Medicines & Healthcare products Regulatory Agency

MHRA Regulating Medicines and Medical Devices

Public Assessment Report

UKPAR

Carbocisteine 375 mg hard Capsules

(Carbocisteine)

UK Licence No: PL 42357/0270

Amneal Pharma Europe Limited.

LAY SUMMARY

Carbocisteine 375 mg hard Capsules
(carbocisteine)

This is a summary of the Public Assessment Report (PAR) for Carbocisteine 375 mg hard Capsules (PL 42357/0270). It explains how Carbocisteine 375 mg hard Capsules 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 Carbocisteine 375 mg hard Capsules.

For practical information about using Carbocisteine 375 mg hard Capsules patients should read the package leaflet or contact their doctor or pharmacist.

What are Carbocisteine 375 mg hard Capsules and what are they used for?
This medicine is used for problems with the breathing passages (respiratory tract). These problems happen when too much mucus is made or the mucus is too sticky.

This application is the same as Carbocisteine Chanelle Medical 375 mg hard Capsules (PL 13931/0113) which is already authorised.

The company (Chanelle Medical) that makes Carbocisteine Chanelle Medical 375 mg hard Capsules (PL 13931/0113) has agreed that its scientific data can be used as a basis for the grant of an identical licence for Carbocisteine 375 mg hard Capsules.

How do Carbocisteine 375 mg hard Capsules work?
This medicine contains the active ingredient carbocisteine. This belongs to a group of medicines called "mucolytics". It works by making mucus (phlegm) less sticky. This makes the mucus easier to cough up.

How are Carbocisteine 375 mg hard Capsules used?
The pharmaceutical form of this medicine is a hard capsule, and the route of administration is oral (by mouth).

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

The recommended dose for adults (including the elderly) is two capsules, 3 times each day. If the patient's symptoms improve, their dose should be lowered to one capsule, 4 times each day.

Carbocisteine 375 mg hard Capsules are not recommended for children.

This medicine can only be obtained with a prescription.

For further information on how Carbocisteine 375 mg hard Capsules are used, refer to the package leaflet and Summary of Product Characteristics available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

What benefits of Carbocisteine 375 mg hard Capsules have been shown in studies?
Carbocisteine 375 mg hard Capsules is considered identical to previously authorised Carbocisteine Chanelle Medical 375 mg hard Capsules (PL 13931/0113) with the same benefits and risks. So, no new studies have been provided for Carbocisteine 375 mg hard Capsules, but reference is made to the studies for Carbocisteine Chanelle Medical 375 mg hard Capsules (PL 13931/0113).

What are the possible side effects from Carbocisteine 375 mg hard Capsules?

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Carbocisteine 375 mg hard Capsules is considered to be identical to the previously authorised application for Carbocisteine Chanelle Medical 375 mg hard Capsules (PL 13931/0113) with the same benefits and risks.

For a full list of all the side effects reported with Carbocisteine 375 mg hard Capsules see section 4 of the package leaflet, available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

For the full list of restrictions, see the package leaflet.

Why was Carbocisteine 375 mg hard Capsules approved?

The MHRA decided that the benefits of Carbocisteine 375 mg hard Capsules are greater than the risks and recommended that they are approved for use.

What measures are being taken to ensure the safe and effective use of Carbocisteine 375 mg hard Capsules?

A Risk Management Plan has been developed to ensure that Carbocisteine 375 mg hard Capsules are 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 Carbocisteine 375 mg hard Capsules 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.

Other information about Carbocisteine 375 mg hard Capsules

A Marketing Authorisation were granted in the UK on 09 October 2018.

The full PAR for Carbocisteine 375 mg hard Capsules follows this summary.

For more information about treatment with Carbocisteine 375 mg hard Capsules read the package leaflet or contact your doctor or pharmacist.

This summary was last updated in October 2018.

TABLE OF CONTENTS

I INTRODUCTION

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Amneal Pharma Europe Limited, a Marketing Authorisation for the medicinal product Carbocisteine 375 mg hard Capsules (PL 42357/0270) on 09 October 2018.

This product is a prescription only medicine (POM) and is a mucolytic agent for the adjunctive therapy of respiratory tract disorders characterised by excessive, viscous mucus, including chronic obstructive airways disease.

This application was submitted as a simple abridged (informed consent) application according to Article 10c of Directive 2001/83/EC, as amended.

The application cross-refers to the medicinal product Carbocisteine Chanelle Medical 375 mg hard Capsules which was first authorised to the marketing authorisation holder (MAH) Chanelle Medical (PL 13931/0113) on 23 November 2016.

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.

No new data were submitted nor were necessary to be submitted for this application, as the data are identical to the data for the previously granted cross-referenced product.

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

II QUALITY ASPECTS

II.1 Introduction

This is an abridged application for Carbocisteine 375 mg hard Capsules (PL 42357/0270) submitted under Article 10c of Directive 2001/83/EC, as amended.

The application cross-refers to the medicinal product Carbocisteine Chanelle Medical 375 mg hard Capsules which was first authorised to the marketing authorisation holder (MAH) Chanelle Medical (PL 13931/0113) on 23 November 2016. The application is considered valid.

II.2. Drug Substance

Drug substance specification

The proposed drug substance specification is consistent with the details registered for the cross-reference product.

II.3. Medicinal Product

Name

The proposed product name for this application is Carbocisteine 375 mg hard Capsules. The product has been named in line with current requirements.

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

Each capsule contains 375 mg of carbocisteine. The finished product is packaged into blister strips formed from PVC/PVDC and aluminium lidding foil or PVC/PE.EVOH.PE/PCTFE and aluminium lidding foil in a pack size of 120 capsules.

The proposed shelf life of the unopened product is 24 months with the storage conditions ‘Store below 30°C.’

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

Legal status

Prescription only medicine (POM).

Marketing Authorisation Holder/Contact Persons/Company

Amneal Pharma Europe Limited, 70 Sir John Rogerson’s Quay, Dublin 2, Ireland.

The Qualified Person (QP) responsible for pharmacovigilance is stated and a satisfactory CV has been provided.

Manufacturers

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

Qualitative and quantitative composition

The proposed composition is consistent with the details registered for the cross-reference product.

Manufacturing process

The proposed manufacturing processes are consistent with the details registered for the cross-reference product and the maximum batch size is stated.

Finished product/shelf-life specification
The proposed finished product specification is in line with the details registered for the cross-reference products.

TSE Compliance
With the exception of gelatin, none of the excipients contain materials of animal or human origin. The suppliers of gelatin have provided Certificates of Suitability from the European Directorate for the Quality of Medicines (EDQM) to show that they are manufactured in-line with current European guidelines concerning the minimising of risk of transmission of Bovine Spongiform Encephalopathy/transmissible Spongiform Encephalopathies (BSE/TSE).

Bioequivalence
No bioequivalence data are required to support this simple abridged application because the proposed product is manufactured to the same formula utilising the same processes as the cross-reference product, Carbocisteine Chanelle Medical 375 mg hard Capsules (PL 13931/0113).

Expert Report
The applicant cross-refers to the data for Carbocisteine Chanelle Medical 375 mg hard Capsules (PL 13931/0113) to which this application is claimed to be identical. This is acceptable.

Product Name and Appearance
See Section II.3 ‘Medicinal Product; Name’ for details of the proposed product name. The appearance of the product is identical to that of the cross-reference product.

II.4 Discussion on chemical, pharmaceutical and biological aspects

The data submitted with this application is acceptable. The grant of a Marketing Authorisation is recommended.

III NON-CLINICAL ASPECTS

Introduction

As this is an abridged application submitted under Article 10c of Directive 2001/83/EC, as amended, no new non-clinical data have been supplied and none are required.

Ecotoxicity/environmental risk assessment (ERA)

Suitable justification has been provided for non-submission of an Environmental Risk Assessment. As the application is an identical version of an already authorised product, it is not expected that environmental exposure will increase following approval of the Marketing Authorisation for the proposed product.

Discussion on the non-clinical aspects

The grant of a Marketing Authorisation is recommended.

IV CLINICAL ASPECTS

Introduction

As this is an abridged application submitted under Article 10c of Directive 2001/83/EC, as amended, no new clinical data have been supplied and none are required.

Risk Management Plan (RMP)

The Applicant has submitted a risk management plan, in accordance with the requirements of Directive 2001/83/EC as amended.

There are no differences from the reference product in terms of proposed uses, maximum pack size / strength or pharmaceutical form / formulation that would have any implications for safety.

In line with the reference product, the applicant proposes only routine pharmacovigilance and routine risk minimisation measures for all safety concerns (labelling in the SmPC and the PIL). This is agreed. The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing Authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the MHRA;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

If the dates for submission of a PSUR and the update of a RMP coincide, they can be submitted at the same time, but via different procedures.

Discussion on the clinical aspects

The grant of a Marketing Authorisation is recommended.

V User consultation

The package leaflet has been evaluated via a user consultation study in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC. The language used for the purpose of user testing the PIL was English.

The results show that the package leaflet meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

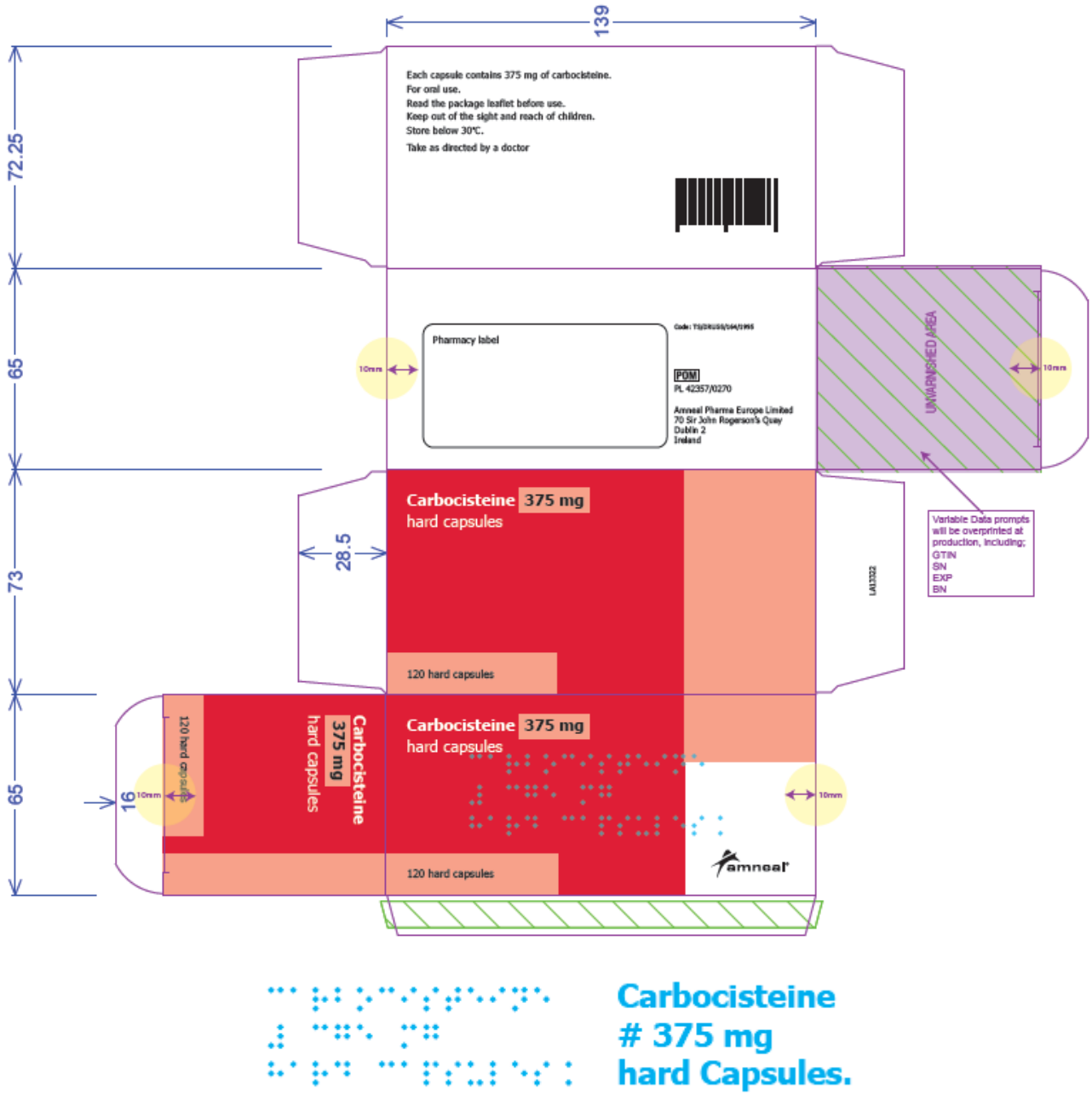
VI Overall conclusion, benefit/risk assessment and recommendation

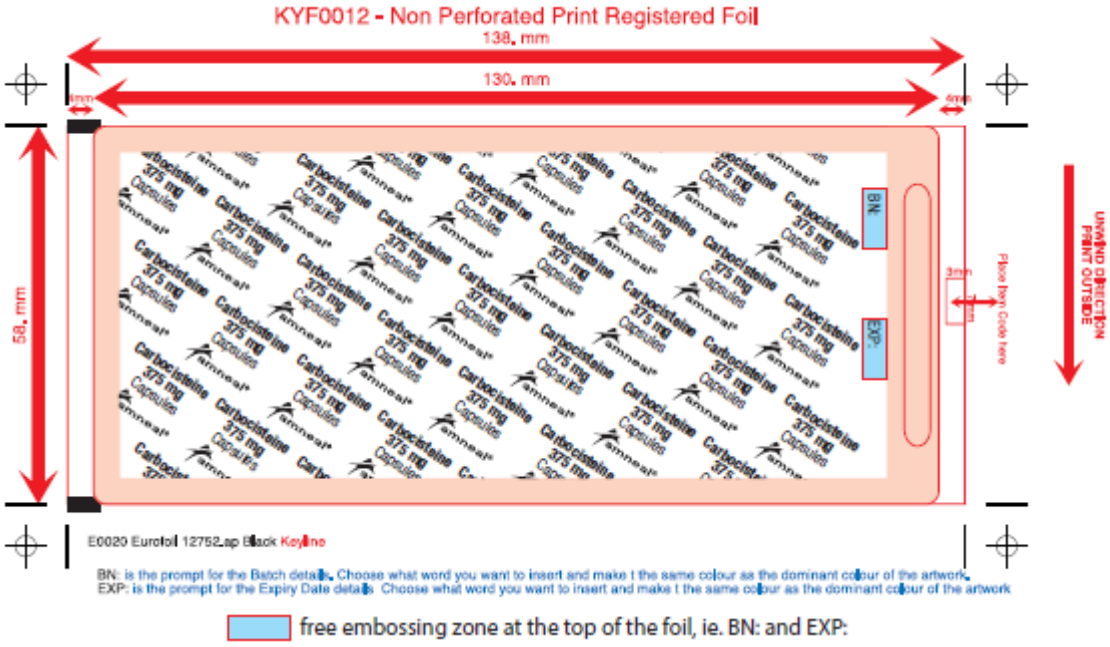
The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. The applicant's product is identical to the cross-reference product. Extensive clinical experience with carbocisteine is considered to have demonstrated the therapeutic value of the compound. The benefit/risk balance is, therefore, considered to be positive.

Summaries of Product Characteristics (SmPC), Patient Information Leaflets (PIL) and Labels
The SmPC and PIL are consistent with the details registered for the cross-reference products.

In accordance with Directive 2010/84/EU the Summaries of Product Characteristics (SmPCs) and Patient Information Leaflets (PILs) for products granted Marketing Authorisations at a national level are available on the MHRA website.

The approved labelling for this medicine is presented below:




KYF0012 - Non Perforated Print Registered Foil
138. mm
130. mm
4mm
4mm
58. mm
BN
EXP
3mm
7mm
Place Pen Circle Here
UNWIND DIRECTION
PRINT OUTSIDE
E0020 Eurofoil 12752.ai Black Keyline
BN: is the prompt for the Batch details. Choose what word you want to insert and make t the same colour as the dominant colour of the artwork.
EXP: is the prompt for the Expiry Date details Choose what word you want to insert and make t the same colour as the dominant colour of the artwork
free embossing zone at the top of the foil, ie. BN: and EXP:

Annex 1

Table of content of the PAR update

Steps taken after the initial procedure with an influence on the Public Assessment Report (Type II variations, PSURs, commitments)

Scope	**Procedure number**	**Product information affected**	**Date of start of the procedure**	**Date of end of procedure**	**Approval/ non approval**	**Assessment report attached Y/N (version)**