MANX BENZOCAINE SORE THROAT SPRAY
PL 15833/0013

UKPAR

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MANX BENZOCAINE SORE THROAT SPRAY
PL 15833/0013

LAY SUMMARY

On 24\textsuperscript{th} March 2009, the MHRA granted Manx Pharma Limited a Marketing Authorisation (licences) for Manx Benzocaine Sore Throat Spray (PL 15833/0013).

Manx Benzocaine Sore Throat Spray contains benzocaine, which is a local anaesthetic. This means that it relieves pain by acting on the surface area treated. The spray is used to relieve the pain of sore throats and minor mouth infections.

No new or unexpected safety concerns arose from this application and it was, therefore, judged that the benefits of taking Manx Benzocaine Sore Throat Spray outweigh the risks; hence a Marketing Authorisation has been granted.
# MANX BENZOCAIN SORE THROAT SPRAY

## SCIENTIFIC DISCUSSION

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**INTRODUCTION**

Based on the review of the data on quality, safety and efficacy, the UK granted a marketing authorisation for the medicinal product Manx Benzocaine Sore Throat Spray (PL 15833/0013) to Manx Pharma Limited on 24th March 2009. This product is a prescription only medicine and is indicated for symptomatic temporary relief of pain associated with sore throat pain and minor mouth infections.

This application for Manx Benzocaine Sore Throat Spray is submitted as an abridged standard application according to Article 10.1 of Directive 2001/83/EC, claiming to be a generic medicinal product to AAA Mouth and Throat Spray, the MA for which is held by the same company, first authorised in September 1997.

The product contains the active substance benzocaine, local anaesthetic of the p-aminobenzoic acid ester class which is used for surface anaesthesia.

The application also included a proposal for the reclassification from P (pharmacy) to GSL (general sales licence) of benzocaine 3% in the form of throat sprays, throat pastilles, throat lozenges and throat tablets, which was rejected.
PHARMACEUTICAL ASSESSMENT

DRUG SUBSTANCE

Benzocaine

INN: Benzocaine
Chemical name: ethyl 4-aminobenzoate
          ethyl p-aminobenzoate
          4-aminobenzoic acid ethyl ester

Structure:

Physical form: White odourless crystals
              Very slightly soluble in cold water, soluble in methanol and diethyl ether.
Molecular formula: C₉H₁₁NO₂
Molecular weight: 165.189

Benzocaine is the subject of a British Pharmacopoeia monograph.

Synthesis of the drug substance from the designated starting materials has been adequately described, and appropriate in-process controls and intermediate specifications are applied. Satisfactory specification tests are in place for all starting materials and reagents, and these are supported by relevant certificates of analysis.

All potential known impurities have been identified and characterised. Appropriate proof of structure data has been supplied for the active pharmaceutical ingredient.

An appropriate specification is provided for the active substance benzocaine. Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications. Batch analysis data are provided and comply with the proposed specification.

Satisfactory certificates of analysis have been provided for working standards used by the active substance manufacturer and finished product manufacturer.

The specifications and typical analytical test reports are provided and are satisfactory.

Satisfactory specifications and certificates of analysis have been provided all aspects of the container-closure system. A declaration has been provided that the primary packaging complies with current regulations concerning contact with foodstuff.

An appropriate retest period has been proposed based on stability data submitted for the active substance benzocaine.
DRUG PRODUCT
Other ingredients
Other ingredients consist of pharmaceutical excipients cetylpyridinium chloride, glycerine, ethanol, clove bud oil, menthol crystals, sodium saccharin 450, peppermint, cremophor RH40, and water. Cetylpyridinium chloride, glycerine, ethanol, sodium saccharin 450 and water comply with their relevant British Pharmacopoeia monographs. Excipients clove bud oil, menthol crystals, peppermint and cremophor RH40 all comply with in-house specifications.

None of the excipients used contain material of animal or human origin.

Product development
The objective of the development programme was to produce a product that could be considered a generic medicinal product of AAA Mouth and Throat Spray (Manx Pharma Limited, September 1997).

The applicant has provided a suitable product development section. Justifications for the use and amounts of each excipient have been provided and are valid. Comparative impurity profiles have been provided for the finished product versus the reference product AAA Mouth and Throat Spray (Manx Pharma Limited).

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

In-process controls are satisfactory based on process validation data and controls on the finished product.

Finished product specification
The finished product specification is satisfactory. Test methods have been described and have been adequately validated, as appropriate. Batch data have been provided and comply with the release specification. Certificates of analysis for all working standards used have been provided and are satisfactory.

Container-Closure System
The product is packaged in white aluminium spray containers with metering pump and high density polyethylene cap, and polypropylene and nitrile rubber nozzle.

Specifications and certificates of analysis for the packaging types used have been provided. All primary product packaging complies with the European Pharmacopoeia monograph. The product is packaged in sizes of not less than 7.3g, which gives approximately 60 metered doses.

Stability
Finished product stability studies have been conducted in accordance with current guidelines. Based on the results, a shelf-life of 24 months has been set, which is satisfactory. Storage conditions are “Keep away from a naked flame” and ‘Do not store above 25°C.’
ADMINISTRATIVE
Expert Report
A pharmaceutical expert report has been written by a suitably qualified person and is satisfactory.

Summary of Product Characteristics (SPC)
This is pharmaceutically satisfactory.

Labelling
These are pharmaceutically satisfactory.

Patient Information Leaflet (PIL)
This is pharmaceutically satisfactory.

A package leaflet has been submitted to the MHRA along with results of consultations with target patient groups ("user testing"), in accordance with Article 59 of Council Directive 2001/83/EC, as amended. The results indicate that the package leaflet is well-structured and organised, easy to understand and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that it contains.

MAA Form
This is pharmaceutically satisfactory.

Conclusion
It is recommended that a Marketing Authorisation is granted for this application.
PRECLINICAL ASSESSMENT

This application for Max Benzocaine Sore Throat Spray was submitted as an abridged standard application according to Article 10.1 of Directive 2001/83/EC, claiming to be a generic medicinal product of AAA Mouth and Throat Spray, the MA for which is held by the same company, first authorised in September 1997.

No new preclinical data have been supplied with this application and none are required for applications of this type.
CLINICAL ASSESSMENT

CLINICAL PHARMACOLOGY
No bioequivalence studies have been performed and none are required for this application, as the product is administered as a topical spray.

EFFICACY
No new data has been provided.

SAFETY
No new data has been provided.

EXPERT REPORTS
The clinical expert report has been written by a suitably qualified person and is satisfactory.

PATIENT INFORMATION LEAFLET (PIL)
This is consistent with that for the reference product and is satisfactory.

LABELLING
These are satisfactory.

APPLICATION FORM (MAA)
This is satisfactory.

SUMMARY OF PRODUCT CHARACTERISTICS (SPC)
This is consistent with that for the reference product and is satisfactory.

DISCUSSION
A bioequivalence study with the reference product is not required for this product and can be justified as a generic medicinal product considering the quantitative and qualitative composition of the product and the route of administration.

MEDICAL CONCLUSION
The grant of a marketing authorisation is recommended for this application.
OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY
The important quality characteristics of Manx Benzocaine Sore Throat Spray are well-defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

PRECLINICAL
No new preclinical data were submitted and none are required for applications of this type.

EFFICACY
Benzocaine is a well-known drug and has been used as a diuretic for many years.
The applicant’s Manx Benzocaine Sore Throat Spray is considered to be bioequivalent to the reference product Lasix AAA Mouth and Throat Spray.

No new or unexpected safety concerns arise from this application.

The SPC, PIL and labelling are satisfactory and consistent with those for the reference product AAA Mouth and Throat Spray.

This product was referred to CMD(h) due to the proposal to amend the legal status from P to GSL.
The Committee is asked to consider whether the proposal to amend the legal status, from P to GSL, of benzocaine (3%), in spray formulation, for internal use is acceptable.

The Committee advised that the GSL order should not be further amended with respect to benzocaine. The Committee considered that the criterion for inclusion in the GSL order according to Section 51 of the Medicines Act was not met by the product for the proposed indications, in that it cannot be sold or supplied with reasonable safety otherwise than by, or under the supervision of, a pharmacist.

The committee gave the following reason for this advice:
The advice of the pharmacist is required to ensure that the patient receives the most appropriate treatment, particularly in the case of fungal mouth infections.

The committee also commented that the lack of specificity in the proposed indications, especially that of ‘pain of minor mouth infections’ was unhelpful for a GSL product.

RISK BENEFIT ASSESSMENT
The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The data submitted supports the claim that the applicant’s product and the reference product are interchangeable. Extensive clinical experience with benzocaine is considered to have demonstrated the therapeutic value of the compound. The benefit/risk is, therefore, considered to be positive.
## STEPS TAKEN FOR ASSESMENT

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<tr>
<td>1</td>
<td>The MHRA received the marketing authorisation application on 19th April 2000. The MHRA also received further response from the MAH regarding the application on 23rd October 2008.</td>
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<td>2</td>
<td>Following standard checks and communication with the applicant the MHRA considered the applications valid on 23rd October 2008.</td>
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<td>3</td>
<td>Following assessment of the applications, the MHRA requested further information relating to the quality dossiers on 12th January and 17th March 2009.</td>
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<td>4</td>
<td>The applicant responded to the MHRA’s requests, providing further information on 9th March and 19th March 2009 for the quality sections.</td>
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<td>5</td>
<td>The applications were determined on 24th March 2009.</td>
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MANX BENZOCAINE SORE THROAT SPRAY
PL 15833/0013

STEPS TAKEN AFTER AUTHORISATION - SUMMARY

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SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Manx Benzocaine Sore Throat Spray.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Benzocaine 1.5 mg per actuation. For excipients please see 6.1.

3 PHARMACEUTICAL FORM
Oromucosal spray.

4 CLINICAL PARTICULARS
4.1 THERAPEUTIC INDICATIONS
Symptomatic temporary relief of pain associated with sore throat pain and minor mouth infections.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION
Adults (including elderly):
Spray two metered doses every two to three hours if required (not more than sixteen doses in every 24 hours) or as directed by the physician.

Children aged 6 and over:
One metered dose every two to three hours if required (not more than eight doses in every 24 hours) or as directed by the physician.
Not suitable for children under 6 years.

Route of administration
Topical application to the mucosa of the mouth and throat by means of a metered dose aerosol.
Product should not be administered for more than 7 consecutive days. The container should be shaken before use.
4.3 CONTRAINDICATIONS
Known hypersensitivity to benzocaine.
Methaemoglobinaemia.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE
This preparation should not be administered to children under 6 years or used for more than seven consecutive days unless directed by a physician.

If the sore throat is severe, persistent or accompanied by fever or headache, a physician should be consulted before the use of this product. Avoid spraying into eyes.

Caution should be exercised in the use of this product if there have been previous allergic reactions with other local anaesthetics or sunscreen products.

Avoid inhalation of the product.
To be used with caution in patients with asthma.
4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION
Benzocaine is an ester which on hydrolysis produces p-aminobenzoic acid so it should not be used in patients being treated with sulphonamides.

4.6 PREGNANCY AND LACTATION
There is no evidence, at present, of hazard from benzocaine in pregnancy. However, only very limited data is available. Therefore it should not be used in pregnancy unless considered essential by a physician.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES
None.

4.8 UNDESIRABLE EFFECTS
Hypersensitivity reactions to benzocaine have been reported. Methaemoglobinaemia can occur rarely.

4.9 OVERDOSE
There have been no reports of overdosage with Manx Benzocaine Sore Throat Spray. Systemic effects are unlikely.

5 PHARMACOLOGICAL PROPERTIES
5.1 PHARMACODYNAMIC PROPERTIES
Benzocaine is a surface anaesthetic of the ester type. It has found frequent use as lozenges or solution to treat pain arising from various throat and mouth conditions.

5.2 PHARMACOKINETIC PROPERTIES
Benzocaine is sparingly soluble in water with toxicity about a tenth that of cocaine. It is not readily absorbed from mucus membranes. It is an ester which on hydrolysis produces p-aminobenzoic acid.

5.3 PRECLINICAL SAFETY DATA
None stated.

6 PHARMACEUTICAL PARTICULARS
6.1 LIST OF EXCIPIENTS
Cetylpyridinium chloride, glycerin, ethanol, clove bud oil, menthol crystals, sodium saccharin 450, peppermint, cremophor RH40, water.

6.2 INCOMPATIBILITIES
None.

6.3 SHELF LIFE
24 months.

6.4 SPECIAL PRECAUTIONS FOR STORAGE
Keep away from a naked flame.
Do not store above 25°C.

6.5 NATURE AND CONTENTS OF CONTAINER
White aluminium spray container with metering pump and high density polyethylene cap, and propylene and nitrilic rubber nozzle.
Pack size: not less than 7.3 g (approximately 60 metered doses).

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL
To help protect the environment, do not dispose of this medicine via wastewater or household waste. Ask a pharmacist for advice on disposal.

7 MARKETING AUTHORISATION HOLDER
Manx Pharma Limited
Taylor Group House
Wedgnock Lane
Warwick
CV34 5YA
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)
15833/0013

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
24/03/2009

10 DATE OF REVISION OF THE TEXT
24/03/2009
PATIENT INFORMATION LEAFLET - INFORMATION FOR THE USER

MANX BENZOCAINE SORE THROAT SPRAY

Benzocaine

Read all of this leaflet carefully because it contains important information for you. This medicine is available without prescription. However, you still need to take Manx Benzocaine Sore Throat Spray carefully to get the best results from it.

- Keep this leaflet. You may need to read it again.
- Ask your pharmacist if you need more information or advice.
- You must contact a doctor if your symptoms worsen or do not improve.
- If any of the side effects get serious, or if you notice any side effect not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet
1. What Manx Benzocaine Sore Throat Spray is and what it is used for
2. Before you use Manx Benzocaine Sore Throat Spray
3. How to use Manx Benzocaine Sore Throat Spray
4. Possible side effects
5. How to store Manx Benzocaine Sore Throat Spray
6. Further information

1. What Manx Benzocaine Sore Throat Spray is and what it is used for

Manx Benzocaine Sore Throat Spray contains benzocaine, which is a local anaesthetic. This means that it relieves pain by acting on the surface area treated. The spray is used to relieve the pain of sore throats and minor mouth infections.

2. Before you use Manx Benzocaine Sore Throat Spray

Do not use the medicine for more than seven days in a row. If the problem does not improve, or you need to take more doses than the number recommended in section 3, you should see your doctor.

Do not use Manx Benzocaine Sore Throat Spray if:
- you have had an allergic (hypersensitive) reaction such as rash, itching or wheezing to benzocaine or any of the other ingredients of Manx Benzocaine Sore Throat Spray (see section 6 for other ingredients).
- you have a rare blood condition called methaemoglobinemia.

Take special care and please tell your doctor or pharmacist if you have:
- a headache or fever (raised temperature) for more than a few days
- a sore throat or mouth symptoms for more than a few days, or if the throat is so sore that you cannot swallow.

Please tell your doctor or pharmacist if you have or have had:
- asthma
- an allergic reaction to any other local anaesthetic
- an allergic reaction to a sunscreen product.

Care should be taken to avoid getting the spray into your eyes or airways (do not breathe it in).

Children under 6 years of age should not use this spray.

Taking other medicines
Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without prescription.
- sulphonamide antibiotics such as co-trimoxazole for an infection.

Pregnancy and breast-feeding
You should not use the spray during pregnancy or breast-feeding.

Ask your doctor or pharmacist for advice before taking any medicines.

Driving and operating machinery
There are no known effects of this medicine on your ability to drive or use machinery.

Important Information about some of the ingredients in this product
This spray contains small amounts of ethanol (alcohol), less than 100mg per metered dose.

3. How to use Manx Benzocaine Sore Throat Spray

Always use Manx Benzocaine Sore Throat Spray as recommended by your doctor or pharmacist. You should check with your doctor or pharmacist if you are not sure.

The usual doses are:
Adults, including the elderly: Spray two doses to the affected part of the mouth or throat and repeat every two or three hours if required. Do not use more than 8 times a day.

(continued overleaf)
Children aged 6 to 12 years: Spray one dose to the affected area and repeat every two to three hours if required. Do not give more than 8 times a day.

The medicine is not recommended for use by children younger than 6 years.

Please follow the handling instructions below:
- shake the container before use

![Fig. 1](image)

**Fig. 1** Resting position (cannot be activated)

![Fig. 2](image)

**Fig. 2** Raise nozzle from vertical to horizontal position

Before use it may be necessary to press the plunger 2-3 times to activate spray.

Do not use the spray near a naked flame.

### 4. Possible side effects

Like all medicines Manx Benzocaine Sore Throat Spray can cause side effects, although not everybody gets them.

If you experience any of the following allergic reactions stop using the spray and speak to your doctor immediately:
- severe rash, itching, swelling of the face, lips or mouth
- shortness of breath or difficulty breathing
- irregular heartbeat, low blood pressure (light-headed feeling when standing)

Methaemoglobinemia (a very rare blood condition) has been reported with benzocaine use.

If you notice any side effects not listed please tell your doctor or pharmacist.

### 5. How to store Manx Benzocaine Sore Throat Spray

Keep out of the reach and sight of children.

Do not store above 25°C and keep away from naked flames.

Do not use the spray after the expiry date which is printed in the packet.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

### 6. Further Information

What Manx Benzocaine Sore Throat Spray contains

Each metered dose of Manx Benzocaine Sore Throat Spray contains the active benzocaine 1.5mg. It also contains cetylpyridinium chloride, glycerin, ethanol, clove bud oil, peppermint, menthol, saccharin sodium 450, cremophor RH40 (polyethoxylated castor oil) and purified water.

What Manx Benzocaine Sore Throat Spray looks like and contents of the pack

This product is available in the white aluminium can with a folding arm activator and cap. Each can contains approximately sixty metered doses of liquid spray.

Marketing Authorisation Holder

Manx Pharma Ltd., Taylor Group House Wedgnock Lane, Warwick, CV34 5YA, United Kingdom.

Manufacturer

Pharmaserve (North West) Ltd., 9 Arkwright Road Astmoor Industrial Estate, Runcorn, Cheshire WA7 1NU, United Kingdom.

This leaflet was last revised in March 2009
Contains 1.5mg Benzocaine per metered dose. Cetylpyridinium Chloride, Glycerin, Ethanol, Clove Bud Oil, Menthol, Saccharin Sodium, Peppermint, Cremophor and Purified Water.

READ THE ACCOMPANYING LEAFLET BEFORE USE

Directions for use: Shake before use. Raise nozzle to horizontal position. Hold your head upright, insert the nozzle well into your mouth and press the plunger once to deliver a single metered dose. See enclosed leaflet for further information.

The usual doses are: Adults, including the elderly: Spray 2 doses to the affected part of the mouth or throat and repeat every 2 or 3 hours if required. Do not use more than 8 times a day.

Children aged 6 to 12 years: Spray 1 dose to the affected area and repeat every 2 to 3 hours if required. Do not give more than 8 times a day.

The medicine is not recommended for use by children younger than 6 years.

Do not use for more than seven days in a row. If symptoms continue, see your doctor. Do not use if you know you are allergic to benzocaine or any of the other ingredients; if you have a rare blood condition called methaemoglobinaemia or if you are pregnant or breast-feeding.

Before use, tell your doctor or pharmacist if you have had a headache, fever, sore throat or mouth symptoms for more than a few days; cannot swallow because your throat is too sore; have asthma, have had an allergic reaction to any other local anaesthetic or to a sunscreen product; are taking any other medicines. Avoid getting the spray into your eyes. Do not breathe it in. Contains small amounts of ethanol (alcohol), less than 100mg per metered dose. Keep all medicines out of the reach and sight of children. Keep away from naked flame. Do not store above 25°C. See base of can for batch number and expiry date. Do not exceed the stated dose.