IPAR

Public Assessment Report for a
Medicinal Product for Human Use

Scientific Discussion

Thamicarb 84mg/ml Oral Solution
Sodium hydrogen carbonate
PA22697/017/001

The Public Assessment Report reflects the scientific conclusion reached by the Health Products Regulatory Authority (HPRA) at the end of the evaluation process and provides a summary of the grounds for approval of a marketing authorisation for a specific medicinal product for human use. It is made available by the HPRA for information to the public, after deletion of commercially sensitive information. The legal basis for its creation and availability is contained in Article 21 of Directive 2001/83/EC, as amended. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the medicinal product for marketing in Ireland.

CONTENTS

I. INTRODUCTION

This product was initially authorised under procedure number UK/H/5407/001/DC with the UK as RMS. The responsibility of RMS was transferred to Ireland on 01/08/2019 under procedure number IE/H/1033/001/DC.
Please note the following detail for the product in IE:
Marketing Authorisation Number: [PA22697/017/001
Marketing Authorisation Holder: [ISYRI Limited, t/a Thame Laboratories

The current Summary of Product Characteristics (SmPC) for this medicinal product is available on the HPRA website at www.hpra.ie.

The UK public assessment report published at the time of the initial marketing authorisation is provided herein.

Based on the review of the data on quality, safety and efficacy, the Reference Member State (RMS) and Concerned Member State (CMS) considered that the application for Thamicarb 84 mg/ml Oral Solution (PL 39307/0005; UK/H/5407/001/DC) for the treatment of hyperacidity, dyspepsia and symptomatic relief of heartburn and peptic ulceration, is approvable.

This application was submitted under Article 10a of Directive 2001/83/EC, as amended, claiming to be an application for a product containing an active substance of well-established use.

With the UK as the RMS in this Decentralised Procedure (UK/H/5407/001/DC), Syri Limited, trading as Thame Laboratories applied for the Marketing Authorisation for Thamicarb 84 mg/ml Oral Solution in the Republic of Ireland.

Sodium bicarbonate is used as an antacid in relief of the symptoms of dyspepsia, heartburn and indigestion caused by excess gastrointestinal acid. Sodium bicarbonate causes neutralisation of gastric acid with the production of carbon dioxide.

Bibliographic data on sodium bicarbonate have been submitted to support this application. No new non-clinical or clinical studies were conducted for this application, which is acceptable given that this is a bibliographic application for a product containing an active ingredient of well-established use.

The RMS has been assured that acceptable standards of GMP are in place for this product type at all sites responsible for the manufacture and assembly of this product.

For manufacturing sites within the Community, the RMS has accepted copies of current manufacturer authorisations issued by inspection services of the competent authorities as certification that acceptable standards of GMP are in place at those sites.

All involved Member States agreed to grant a Marketing Authorisation for the above product at the end of the procedure (Day 210 – 28th August 2014). After a subsequent national phase, the UK granted a Marketing Authorisation for this product on 29th September 2014 (PL 39307/0005).

The legal status of this product was updated to prescription only (POM) during variation PL 39307/0005 – 0025; UK/H/5407/II/017/G.

II. QUALITY ASPECTS

II QUALITY ASPECTS

II.1 Introduction

Each 1 ml of solution contains 84mg of sodium bicarbonate (equivalent to 1mmol/ml sodium and bicarbonate).

In addition to sodium bicarbonate this product also contains purified water.

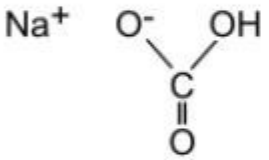
The finished product is packaged in an amber glass bottle which has a white tamper-evident child-resistant polypropylene cap with HDPE-EPE wadding, containing 100 ml or 500 ml of solution.

A dosing device is also included in the packaging which consists of a 20ml white polypropylene oral syringe with 1ml graduation marks and LDPE syringe adaptor.

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

II.2 ACTIVE SUBSTANCE

INN: Sodium bicarbonate
Chemical Names: Sodium bicarbonate
Structure:



Molecular formula: $NaHCO_3$
Molecular weight: 84.0 g/mol
Physical form: White or almost white, crystalline powder.
Solubility: sparingly soluble in water and practically insoluble in ethanol.

Sodium bicarbonate is the subject of a European Pharmacopoeia monograph.

All aspects of the manufacture and control of the active substance sodium bicarbonate are covered by a European Directorate for the Quality of Medicines and Healthcare (EDQM) Certificate of Suitability.

II.3 DRUG PRODUCT

Pharmaceutical development
The objective of the development programme was to formulate a safe, efficacious, stable oral solution containing 84 mg/ml of sodium bicarbonate.

Suitable pharmaceutical development data have been provided for this application.

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.

A satisfactory batch formula has 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 Specification
The finished product specification is satisfactory. The test methods have been described and adequately validated. Batch data have been provided that comply with the release specification.

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 12 months with storage conditions "Do not store above 25°C", "Do not refrigerate or freeze", "Do not use if crystals are observed in the product" and "Keep out of the sight and reach of children" have been set. The proposed in-use shelf life storage recommendations are "Discard your medicine 3 days after first opening" (100 ml bottles) and "Discard your medicine 7 days after first opening" (500 ml bottles). The proposed shelf lives and the storage conditions are satisfactory.

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 NON-CLINICAL ASPECTS

III.1 Introduction
The pharmacological, pharmacokinetic and toxicological properties of sodium bicarbonate are well-known.

No new non-clinical data have been supplied with this application and none are required for applications of this type. The non-clinical expert report has been written by an appropriately qualified person and is a suitable summary of the non-clinical aspects of the dossier.

There are no objections to the approval of this product from a non-clinical point of view.

III.2 Pharmacology
Not applicable for this product type. Refer to section 'III.1; Introduction' detailed above.

III.3 Pharmacokinetics
Not applicable for this product type. Refer to section 'III.1; Introduction' detailed above.

III.4 Toxicology
Not applicable for this product type. Refer to section 'III.1; Introduction' detailed above.

III.5 Ecotoxicity/Environmental Risk Assessment
Suitable justification has been provided for non-submission of an Environmental Risk Assessment. As the application is for a product containing an active substance of well-established use that will be used in place of existing products, 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 is recommended.

IV. CLINICAL ASPECTS

IV CLINICAL ASPECTS

IV.1 Introduction

The pharmacology, pharmacodynamics and pharmacokinetics of sodium bicarbonate are well known. No new clinical pharmacology, pharmacodynamics and pharmacokinetics data have been submitted and none are required for applications of this type. The clinical pharmacology of sodium bicarbonate is well-known.

IV. 2 Pharmacokinetics

After oral administration, sodium bicarbonate acts very rapidly and neutralises gastric acid. The un-neutralised sodium bicarbonate rapidly goes into the small intestine where it is absorbed. Following oral administration, sodium bicarbonate is usually excreted within 3-4 hours. Elimination of sodium bicarbonate occurs principally via the kidney.

No new safety data were supplied or required for this bibliographic application. Safety is adequately reviewed in the clinical overview. The safety profile of sodium bicarbonate is well-known.

IV.3 Pharmacodynamics

Sodium bicarbonate has a potent antacid action. Once it reaches the stomach sodium bicarbonate rapidly reacts with hydrochloric acid to form sodium chloride, carbon dioxide and water. Excess bicarbonate that does not neutralise gastric acid rapidly empties into the small intestine and is absorbed.

Sodium bicarbonate is an alkalinising agent which dissociates to provide bicarbonate ion. Bicarbonate is the conjugate base component of the principal extracellular buffer in the body, the bicarbonate: carbonic acid buffer. At a given pH, the ratio of bicarbonate: carbonic acid is constant.

IV.4 Clinical efficacy

No new efficacy data have been submitted and none are required for applications of this type. The clinical efficacy of sodium bicarbonate is well-established. Efficacy is adequately reviewed in the clinical overview.

The applicant has provided a review of a number of publications. No clinical studies with sodium bicarbonate oral solution have been conducted by the applicant.

Sodium bicarbonate is quick acting and widely used as antacid in the form of reconstituted powder or granules (publication review). Sodium bicarbonate is also a constituent of many proprietary preparations that are used to relieve hyperacidity, dyspepsia and symptomatic

relief of heartburn and peptic ulceration. Such formulations are alginate raft forming oral suspensions containing sodium alginate, sodium bicarbonate and calcium carbonate (publication reviews) and Zegerid powder containing omeprazole with sodium bicarbonate (publication reviews).

IV.6 Risk Management Plan (RMP)

The Applicant has submitted an RMP, in accordance with the requirements of Directive 2001/83/EC, 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

No new clinical data were submitted, and none were required for an application of this type.

The published literature supports the efficacy of this product in the proposed indications. The efficacy of sodium bicarbonate is well-known. The presented evidence for well-established use of the active substance is sufficient.

The safety profile of sodium bicarbonate is well-known. The literature review identified no new or unexpected safety issues or concerns.

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

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 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.

V. OVERALL CONCLUSIONS

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 from the literature. Extensive clinical experience with sodium bicarbonate 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), Patient Information Leaflet (PIL) and labelling are satisfactory, and in line with current guidelines.

VI. REVISION DATE

23/02/2022

VII. UPDATES

This section reflects the significant changes following finalisation of the initial procedure.

SCOPE	PROCEDURE NUMBER	PRODUCT INFORMATION AFFECTED	DATE OF START OF PROCEDURE	DATE OF END OF PROCEDURE
RMS transfer	From Uk/H/5407/001/DC to IE/H/1033/001/DC			