Medicines & Healthcare products Regulatory Agency

MHRA

Public Assessment Report

National Procedure

Carbocisteine 250 mg/5 ml Adult Syrup

(carbocisteine)

PL 25298/0266

Brown & Burk UK Ltd

LAY SUMMARY

Carbocisteine 250 mg/5 ml Adult Syrup (carbocisteine)

This is a summary of the Public Assessment Report (PAR) for Carbocisteine 250 mg/5 ml Adult Syrup. 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.

This product will be referred to as Carbocisteine Syrup in this lay summary for ease of reading.

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

What is Carbocisteine Syrup and what is it used for?
This application is the same as Carbocisteine 250 mg/5 ml Adult Syrup (PL 25298/0082) which is already authorised.

The Company responsible for Carbocisteine 250 mg/5 ml Adult Syrup has agreed that its scientific data can be used as the basis for the grant of an identical licence for Carbocisteine Syrup.

Carbocisteine Syrup is used for problems with the breathing passages (respiratory tract) caused by too much sticky mucus.

How does Carbocisteine Syrup work?
This medicine contains the active substance carbocisteine. This belongs to a group of medicines called 'mucolytics' which work by making mucus (phlegm) less sticky. This makes the mucus easier to cough up.

How is Carbocisteine Syrup used?
The pharmaceutical form of this medicine is a syrup and the route of administration oral (via the mouth). Carbocisteine Syrup comes with a measuring beaker. If the patient feels that this medicine is too weak or too strong, they should not change the dose themselves, but ask their doctor.

How much to take
Adults (including the elderly)

- Usual dose is 15 ml three times each day

If the patient’s symptoms improve, their dose may be lowered to 10 ml, three times, each day.

Children
Carbocisteine Syrup is not recommended for children.
This medicine is not recommended for use in children and adolescents under the age of 18 years due to the alcohol content.

For further information on how Carbocisteine Syrup 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 only be obtained with a prescription.

The patient should always take the 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 Carbocisteine Syrup have been shown in studies?
Carbocisteine Syrup is considered identical to the previously authorised product with the same benefits and risks. No new studies have been provided for Carbocisteine Syrup, however, reference is made to the studies for Carbocisteine 250 mg/5 ml Adult Syrup.

What are the possible side effects of Carbocisteine Syrup?
For the full list of all side effects reported with this medicine, 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 behalf of someone else they care for, directly via the Yellow Card scheme at www.mhra.gov.uk/yellowcard or search for 'MHRA Yellow Card' online. By reporting side effects, patients can help provide more information on the safety of this medicine.

Carbocisteine Syrup is considered to be identical to the previously authorised product/products with the same benefits and risks.

Why was Carbocisteine Syrup approved?
The MHRA decided that the benefits of Carbocisteine Syrup 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 Carbocisteine Syrup?
A Risk Management Plan (RMP) has been developed to ensure that Carbocisteine Syrup is used as safely as possible. Based on this plan, safety information has been included in the SmPC and the PIL, 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 and reviewed continuously.

Other information about Carbocisteine Syrup
A Marketing Authorisation was granted in the United Kingdom (UK) on 30 March 2021.

The full PAR for Carbocisteine Syrup follows this summary.

This summary was last updated in May 2021.

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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 Carbocisteine 250 mg/5 ml Adult Syrup (PL 25298/0266) could be approved.

The product is approved for the following indication:
Carbocisteine is a mucolytic agent for the adjunctive therapy of respiratory tract disorders characterised by excessive, viscous mucus, including chronic obstructive airways disease.

This medicine is not recommended for use in children and adolescents under the age of 18 years due to the alcohol content.

Carbocisteine (S-carboxymethyl L-cysteine) has been shown in normal and bronchitic animal models to affect the nature and amount of mucus glycoprotein which is secreted by the respiratory tract. An increase in the acid:neutral glycoprotein ratio of the mucus and a transformation of serous cells to mucus cells is known to be the initial response to irritation and will normally be followed by hypersecretion. The administration of carbocisteine to animals exposed to irritants indicates that the glycoprotein that is secreted remains normal; administration after exposure indicates that return to the normal state is accelerated. Studies in humans have demonstrated that carbocisteine reduces goblet cell hyperplasia. carbocisteine can therefore be demonstrated to have a role in the management of disorders characterised by abnormal mucus.

This a national abridged application submitted 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 cross-reference product Carbocisteine 250 mg/5 ml Adult Syrup (PL 25298/0082) currently held by Brown & Burk UK Limited, which was originally granted in the UK to the Marketing Authorisation Holder on 01/02/2019.

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 versionof 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 (UK) on 30 March 2021.

II. EXPERT REPORT

The applicant cross-refers to the data for Carbocisteine 250 mg/5 ml Adult Syrup (PL 25298/0082; Brown & Burk UK Limited) which this application is claimed to be identical. This is acceptable.

III. ASSESSOR'S COMMENTS ON THE PRODUCT INFORMATION

SUMMARY OF PRODUCT CHARACTERITICS (SmPC)

The SmPC is in line with that for Carbocisteine 250 mg/5 ml Adult Syrup (PL 25298/0082), dated 02/2019.

PATIENT INFORMATION LEAFLET

A leaflet mock-up has been provided which has been aligned with that for Carbocisteine 250 mg/5 ml Adult Syrup (PL 25298/0082), dated for 02/2019. The user test report submitted for PL 25298/0082 has been provided.

LABEL

Label mock-ups have been provided.

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

Carbocisteine 250 mg/5 ml Adult Syrup is available in Type III amber glass bottles closed with a polypropylene cap equipped with a low density polyethylene plug/seal. A polypropylene measuring cup is supplied with each bottle. The medicinal product is available in pack sizes of 200 ml, 250 ml, 300 ml bottles. Not all pack sizes may be marketed.

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

The proposed shelf life of the product is 36 months for the unopened bottle with the recommended storage conditions 'Do not store above 25 °C. Store in the original container and keep the bottle in outer carton in order to protect from light.' The in use shelf-life is 15 days after first opening the bottle.

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

Legal status

Prescription only medicine (POM).

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 composition
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 (GMO).

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 full colour mock-up of the Patient Information Leaflet (PIL) has been provided with the application in accordance with the requirements of Regulation 267 of The Human Medicines Regulations 2012, as amended (previously article 61(1) of Council Directive 2001/83/EC).

The PIL has been evaluated via a user consultation with target patient groups in accordance with the requirements of Regulation 260(3) of The Human Medicines Regulations 2012, as amended (previously Article 59(3) of Council Directive 2001/83/EC) on the basis of a bridging report making reference to Carbocisteine 250 mg/5 ml Adult Syrup(PL 25298/0082; Brown & Burk UK Limited). The bridging report submitted by the applicant is acceptable.

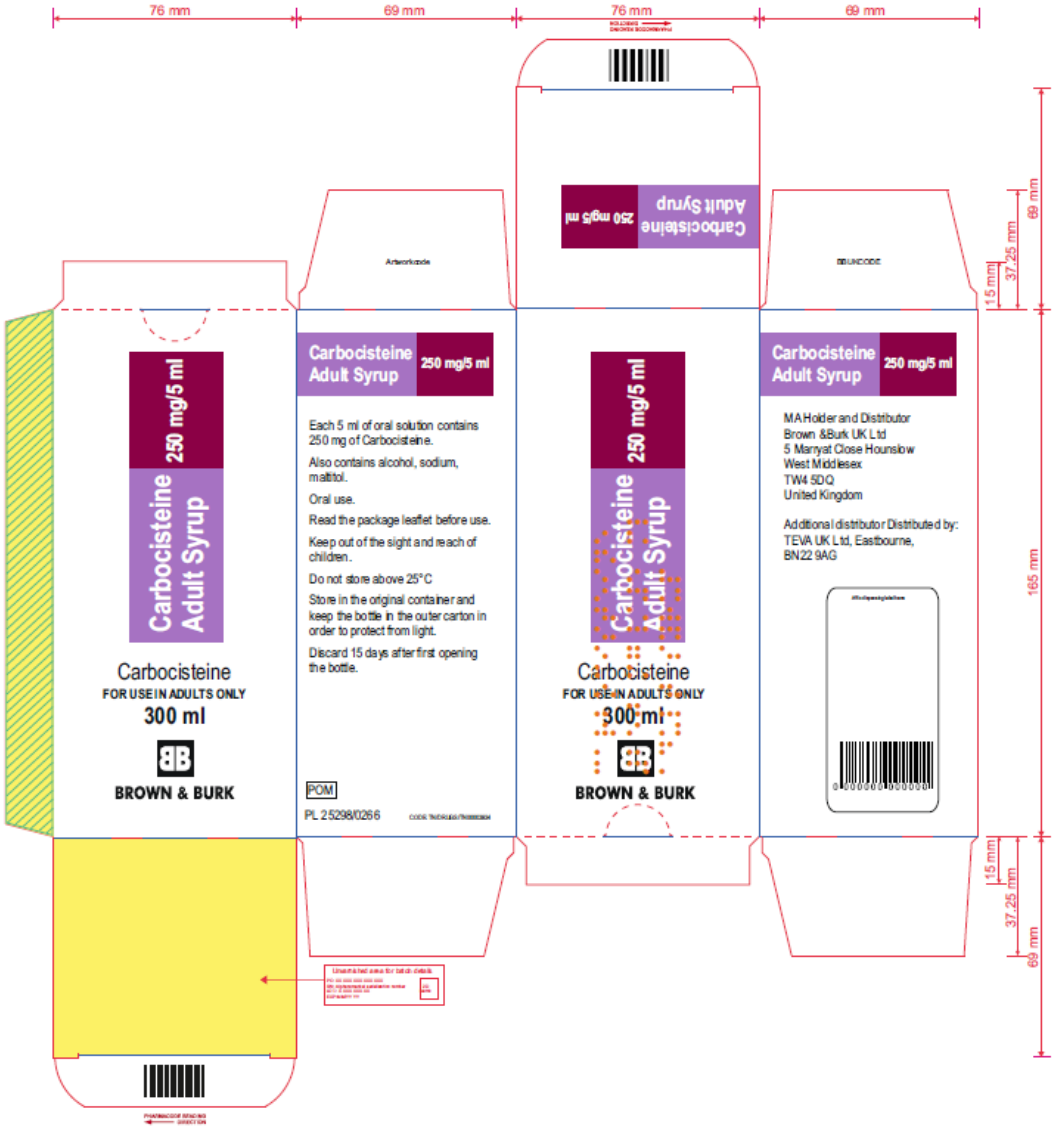
IX. OVERALL CONCLUSION, BENEFIT/RISK AND RECOMMENDATION
The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. The applicant’s product is identical to the cross-reference product. The benefit/risk balance is, therefore, considered to be the same as for the cross-reference product

and positive.

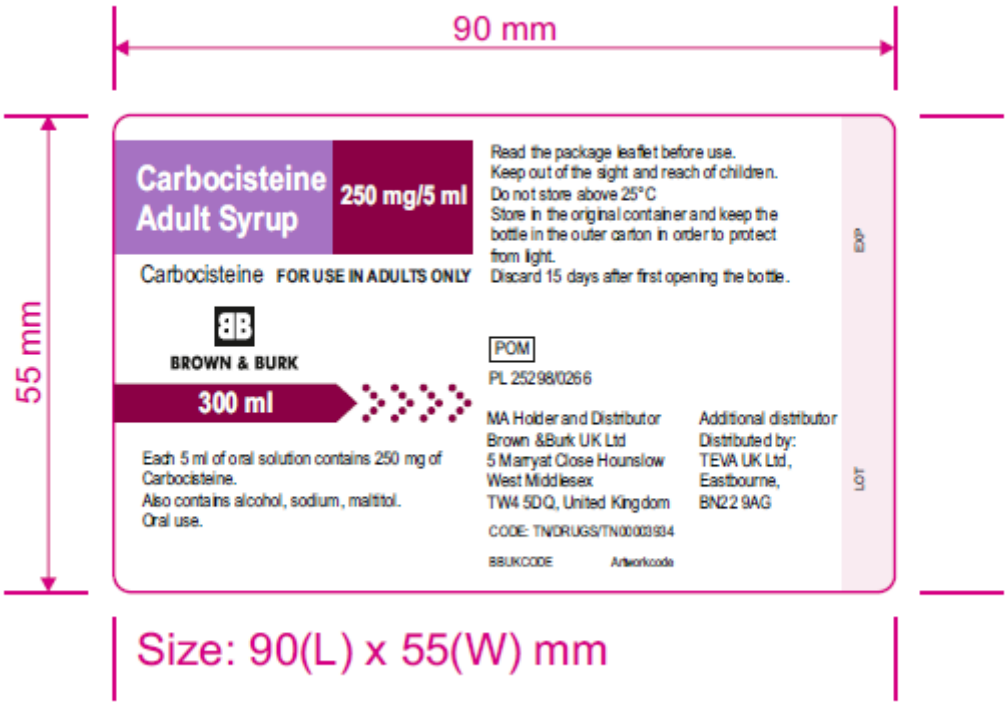
The Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and labelling are satisfactory, in line with current guidelines and consistent with the cross-reference product.

In accordance with Regulation 203(2) of The Human Medicines Regulation 2012, as amended, the current approved UK versions of the SmPC and PIL for this product is available on the MHRA website.

Representative copies of the labels at the time of licensing are provided below.



Carbocisteine
#250 mg/#5 ml
Adult Syrup



Size: 90(L) x 55(W) mm

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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**