Medicines & Healthcare products Regulatory Agency

MHRA

Public Assessment Report

National Procedure

Sodium Citrate 0.3M Oral Solution
Sodium citrate

PL 48259/0056

Northumbria Pharma Limited

LAY SUMMARY

Sodium Citrate 0.3M Oral Solution
(sodium citrate)

This is a summary of the Public Assessment Report (PAR) for Sodium Citrate 0.3M Oral Solution. It explains how 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 Sodium citrate oral solution in this lay summary for ease of reading.

For practical information about using Sodium citrate oral solution, patients should read the Patient Information Leaflet (PIL) or contact their doctor or pharmacist.

What is Sodium citrate oral solution and what is it/are they used for?
This application is for a generic medicine. This means that this medicine is the same as, and considered interchangeable with, a reference medicine already authorised, called Sodium Citrate 0.3M Oral Solution (PL 01883/0343).

Sodium citrate oral solution is used as an antacid prior to anaesthesia for caesarean section.

How does Sodium citrate oral solution work?
Sodium citrate oral solution is used as an antacid prior to anaesthesia for caesarean section.

How is Sodium citrate oral solution used?
The pharmaceutical form of this medicine is an oral solution, and the route of administration is oral (taken by mouth).

The patient's doctor or nurse will give the patient a whole container of Sodium citrate oral solution for them to drink.

For further information on how Sodium citrate oral solution 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 Sodium citrate oral solution have been shown in studies?
Sodium citrate oral solution is a generic medicine that fulfils criteria meaning that no additional studies are required. Sodium citrate oral solution has been considered a generic medicine of the reference medicine based on a comparison of their physical and chemical characteristics.

What are the possible side effects of Sodium citrate oral solution?
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.

As Sodium citrate oral solution is a generic medicine, its benefits and possible side effects are considered to be the same as for the reference medicine.

Why was Sodium citrate oral solution approved?
It was concluded that, Sodium citrate oral solution has been shown to be comparable 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 Sodium citrate oral solution?
As for all newly authorised medicines, a Risk Management Plan (RMP) has been developed for Sodium citrate oral solution. The RMP details the important risks of Sodium citrate oral solution, how these risks can be minimised, any uncertainties about Sodium citrate oral solution (missing information), and how more information will be obtained about the important risks and uncertainties.

There are no safety concerns associated with use of Sodium citrate oral solution.

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 Sodium citrate oral solution 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 Sodium citrate oral solution
A Marketing Authorisation for Sodium citrate oral solution was granted in the United Kingdom (UK) on 15 December 2022.

The full PAR for Sodium citrate oral solution follows this summary.

This summary was last updated in March 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 Sodium Citrate 0.3M Oral Solution (PL 48259/0056) could be approved.

The product is approved for the following indication:

- Non-particulate antacid for use by mouth prior to general anaesthesia for caesarean section.

The active substance, sodium citrate, has no relevant pharmacodynamic activity other than that caused by its alkalinity (e.g. its gastric acid neutralising capacity).

This application was approved under Regulation 51B of The Human Medicines Regulation 2012, as amended (previously Article 10(1) of Directive 2001/83/EC, as amended), as a generic medicine of a suitable originator medicinal product, Sodium Citrate 0.3M Oral Solution (PL 01883/0343), that has been licensed for a suitable time, in line with the legal requirements.

No new non-clinical studies were conducted, which is acceptable given that the application is for a generic medicinal product of a suitable reference product.

A biowaiver was submitted with this application, which was accepted. No bioequivalence study was required, and no new clinical studies 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 Marketing Authorisation for Sodium Citrate 0.3M Oral Solution wase granted in the United Kingdom (UK) on 15 December 2022.

II QUALITY ASPECTS

II.1 Introduction

This product contains 2.647 g of the active substance, sodium citrate, in each 30 ml of oral solution.

In addition to sodium citrate, this product also contains the excipients purified water and glycerol.

The finished product is packaged in amber terephthalate (PET) 30 ml bottles, each with a tamper evident high-density polyethylene (HDPE) cap with a low-density polyethylene (LDPE liner), in pack sizes of 1 or 10 bottles per carton.

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.

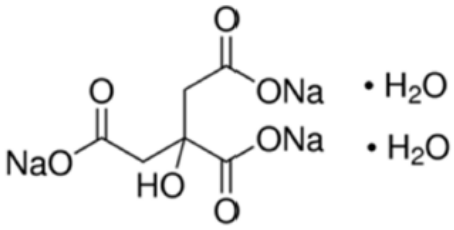
II.2 ACTIVE SUBSTANCE

rINN: Trisodium citrate dihydrate

Chemical Name: Trisodium 2-hydroxypropane-1,2,3-tricarboxylate dihydrate

Molecular Formula: $C_6H_5Na_3O_7,2H_2O$

Chemical Structure:



Molecular Weight: 294.1 g/mol

Appearance: White or almost white, crystalline powder or white or almost white, granular crystals, slightly deliquescent in moist air

Solubility: Freely soluble in water, practically insoluble in ethanol (96 per cent)

The information related to the active substance was provided in an Active Substance Master File (ASMF). The active substance is the subject of a Ph.Eur. monograph.

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 specification. 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 complies with the 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 was provided.

All excipients comply with their respective European/national Pharmacopoeia monographs. Satisfactory Certificates of Analysis were provided for all excipients.

No excipients of animal or human origin are used in the final 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 24 months, with the storage conditions 'Do not store above 25°C. Store in the original bottle in order to protect from light. Keep the bottle tightly closed.', is acceptable.

The product is for single use only. Any remaining solution should be discarded.

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 was recommended.

III NON-CLINICAL ASPECTS

III.1 Introduction
As the pharmacodynamic, pharmacokinetic and toxicological properties of sodium citrate 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
A suitable justification was provided for non-submission of an Environmental Risk Assessment. As the application is for generic version of an already authorised product, an increase in environmental exposure is not anticipated following approval of the marketing authorisation for the proposed product.

III.6 Discussion on the non-clinical aspects
The grant of a Marketing Authorisation was recommended.

IV CLINICAL ASPECTS

IV.1 Introduction

The clinical pharmacology, efficacy and safety of sodium citrate are well-known. According to the regulatory requirements, the applicant has provided a suitable biowaiver and a bioequivalence study is not required for this product. An overview based on a literature review is, thus, satisfactory.

IV. 2 Pharmacokinetics

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

IV.3 Pharmacodynamics

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

IV.4 Clinical efficacy

No new efficacy data were submitted with 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 Sodium Citrate 0.3M Oral Solution (PL 01883/0343).

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 was 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 was acceptable, and no new non-clinical or clinical safety concerns have been identified. Extensive clinical experience with sodium citrate is considered to have demonstrated the therapeutic value of the compound. The benefit/risk is, therefore, considered to be positive.

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

In accordance with legal requirements, the current approved UK 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, is 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**