Summary Public Assessment Report

Generics

Benzydamine hydrochloride/Cetylpyridinium chloride Farmak 1.5 mg/5 mg/ml oromucosal spray, solution

Benzydamine hydrochloride, cetylpyridinium chloride

LT/H/0168/001/DC

Date: 08/11/2023

Summary Public Assessment Report

Generics

Benzydamine hydrochloride/Cetylpyridinium chloride Farmak 1.5 mg/5 mg/ml oromucosal spray, solution

Active substance: benzydamine hydrochloride, cetylpyridinium chloride

This is a summary of the public assessment report (PAR) for Benzydamine hydrochloride/Cetylpyridinium chloride Farmak 1.5 mg/5 mg/ml oromucosal spray, solution. It explains how Benzydamine hydrochloride/Cetylpyridinium chloride Farmak 1.5 mg/5 mg/ml oromucosal spray, solution 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 Benzydamine hydrochloride/Cetylpyridinium chloride Farmak 1.5 mg/5 mg/ml oromucosal spray, solution.

For practical information about using Benzydamine hydrochloride/Cetylpyridinium chloride Farmak 1.5 mg/5 mg/ml oromucosal spray, solution patients should read the package leaflet or contact their doctor or pharmacist.

What is Benzydamine hydrochloride/Cetylpyridinium chloride Farmak and what is it used for?

Benzydamine hydrochloride/Cetylpyridinium chloride Farmak is a 'generic medicine'. This means that Benzydamine hydrochloride/Cetylpyridinium chloride Farmak is similar to a 'reference medicines' already authorised in the European Union (EU) called Gola Action 1.5/5.0 mg/ml oromucosal spray, solution.
Benzydamine hydrochloride/Cetylpyridinium chloride Farmak 1.5 mg/5 mg/ml oromucosal spray, solution is indicated in adults and adolescents over 12 years of age for anti-inflammatory, analgesic and antiseptic treatment of irritations in the throat, mouth and gums, in gingivitis and pharyngitis and before and after tooth extractions.

How does Benzydamine hydrochloride/Cetylpyridinium chloride Farmak work?

Benzydamine hydrochloride/Cetylpyridinium chloride Farmak contains two active ingredient:
- benzydamine hydrochloride is a molecule with a nonsteroidal chemical structure with anti-inflammatory and analgesic properties and
- cetylpyridinium chloride is active against gram-positive bacteria and less active against gram-negative bacteria, and therefore performs an optimum antiseptic and germicidal action. It also has antifungal properties.

How is Benzydamine hydrochloride/Cetylpyridinium chloride Farmak used?

The pharmaceutical form of Benzydamine hydrochloride/Cetylpyridinium chloride Farmak is oromucosal spray, solution and the route of administration is oral.
Before the first use of Benzydamine hydrochloride/Cetylpyridinium chloride Farmak oromucosal spray, solution, press the spray head at least 3-4 times in order to obtain even delivery. If the spray has not been used for a long period of time (like at least for one week), press the spray head 1-2 times in order to obtain even delivery.

Open your mouth wide, point the spray nozzle towards your throat and press the spray head 1-2 times. Hold your breath while spraying.

Adults: For a single dose, the spray head should be pressed once to twice. This may be repeated every 2 hours, 3-5 times a day.

For optimal effect, it is not recommended to use the product immediately before or after cleaning teeth.
The stated dose should not be exceeded.
Benzydamine hydrochloride/Cetylpyridinium chloride Farmak can be used for up to 7 days.

Elderly patients
The recommended dose is the same as for adults.

Paediatric population
Adolescents over 12 years of age: For a single dose, the spray head should be pressed once to twice. This may be repeated every 2 hours, 3-5 times a day.

Benzydamine hydrochloride/Cetylpyridinium chloride Farmak is contraindicated in children under 6 years of age.

Benzydamine hydrochloride/Cetylpyridinium chloride Farmak should not be used in children aged 6 to 12 years, unless otherwise prescribed by a doctor.

What benefits of Benzydamine hydrochloride/Cetylpyridinium chloride Farmak have been shown in studies?

No additional studies were needed as Benzydamine hydrochloride/Cetylpyridinium chloride Farmak is generic medicine that are given as oral solution and contain the same active substances as reference medicine called Gola Action.

What are the possible side effects of Benzydamine hydrochloride/Cetylpyridinium chloride Farmak?

Because Benzydamine hydrochloride/Cetylpyridinium chloride Farmak is a generic medicine and bioequivalent to the reference medicine, its benefits and possible side effects are taken as being the same as the reference medicine.
Prolonged use of the medication may lead to sensitisation, oral mucosal irritation, burning oral sensation and various alergic reaction in which case treatment must be suspended and a suitable therapy instated.
For the full list of restrictions, see the package leaflet.

Why is Benzydamine hydrochloride/Cetylpyridinium chloride Farmak approved?

It was concluded that, in accordance with EU requirements, Benzydamine hydrochloride/Cetylpyridinium chloride Farmak has been shown to have comparable quality to reference medicine. Therefore, the State Medicines Control Agency of Lithuania decided that, as for reference medicine called Gola Action 1.5/5.0 mg/ml oromucosal spray, solution, the benefits are greater than its risk and recommended that it can be approved for use.

What measures are being taken to ensure the safe and effective use of Benzydamine hydrochloride/Cetylpyridinium chloride Farmak?

A risk management plan has been developed to ensure that Benzydamine hydrochloride/Cetylpyridinium chloride Farmak 1.5 mg/5 mg/ml oromucosal spray, solution is used as safely as possible. Based on this plan, safety information has been included in the summary of product characteristics and the package leaflet for Flubiprofen Farmak, including the appropriate precautions to be followed by healthcare professionals and patients.

Known side effects are continuously monitored. Furthermore new safety signals reported by patients/healthcare professionals will be monitored/reviewed continuously as well.

Other information about Benzydamine hydrochloride/Cetylpyridinium chloride Farmak

The marketing authorisation for Benzydamine hydrochloride/Cetylpyridinium chloride Farmak was granted after completion of Decentralized Procedure on July 19, 2023.

The full PAR for Benzydamine hydrochloride/Cetylpyridinium chloride Farmak can be found on the website https://mri.cts-mrp.eu/portal/home?domain=h. For more information about Benzydamine hydrochloride/Cetylpyridinium chloride Farmak, read the package leaflet (*link*) or contact your doctor or pharmacist.

This summary was last updated in 11/2023.

Public Assessment Report

Scientific discussion

Benzydamine hydrochloride/Cetylpyridinium chloride Farmak 1.5 mg/5 mg/ml oromucosal spray, solution

Benzydamine hydrochloride, cetylpyridinium chloride

LT/H/0168/001/DC

Date: 08/11/2023

This module reflects the scientific discussion for the approval of I Benzydamine hydrochloride/Cetylpyridinium chloride Farmak 1.5 mg/5 mg/ml oromucosal spray, solution. The procedure was finalised at Day 210, 19/07/2023. 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 Benzydamine hydrochloride/Cetylpyridinium chloride Farmak 1.5 mg/5 mg/ml oromucosal spray, solution, from Farmak International Sp. z o.o., Poland.

Benzydamine hydrochloride/Cetylpyridinium chloride Farmak 1.5 mg/5 mg/ml oromucosal spray, solution is indicated in adults and adolescents over 12 years of age for anti-inflammatory, analgesic and antiseptic treatment of irritations in the throat, mouth and gums, in gingivitis and pharyngitis and before and after tooth extractions.

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

This decentralised procedure concerns a hybrid application claiming similarity with European reference medicinal product Gola Action 1.5/5.0 mg/ml oromucosal spray, solution, registered by IODOSAN S.p.A. (Italy), since 1999
The concerned member state (CMS) involved in this procedure was Poland.

The marketing authorisation has been granted pursuant to Article 10(3) of Directive 2001/83/EC.

II. QUALITY ASPECTS

II.1 Introduction

Benzydamine hydrochloride/Cetylpyridinium chloride Farmak 1.5 mg/5 mg/ml oromucosal spray, solution is clear colourless liquid. pH 4.5 to 6.5

Benzydamine hydrochloride/Cetylpyridinium chloride Farmak 1.5 mg/5 mg/ml oromucosal spray, solution is packed in polyethylene bottle with a dosing pump and spray actuator: 30 ml of oromucosal spray, solution, in a box. Not less than 250 actuations per container.

The excipients are glycerol (E422), saccharin sodium, macrogolglycerol hydroxystearate, mint flavour (contains: natural mint essential oil, mint natural extract, maltodextrines, menthofuran, pulegon, arabic gum (E414)) and purified water.

II.2 Drug Substance

Benzydamine hydrochloride/Cetylpyridinium chloride Farmak 1.5 mg/5 mg/ml oromucosal spray, solution contains 1.5 mg benzydamine hydrochloride and 5 mg cetylpyridinium chloride as the active ingredients in each ml.
All the active substances are well known and widely used as over-the-counter drugs for many years.

The drug substance benzydamine hydrochloride is described in the European Pharmacopoea (EP). Benzydamine hydrochloride is white or almost white crystalline powder, odourless; very soluble in water, freely soluble in ethanol (96 %) and methylene chloride, slightly

soluble in acetone, practically insoluble in heptane. Benzydamine hydrochloride does not exhibit polymorphism.
The ASMF procedure is applied for the drug substance benzydamine hydrochloride. The manufacturing process of benzydamine hydrochloride involves four stages of operation. Detailed description of manufacturing process, including scheme and flow chart diagram has been provided. The structure of Benzydamine hydrochloride molecule has been adequately elucidated and discussion on possible impurities have been provided.
The drug substance specification has been justified based on the EP. monograph for Benzydamine hydrochloride. All analytical methods used have been adequately described and validated as per ICH Q2 guideline requirements.
Benzydamine Hydrochloride for commercial dispatch is packed in double transparent polyethylene bag (LDPE) and finally kept in a high density polyethelene (HDPE) container.
Stability data on the drug substance have been provided. Benzydamine hydrochloride is found to be stable for 6 months under accelerated conditions and 60 months under long-term conditions. All results are well within set specification and there are no observable trends in the stability data results. The proposed re-test period is 5 years. Although, active substance is stable under long-term, accelerated and force conditions, the stringent storage conditions "Stored at room temperature (25±5ºC) in tight containers", as requested by the manufacturer, is acceptable.
The active substance specification used by the finished product manufacturer includes tests required by the EP monograph for benzydamine hydrochloride and additional test for residual solvents. The quality of specification of the active substance is acceptable. Batch analytical data demonstrating compliance with this specification have been provided.

The drug substance cetylpyridinium chloride is described in the European Pharmacopoea (EP). Cetylpyridinium chloride is white or almost white powder, slightly soapy to the touch. Soluble in water and in alcohol. An aqueous solution froths copiously when shaken. Cetylpyridinium chloride does not exhibit polymorphism.
The ASMF procedure is not applied for the drug substance cetylpyridinium chloride, the full information for the active substance is provided by the applicant.
Sufficient information on manufacturing process and process control, control of materials, control of critical steps and intermediates have been provided.
Cetylpyridinium chloride specification by active substance manufacturer is determined as stated in the British Pharmacopoea (BP). The limit set for the residual solvent acetone is in line with requirements of ICH Q3C guideline.
The drug substance cetypyridinium chloride is packed in polyethylene (LDPE) bags and kept in HDPE containers.
Since the solvent has been changed, the currently available data of stability studies under long-term (for 12 months) and accelerated (for 6 months) conditions with newly produced batches using acetone as solvent, has been provided. All critical parameters tested are within the acceptable specifications. Since the API manufacturer has not changed the synthesis of cetypyridinium chloride, only changed the filtration media in the manufacturing of cetylpyridinium chloride. The drug substance is stable and the risk is negligible. So, the API manufacturer keeps the retest period of 3 years. Nevertheless, the API manufacturer provided the declaration in that the retest period of cetylpyridinium chloride will be 2 years until stability data of 2 years for cetylpyridinium chloride is available at the end of 2023. This is acceptable. The approved storage conditions are "The product must be stored in well closed containers".
The active substance specification used by the finished product manufacturer includes tests required by the EP monograph for cetylpyridinium chloride and additional test for residual

solvent. The quality of specification of the active substance is acceptable. Batch analytical data demonstrating compliance with this specification have been provided

II.3 Medicinal Product

The formulation development has been described with detail. During the pharmaceutical development, it was taken into account that the drug product Benzydamine hydrochloride/cetylpyridinium chloride, 1.5 mg/5.0 mg/ml, oromucosal spray, solution should be similar to the reference medicinal product Gola Action 150mg/100ml + 500mg/100ml spray per mucosa orale. Selection of active substances, excipients and their concentrations have been justified.
The qualitative and quantitative composition of the Benzydamine hydrochloride/cetylpyridinium chloride, 1.5 mg/5.0 mg/ml oromucosal spray, solution corresponds to the composition of reference product. The pharmaceutical equivalence of developed product and reference product have been demonstrated.
A brief flow chart of the manufacturing process has been provided outlining the production steps and in-process controls. The manufacturing process involves preparation of materials, preparation and filtration of solution, filling bottles, labelling and packaging. The preparation of Benzydamine hydrochloride/Cetylpyridinium chloride 1.5 mg/5.0 mg/ml oromusocal spray, solution is not complicated and complies with general technological principles for the preparation of oromucosal solution. The process validation scheme to be followed have been included in the dossier. The scheme includes a flow chart of the manufacturing process, the tests to be performed and acceptance criteria and the data to be collected.
The excipients used are well known and commonly used in the composition of the oromucosal sprays, solutions. All excipients comply to EP requirements except mint flavour which is controlled according to the in-house specification. Satisfactory certificates of analysis as tested by the drug product manufacturer are provided demonstrating compliance of the excipients against their EP monographs or against the in-house specification.
The Applicant has provided one specification for release and shelf-life. The proposed drug product specification in general follows recommendations provided in ICH guidelines Q6A and European Pharmacopoeia. Description and validations of the analytical methods have been presented. Batch analysis has been performed of four pilot scale batches. The batches comply with the proposed specification. The specification is justified based on scientific rationale in combination with batch analysis data and stability data.
The medicinal product Benzydamine hydrochloride/cetylpyridinium chloride, 1.5 mg/5.0 mg/mL oromucosal spray, solution is packed in a 54 ml polyethylene bottle (HDPE) fitted with a dosing pump (PE/POM/EVA/stainless steel/aluminium/silicone emulsion) and a spray actuator (PP, HDPE).
The stability studies of the drug product were conducted on four pilot scale batches under ICH storage conditions. Currently available result of 18 months of long-term stability studies have been provided for batches size of 300 L. The results of the stability study demonstrate that the chosen primary container is suitable to preserve the microbiological and physical-chemical characteristics of the drug product. An in-use stability study at the beginning and closely to the end of the shelf life is concluded. 6 months results are available. On basis of the data submitted, a shelf life was granted of 2 years, with storage conditions “no special storage conditions are required for the products”. The shelf-life after first opening of bottle is 6 months.

II.4 Discussion on chemical, pharmaceutical and biological aspects

Based on the submitted dossier, the member states consider that Benzydamine hydrochloride/cetylpyridinium chloride, 1.5 mg/5.0 mg/mL oromucosal spray, solution have a proven chemical-pharmaceutical quality. Sufficient controls have been laid down for the active substance and finished product.

The following post-approval commitments were made:

Description	Due date
The applicant commits to submit a post approval variation to validate in-house GC method used by the active substance manufacturer Unilab Chemicals and Pharmaceuticals Pvt. Ltd., India for the control of purity of starting materiał cetyl chloride	till the end of July, 2024
The applicant commits to submit a post approval variation to validate in-house GC method used by the active substance manufacturer Unilab Chemicals and Phannaceuticals Pvt. Ltd., India for the control of purity of starting materiał pyridine	till the end of July, 2024
The applicant commits to submit a post approval variation for the introduction of the new LC-MS method for testing impurity G for benzydamine hydrochloride drug substance according to requirements of corresponding Ph. Eur. 11.1 monograph.	till the end of July, 2024
The applicant commits to submit a post approval variation for the introduction of to submit the declaration that polyethylene bottle and spray actuator materials comply with the requirements of Ph.Eur. 3.1.3 and Ph.Eur 3.2.2.	till the end of 2024

III. NON-CLINICAL ASPECTS

III.1 Introduction

Pharmacodynamic, pharmacokinetic and toxicological properties of benzydamine hydrochloride and cetylpyridinium chloride are well known. As benzydamine hydrochloride and cetylpyridinium chloride are widely used, well-known active substances, the applicant has not provided additional studies and further studies are not required. The non-clinical overview on the pre-clinical pharmacology, pharmacokinetics and toxicology based on literature review is, thus, appropriate.

III.2 Ecotoxicity/environmental risk assessment (ERA)

Since Benzydamine hydrochloride/Cetylpyridinium chloride Farmak 1.5 mg/5 mg/ml oromucosal spray, solution is a hybrid product of a reference product The European reference medicinal product is Gola Action 1.5/5.0 mg/ml oromucosal spray, solution (1,5 mg/ml benzydamine hydrochloride and 5,0 mg/ml cetylpyridinium chloride) by IODOSAN S.p.A. (Italy), registered since 1999, the applicant did not submit an environmental risk assessment (ERA). The need for ERA study can be waived because this hybrid application will lead to substitution of existing products on the market. The approval of this medicine will not lead to an increased exposure to the environment. An environmental risk assessment is therefore not deemed necessary.

III.3 Discussion on the non-clinical aspects

Benzydamine hydrochloride/Cetylpyridinium chloride oromucosal spray, solution is a hybrid product of a reference product Gola Action 150 mg/100 ml+500mg/100ml oramucosal spray by Iodosan S.p.A., authorized since 10/11/1999 in Italy. A non-clinical overview on the

pharmacology, pharmacokinetics and toxicology has been provided, which is based on up-to-date and adequate scientific literature. The overview justifies why there is no need to generate additional nonclinical pharmacology, pharmacokinetics and toxicology data. Therefore, the member state agreed that no further non-clinical studies are required.

IV. CLINICAL ASPECTS

IV.1 Introduction

Benzydamine hydrochloride and cetylpyridinium chloride are well known active substances with established efficacy and tolerability. A clinical overview has been provided, which is based on scientific literature. The overview justifies why there is no need to generate additional clinical data. Therefore, the member state agreed that no further clinical studies are required.
The bioequivalence study has not been performed. Biowaiver is discussed below.

IV.2 Pharmacokinetics

No new pharmacokinetic studies have been submitted. No data are required for this application.

The applicant has provided the following justification in support of a biowaiver:

- The two products are pharmaceutical equivalents as they contain the same amount of the same active ingredients in the same dosage form, i.e. 1,5 mg benzydamine hydrochloride and 5 mg cetylpyridinium chloride in 1 ml and 100ml of solution/spray accordingly.
- The qualitative and quantitative compositions in terms of active substances and excipients are the same for the corresponding products.
- The drug products and reference products are all aqueous solutions of benzydamine hydrochloride and cetylpyridinium chloride.
- Benzydamine hydrochloride/Cetylpyridinium chloride Farmak 1.5 m/5 mg/ml oromucosal spray, solution and Gola Action 150 mg/100 ml + 500 mg/100 ml oromucosal spray are all locally acting drug products.
- The systemic absorption of benzydamine hydrochloride and cetylpyridinium chloride applied topically is very low.
- As Benzydamine hydrochloride/Cetylpyridinium chloride Farmak 1.5 m/5 mg/ml, and also Gola Action 150 mg/100 ml + 500 mg/100 ml oromucosal spray are all solutions when administrated to the oral cavity, no in vivo studies are deemed necessary in view of the self-evident bioequivalence of solutions as described in the Appendix II of “Guideline on the investigation of bioequivalence” (CPMP/EWP/QWP/1401/98 Rev.1/Corr**).
- According to the “Guideline On The Investigation Of Bioequivalence” CPMP/EWP/QWP/1401/98 Rev. 1/ Corr (London, 20 January 2010) the equivalence of the locally acting locally applied products in the solutions form does not need to be demonstrated in the study.

Taking into consideration all the data provided, it can be concluded that the proposed and the reference drugs are bioequivalent.

Therefore, the proposed product satisfies the criteria of a generic product and is applicable for submission under paragraph 3 of Article 10 of Directive 2001/83/EC.

IV.3 Pharmacodynamics

No new data have been submitted. No data are required for this application.

IV.4 Clinical efficacy

No new data have been submitted. To support the clinical efficacy, the reference is made to the clinical studies and experience with the reference product Gola Action 150 mg/100 ml + 500 mg/100 ml oromucosal spray.

IV.5 Clinical safety

No new data have been submitted. To support the clinical safety, the reference is made to the clinical studies and experience with the reference product Gola Action 150 mg/100 ml + 500 mg/100 ml oromucosal spray.

IV.6 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 Benzydamine hydrochloride/Cetylpyridinium chloride Farmak 1.5 mg/5 mg/ml oromucosal spray, solution.

Summary table of safety concerns as approved in RMP

Important identified risks	None
Important potential risks	None
Missing information	None

IV.7 Discussion on the clinical aspects

For these marketing authorisation, references are made to the clinical studies and experience with the reference product Gola Action 150 mg/100 ml + 500 mg/100 ml oromucosal spray. No new clinical studies were conducted. The bioequivalence study was not carried out as both products are oromucosal spray (solutions) at the time of administration. The applicant demonstrated that according to CPMP/EWP/QWP/1401/98 Rev. 1/Corr. “Guideline on the Investigation of Bioequivalence” that Benzydamine Hydrochloride/Cetylpyridinium Chloride 1.5 mg/5 mg/mL oromucosal spray and the reference product Gola Action 150 mg/100 ml + 500 mg/100 ml oromucosal spray are bioequivalent.
Risk management is adequately addressed.

V. USER CONSULTATION

A user consultation with target patient groups on the package information leaflet (PL) has been performed The PL user testing is considered acceptable.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

Benzydamine hydrochloride/Cetylpyridinium chloride Farmak 1.5 mg/5 mg/ml oromucosal spray, solution have a proven chemical-pharmaceutical quality and are generic form of reference medicinal product Gola Action 1.5/5.0 mg/ml oromucosal spray, solution. Gola Action is well-known medicinal product with established favourable efficacy and safety profiles.

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

The Decentralized procedure was finalised with a positive outcome on 19/07/2023.

Viešojo vertinimo protokolo apžvalga

Benzydamine hydrochloride/Cetylpyridinium chloride Farmak 1,5 mg/5 mg/ml burnos gleivinės purškalas (tirpalas)

benzidamino hidrochloridas/cetilpiridinio chloridas

Trumpa kokybinės dalies apžvalga

Vaistinio preparato veikliosios medžiagos yra benzidamino hidrochloridas ir cetilpiridinio chloridas. Abi veikliosios medžiagos aprašytos Europos Farmakopėjoje. Benzidamino hidrochlorido gamintojas pateikė veikliosios medžiagos gamybos bylą (ASMF). Vaistinei medžiagai cetilpiridinio chloridui ASMF procedūra netaikoma, visą informaciją apie veikliąją medžiagą pateikia pareiškėjas. Gatavo produkto gamintojo veikliosiųjų medžiagų benzidamino hidrochlorido ir cetilpiridinio chlorido specifikacijos yra tinkamos kokybės ir atitinka ES gairių reikalavimus. Pateikti serijų analizės sertifikatai atitinka patvirtintų specifikacijų reikalavimus. Remiantis veikliosios medžiagos gamybos bylos duomenimis, nustatytas veikliosios medžiagos benzidamino hidrochlorido pakartotinės patikros laikotarpis yra 5 metai, laikant kambario temperatūroje (25±5ºC) sandariuose induose. Cetilpiridinio chloridui nustatytas 2 metų pakartotinės patikros laikotarpis iki 2023 m. pabaigos, vėliau – 3 metai, laikant gerai uždarytose talpyklėse.
Benzydamine hydrochloride/Cetylpyridinium chloride Farmak 1,5 mg/5 mg/ml burnos gleivinės purškalas (tirpalas) yra skaidrus, bespalvis tirpalas. pH nuo 4.5 iki 6.5. Gatavo produkto sudėtyje yra šios pagalbinės medžiagos: glicerolis (E422), sacharino natrio druska, makrogolglicerolio hidroksisteratas, mėtų skonio medžiaga (sudėtyje yra: natūralus mėtų eterinis aliejus, natūralus mėtų ekstraktas, maltodekstrinai, mentofuranas, pulegonas, gumiarabikas (E414)) ir išgrynintas vanduo. Pagalbinių medžiagų pasirinkimas yra pagrįstas, jos yra plačiai naudojamos farmacinių preparatų gamyboje. Palyginamieji in vitro tirpumo tyrimai atlikti su referenciniu vaistiniu preparatu Gola Action 1,5/5,0 mg/ml burnos gleivinės purškalas, tirpalas. Bioekvivalentiškumo tyrimai neatlikti, nes abu vaistiniai preparatai yra vandeniniai tirpalai vartojami ant burnos gleivinės. Gamybos procesą sudaro medžiagų paruošimas, tirpalo paruošimas ir filtravimas, butelių užpildymas, ženklinimas ir pakavimas. Produktas gaminamas naudojant įprastines gamybos technologijas. Gatavo produkto išleidimo ir tinkamumo laiko pabaigos specifikacijų kokybė atitinka ES gairių reikalavimus. Analizės procedūrų aprašymai pateikti, metodai validuoti. Serijų analizės sertifikatai atitinka specifikacijos reikalavimus. Gatavas produktas pakuojamas į polietileno buteliuką su dozavimo pompa ir purkštuvu; buteliuke yra 30 ml burnos gleivinės purškalo (tirpalo). Kartono dėžutėje yra vienas buteliukas. Buteliuke yra ne mažiau kaip 250 išpurškimų. Gatavo produkto stabilumo tyrimai atlikti pagal ES gairių reikalavimus. Remiantis stabilumo tyrimų duomenimis nustatytas 2 metų tinkamumo laikas. Tinkamumo laikas po pirmojo atidarymo: 6 mėnesiai. Šiam vaistiniam preparatui specialių laikymo sąlygų nereikia.

Trumpa ikiklinikinės ir klinikinės dalies apžvalga

Benzydamine hydrochloride/Cetylpyridinium chloride Farmak 1,5 mg/5 mg/ml burnos gleivinės purškalas (tirpalas) yra nereceptinis vaistinis preparatas, skirtas suaugusiųjų ir vyresnių kaip 12 metų paauglių uždegimui slopinti ir analgeziniam bei antiseptiniam poveikiui sukelti, jei yra ryklės, burnos ir dantenų dirginimas, sergant gingivitu ir faringitu bei prieš dantų traukimą arba po jo.

Benzydamine hydrochloride/Cetylpyridinium chloride Farmak 1,5 mg/5 mg/ml burnos gleivinės purškalą (tirpalą) sudaro dvi veikliosios medžiagos:
- benzidamino hidrochloridas, kuris sukelia uždegimą slopinantį ir analgezinį poveikį. Pasireiškia lokalus uždegimo požymių (pvz., skausmo, paraudimo, patinimo, karščio ir funkcijos sutrikimo) lengvinimas;
- cetilpiridinio chloridas veikia gramteigiamas bakterijas ir kiek silpniau gramneigiamas bakterijas, todėl pasireiškia optimalus antiseptinis ir germicidinis poveikis. Be to, pasireiškia ir poveikis nuo grybelių.
Benzidamino hidrochlorido ir cetilpiridinio chlorido farmakodinaminės, farmakokinetinės ir toksikologinės savybės yra gerai žinomos, Paraiška registruoti vaistinį preparatą pateikta pagal Direktyvos 2001/83/EB 10 str. 3d. („hibridinis“), naujų ikiklinikinių tyrimų duomenų pareiškėjas nepateikė. Pateikti ikiklinikiniai tyrimų duomenys pagrįsti literatūros šaltinių duomenimis.
Paraiška registruoti vaistinį preparatą pateikta pagal Direktyvos 2001/83/EB 10 str. 3d. („hibridinis“). Remiantis EK patvirtintomis Biologinio ekvivalentiškumo gairėmis (CPMP/EWP/QWP/1401/98 Rev. 1/ Corr **, of January 2010) vaistinis prepratas Benzydamine hydrochloride/Cetylpyridinium chloride Farmak 1,5 mg/5 mg/ml burnos gleivinės purškalas (tirpalas) ir referencinis vaistinis prepratas Gola Action 150 mg/100 ml + 500 mg/100 ml burnos gleivinės purškalas yra pakankamai panašūs (kiekybinė sudėtis, farmacinė forma, veikimo vieta ir t.t.). Biologinio ekvivalentiškumo tyrimas neatliktas, nes minėti vaistiniai preparatai vartojami geriamojo tirpalo forma, jų kokybinė sudėtis vienoda, o pagalbinės medžiagos nedaro įtakos vaistinių preparatų biologiniam prieinamumui.

Benzydamine hydrochloride/Cetylpyridinium chloride Farmak 1,5 mg/5 mg/ml burnos gleivinės purškalo (tirpalas) naudojimo saugumui užtikrinti yra pateiktas rizikos valdymo planas. Saugumo informacija pateikiama preparato charakteristikų santraukoje ir informaciniame lapelyje. Šiam vaistiniam preparatui taikomos įprastos rizikos valdymo priemonės.
Nepageidaujami reiškiniai yra nuolat analizuojami po vaistinio preparato registracijos.

Remiantis pateiktais kokybės, saugumo ir veiksmingumo duomenimis, decentralizuotoje procedūroje dalyvaujančios referencinė valstybė narė (Lietuva) ir pripažįstanti valstybė narė (Lenkija) nutarė, kad vaistinį preparatą Benzydamine hydrochloride/Cetylpyridinium chloride Farmak 1,5 mg/5 mg/ml burnos gleivinės purškalas (tirpalas) registruoti galima ir europinė fazė buvo sėkmingai baigta (210 dieną) 2022-07-19.
Lietuvoje vaistinis preparatas užregistruotas 2022-08-14.