorised product with the same benefits and risks.

Why was Benzydamine Hydrochloride Spray approved?
The MHRA decided that the benefits of Benzydamine Hydrochloride Spray are greater than the risks and recommended that this medicine is approved for use.

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

The following safety concerns have been recognised for Benzydamine Hydrochloride Spray:

Summary of safety concerns	
Important identified risks	• Hypersensitivity reactions (including anaphylactic reactions) • Bronchospasm
Important potential risks	• None
Missing information	• Use during pregnancy and lactation • Safety in paediatric population

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 Benzydamine Hydrochloride Spray 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 this application and are satisfactory.

Other information about Benzydamine Hydrochloride Spray

A marketing authorisation was granted in the UK for Benzydamine Hydrochloride 0.15 % w/v Oromucosal Spray on 06 September 2023. A subsequent change of ownership procedure took place on 16 January 2024 from the original marketing authorisation holder (MAH); Abdi Farma, Unip. Lda (PL 39360/0040) to the current MAH, Zentiva Pharma UK Limited (PL 17780/1251).

The full PAR for Benzydamine Hydrochloride Spray follows this summary.

This summary was last updated in February 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 application for Benzydamine Hydrochloride 0.15 % w/v Oromucosal Spray (PL 39360/0040) could be approved.

The product is approved for the following indications:
Benzydamine Hydrochloride 0.15 % w/v Oromucosal Spray is a locally acting analgesic and anti-inflammatory treatment for the throat and mouth.

It is used to treat various painful oropharyngeal conditions such as mouth ulcers, sore throat, sore mouth or gums, and dental pain.

The name of the active substance is Benzydamine, classified as other anti-inflammatory and antirheumatic agent, steroids; it acts on the local mechanisms of inflammation such as pain, oedema or granuloma. Benzydamine topically applied demonstrates anti-inflammatory activity, reducing oedema as well as exudate and granuloma formation. Further, it exhibits analgesic properties if the pain is caused by an inflammatory condition and local anaesthetic activity. Hyperthermia, which is indicative of systemic functional involvement, is poorly affected by benzydamine.

The indazole analogue benzydamine has physicochemical properties and pharmacological activities which differ from those of the aspirin-like NSAIDs. Unlike aspirin-like NSAIDs which are acids or metabolised to acids, benzydamine is a weak base. In further contrast, benzydamine is a weak inhibitor of the prostaglandin synthesis. Only at concentration of 1mM and above benzydamine effectively inhibits cyclooxygenase and lipooxygenase enzyme activity. It mostly exerts its effects through inhibition of the synthesis of proinflammatory cytokines including tumour necrosis factor-alpha (TNF-α) and Interleukin-1β (IL-1β) without significantly affecting other proinflammatory (IL-6 and 8) or anti-inflammatory cytokines (IL-10, IL-1 receptor antagonist). Further mechanisms of action are hypothesised including the inhibition of the oxidative burst of neutrophils as well as membrane stabilisation as demonstrated by the inhibition of granule release from neutrophils and the stabilization of lysosomes. The local anaesthetic activity of the compound has been related to an interaction with cationic channels.

This is a national abridged application approved under Regulation 56 of The Human Medicines Regulation 2012, as amended (previously Article 10c of Directive 2001/83/EC, as amended) as an informed consent application. The application cross-refers to the reference product Benzydamine Hydrochloride 0.15 % w/v Oromucosal Spray, PL 39360/0012.

No new non-clinical or clinical data have been supplied and none are required for this informed consent application.

Suitable justification has been provided for non-submission of an Environmental Risk Assessment (ERA). As the application is for an identical version of an already authorised product, no increase in environmental exposure is anticipated and no ERA is required.

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

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

A national marketing authorisation was granted in the United Kingdom on 6 September 2023

II. EXPERT REPORT

The applicant cross-refers to the data for Benzydamine Hydrochloride 0.15 % w/v Oromucosal Spray PL 39360/0012 currently held by Abdi Farma Unipessoal Lda. to which this application is claimed to be identical. This is acceptable.

III. ASSESSOR'S COMMENTS ON THE PRODUCT INFORMATION

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

The SmPC is in line with that for Benzydamine Hydrochloride 0.15 % w/v Oromucosal Spray dated 03/2022.

PATIENT INFORMATION LEAFLET

A leaflet text has been provided which has been aligned with that for Benzydamine Hydrochloride 0.15 % w/v Oromucosal Spray, dated for 02/2020. The user test report submitted for PL 39360/0012 has been provided.

LABEL

Text versions of the labels were submitted for the only pack size proposed (30 ml bottle).

IV. QUALITY ASPECTS

IV.1 Drug Substance

Drug substance specification

The source of the active substance is in line with the cross-reference product. The proposed drug substance specification is consistent with the details registered for the cross-reference product.

IV.2. Drug Product Name

The product has been named in line with current requirements.

Strength, pharmaceutical form, route of administration, container and pack sizes

Benzydamine Hydrochloride 0.15 % w/v Oromucosal Spray is available in an amber glass bottle (Type III) with a metered dose pump, in a pack size of 30 ml.

The appearance of the product is identical to that of the cross-reference product.

The proposed shelf life of the product is 3 years with no special storage conditions and to 'Do not freeze'and with a shelf life of 6 months after opening.

The proposed packaging, shelf life and storage conditions are consistent with the details registered for the reference product.

Legal status

Pharmacy (P) medicine.

Manufacturers
The proposed manufacturing site are consistent with the details registered for the cross-reference product and evidence of Good Manufacturing Practice (GMP) compliance has been provided.

Qualitative and quantitative compositions
The composition of the proposed product is consistent with the details registered for the cross-reference product.

Manufacturing process & control of critical steps
The proposed manufacturing processes and process controls are consistent with the details registered for the reference product and the maximum batch size is stated.

Finished product release/shelf life specifications
The finished product specifications at release and shelf-life are in line with the details registered for the cross-reference product.

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

This product does not contain or consist of genetically modified organisms (GMOs).

V. NON-CLINICAL ASPECTS
As this application is submitted under Regulation 56 of The Human Medicines Regulation 2012, as amended, (as an informed consent application) no new non-clinical data have been supplied and none are required.

VI. CLINICAL ASPECTS
As this application is submitted under Regulation 56 of The Human Medicines Regulation 2012, as amended (as an informed consent application), no new clinical data have been supplied, and none are required.

VII. 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.

VIII. USER CONSULTATION
A text version of the Patient Information Leaflet (PIL) has been provided with the application in accordance with legal requirements.

The PIL has been evaluated via a user consultation with target patient groups, in accordance with legal requirements, on the basis of a bridging report making reference to Benzydamine Hydrochloride 0.15 % w/v Oromucosal Spray (PL 36390/0012; Abdi Farma Unipessoal Lda.). The bridging report submitted by the applicant is acceptable.

IX. OVERALL CONCLUSION, BENEFIT/RISK AND RECOMMENDATION

The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. The applicant's product is identical to the cross-reference product. The benefit/risk balance is, therefore, considered to be the same as for the cross-reference product and positive.

The Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and labelling are satisfactory, in line with current guidelines and consistent with the cross-reference product.

In accordance with legal requirements, the current approved UK version of the SmPC and PIL for this product are available on the MHRA website.

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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**