Medicines & Healthcare products
Regulatory Agency

Public Assessment Report

National Procedure

Sevelamer carbonate 800 mg film-coated tablets

sevelamer carbonate

PL 35533/0156

Aspire Pharma Ltd

LAY SUMMARY

Sevelamer carbonate 800 mg film-coated tablets
sevelamer carbonate

This is a summary of the Public Assessment Report (PAR) for Sevelamer carbonate 800 mg film-coated tablets. 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 Sevelamer carbonate tablets in this lay summary for ease of reading.

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

What is Sevelamer carbonate tablets and what is it used for?
This application is for a hybrid medicine. This means that the medicine is similar to a reference medicine already authorised, called Renvela 800 mg, film-coated tablets.

This medicine is used to control hyperphosphataemia (high blood phosphate levels) in:

- adult patients on dialysis (a blood clearance technique). It can be used in patients undergoing haemodialysis (using a blood filtration machine) or peritoneal dialysis (where fluid is pumped into the abdomen and an internal body membrane filters the blood);
- patients with chronic (long-term) kidney disease who are not on dialysis and have a serum (blood) phosphorus level equal to or above 1.78 mmol/l.

This medicine should be used with other treatments such as calcium supplements and vitamin D to prevent the development of bone disease.

How does Sevelamer carbonate tablets work?
Increased levels of serum phosphorus can lead to hard deposits in your body called calcification. These deposits can stiffen your blood vessels and make it harder for blood to be pumped around the body. Increased serum phosphorus can also lead to itchy skin, red eyes, bone pain and fractures.

This medicine contains sevelamer carbonate as the active substance. It binds phosphate from food in the digestive tract and so reduces serum phosphorus levels in the blood.

How is Sevelamer carbonate tablets used?
The pharmaceutical form of this medicine is tablets and the route of administration is oral (by mouth)

This medicine must be taken as prescribed by the patient's doctor. The doctor will base the dose on the patient's serum phosphorus level.

The recommended starting dose of sevelamer carbonate tablets for adults and elderly is one to two tablets of 800mg with each meal, 3 times a day.

This medicine should be taken after a meal or with food.

The tablets must be swallowed whole. The tablets must not be crushed, chewed or broken into pieces.

Initially, the patient's doctor will check the levels of phosphorus in the blood every 2-4 weeks and may adjust the dose of sevelamer carbonate when necessary to reach an adequate phosphate level.

The patient should follow the diet prescribed by their doctor.

For further information on how Sevelamer carbonate tablets 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 this 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 Sevelamer carbonate tablets have been shown in studies?
No additional studies were needed as Sevelamer carbonate tablets contain the same active substance as the reference medicine, and satisfactory data to justify the differences have been provided.

What are the possible side effects of Sevelamer carbonate tablets?
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 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.

Because Sevelamer carbonate tablets is a hybrid medicine and is therapeutically equivalent to the reference medicine, its benefits and possible side effects are taken as being the same as the reference medicine.

Why was Sevelamer carbonate tablets approved?
It was concluded that Sevelamer carbonate tablets has been shown to be therapeutically equivalent to the reference medicine. Therefore, the MHRA decided that, as for the reference medicine, the benefits are greater than the risks and recommended that it can be approved for use.

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

The following safety concerns have been recognised for Sevelamer carbonate tablets:

Summary of safety concerns	
Important identified risks	• Intestinal perforation, obstruction and ileus
Important potential risks	• Serious gastrointestinal disorders associated with sevelamer crystals • Hypersensitivity reactions, including angioedema and anaphylactic reactions • Difficulty swallowing tablets • Vitamin deficiency • Drug interactions with levothyroxine, ciprofloxacin, immunosuppressants, antiarrhythmics, anticonvulsants and antifungal drugs
Missing information	• Use in pregnancy and lactation • Use in hepatic impairment and in immunocompromised patients

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 Sevelamer carbonate tablets 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 Sevelamer carbonate tablets
A marketing authorisation for Sevelamer carbonate tablets was granted in the United Kingdom (UK) on 29 April 2024.

The full PAR for Sevelamer carbonate tablets follows this summary.

This summary was last updated in June 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 Sevelamer carbonate 800 mg film-coated tablets(PL 35533/0156) could be approved.

The product is approved for the following indications:
Sevelamer carbonate is indicated for the control of hyperphosphataemia in adult patients receiving haemodialysis or peritoneal dialysis.

Sevelamer carbonate is also indicated for the control of hyperphosphataemia in adult patients with chronic kidney disease (CKD) not on dialysis with serum phosphorus ≥ 1.78 mmol/l.

Sevelamer carbonate should be used within the context of a multiple therapeutic approach, which could include calcium supplement,1,25-dihydroxy Vitamin D3 or one of its analogues to control the development of renal bone disease.

Mechanism of action
Sevelamer carbonate contains sevelamer, a non-absorbed phosphate binding crosslinked polymer, free of metal and calcium. Sevelamer contains multiple amines separated by one carbon from the polymer backbone which become protonated in the stomach. These protonated amines bind negatively charged ions such as dietary phosphate in the intestine.

This application was approved under Regulation 52B of The Human Medicines Regulation 2012, as amended (previously Article 10(3) of Directive 2001/83/EC, as amended), claiming to be a hybrid medicinal product of a suitable originator product, Renvela 800 mg, film-coated tablets (PLGB 04425/0785) that has been licensed for a suitable time, in line with the legal requirements.

A biowaiver was submitted with this application which was accepted. No bioequivalence or therapeutic equivalence studies were required and none were provided with this application.

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 29 April 2024.

II QUALITY ASPECTS

II.1 Introduction

What this medicine contains

The active substance is sevelamer carbonate. Each film-coated tablet contains 800mg of sevelamer carbonate. The other ingredients are colloidal silicon dioxide, pregelatinised starch, magnesium stearate, hypromellose, acetylated monoglycerides and blue printing ink.

The contents of the pack

The tablets are packed in high density polyethylene bottles with a polypropylene cap and an induction seal. Pack sizes: Each carton contains a bottle of 30, 180, 200 or 210 tablets. Not all pack sizes may be marketed.

Satisfactory specifications and Certificates of Analysis have been provided for all packaging components. All primary packaging complies with the current regulations concerning materials in contact with food.

II.2 ACTIVE SUBSTANCE

rINN: sevelamer carbonate

Chemical Name:

Poly (Allylamine-co-N,N'-diallyl-1,3-diamino-2-hydroxypropane) Carb

Molecular Formula:

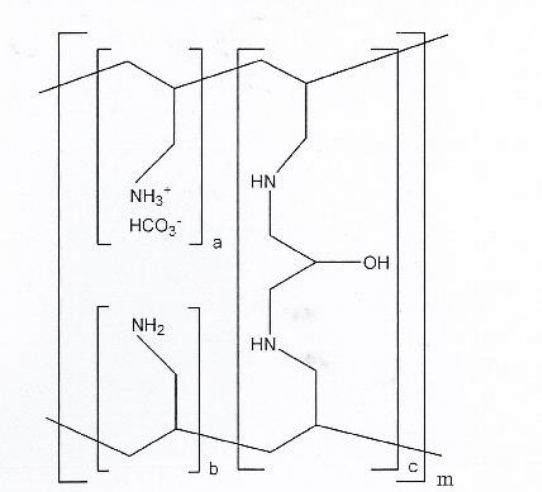
$[(C_3H_7N)_{(a+b)}(C_9H_{18}N_2O)_c \cdot a\ H_2CO_3]_m$ Where (a+b):c=9:1

Assuming 11 amino groups as the starting unit, the "c" represents the cross-linking unit. Total 0.09 equivalents of ECH is used in the cross-linking reaction. Therefore "c x 0.09 = 0.99 =1 (Note, "c" group cross-linked 2 amine units).

The "a" and "b" represent the number of primary amine unit, which means the non-linking amine unit, and a + b = 11 – 2 = 9.

Therefore a+b: c =9:1

Chemical Structure:



a,b = number of primary amine groups a + b = 9

c = number of crosslinking groups c = 1

m = large number to indicate extended polymer network groups

Molecular Weight:

Sevelamer Carbonate as a cross-linked polymer, the molecular weight range is 1.39 x - 2.09×10^{16}.

Appearance: white to off-white powder
Solubility: Water insoluble compound

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

Appropriate proof-of-structure data have been supplied for the active substance. All potential known impurities have been identified and characterised.

An appropriate specification is provided for the active substance. 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 all working standards.

Suitable specifications have been provided for all packaging used. The primary packaging has been shown to comply with current regulations concerning materials in contact with food.

Appropriate stability data have been generated supporting a suitable retest period when stored in the proposed packaging.

II.3 DRUG PRODUCT

Pharmaceutical development

A satisfactory account of the pharmaceutical development has been provided.

Comparative *in vitro* disintegration (in place of dissolution studies) and impurity profiles have been provided for the proposed and reference products.

All excipients comply with either their respective European/national monographs, or a suitable in-house specification. Satisfactory Certificates of Analysis have been provided for all excipients.

No excipients of animal or human origin are used in the finished product.

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

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

Satisfactory batch formulation data have been provided for the manufacture of the product, along with an appropriate account of the manufacturing process. The manufacturing process has been validated and has shown satisfactory results.

Finished Product Specifications
The finished product specifications at release and shelf-life are satisfactory. The test methods have been described and adequately validated. Batch data have been provided that comply with the release specifications. Certificates of Analysis have been provided for any working standards used.

Stability
Finished product stability studies have been conducted in accordance with current guidelines, using batches of the finished product stored in the packaging proposed for marketing. Based on the results, a shelf-life of 30 months, without any special storage conditions, is acceptable.

Suitable post approval stability commitments have been provided to continue stability testing on batches of finished product.

II.4 Discussion on chemical, pharmaceutical and biological aspects
The grant of a marketing authorisation is recommended.

III NON-CLINICAL ASPECTS

III.1 Introduction
As the pharmacodynamic, pharmacokinetic and toxicological properties of sevelamer carbonate is well-known, no new non-clinical studies are required, and none have been provided. An overview based on the literature review is, thus, appropriate.

III.2 Pharmacology
No new pharmacology data were provided and none were required for this application.

III.3 Pharmacokinetics
No new pharmacokinetic data were provided and none were required for this application.

III.4 Toxicology
No new toxicology data were provided and none were required for this application.

III.5 Ecotoxicity/Environmental Risk Assessment

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

III.6 Discussion on the non-clinical aspects

The grant of a marketing authorisation is recommended.

IV CLINICAL ASPECTS

IV.1 Introduction

In accordance with the regulatory requirements, the applicant has provided a suitable biowaiver. No bioequivalence or therapeutic equivalence studies have been submitted with this application.

IV. 2 Pharmacokinetics

No new pharmacokinetic data have been submitted for this application and none were required.

IV.3 Pharmacodynamics

No new pharmacodynamic data have been submitted for this application and none were required.

IV.4 Clinical efficacy

No new efficacy data have been submitted for this application and none were required.

IV.5 Clinical safety

No new safety data were submitted with this application and none were required. The safety profile for this product is considered to be the same as Renvela 800 mg, film-coated tablets.

IV.6 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.

IV.7 Discussion on the clinical aspects

The grant of a marketing authorisation is recommended for this application.

V USER CONSULTATION

A full colour mock-up of the Patient Information Leaflet (PIL) was provided with the application in accordance with legal requirements, including user consultation.

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. Extensive clinical experience with sevelamer carbonate is considered to have demonstrated the therapeutic value of the product.

The benefit/risk is, therefore, considered to be positive.

The Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and labelling are satisfactory and in line with current guidelines.

In accordance with legal requirements, the current approved versions 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**