# SODIUM BICARBONATE 500 MG CAPSULES, HARD

**PL 30464/0063**

**UKPAR**

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SODIUM BICARBONATE 500 MG CAPSULES, HARD

PL 30464/0063

LAY SUMMARY

On 6th September 2012, the MHRA granted Athlone Pharmaceuticals Limited a Marketing Authorisation (licence) for the medicinal product Sodium Bicarbonate 500 mg Capsules, Hard (PL 30464/0063). This is a Prescription-only medicine (POM).

Sodium Bicarbonate 500 mg Capsules are part of a group of medicines called antacids which are used to reduce the effects of excess acid produced in the stomach. Sodium Bicarbonate 500 mg Capsules are used to treat indigestion and acidosis (too much acid produced by the body, or acid not removed by the kidneys).

No new or unexpected safety concerns arose from this application and it was, therefore, judged that the benefits of taking Sodium Bicarbonate 500 mg Capsules, Hard outweigh the risks. Hence, a Marketing Authorisation has been granted.
SODIUM BICARBONATE 500 MG CAPSULES, HARD

PL 30464/0063

SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the UK granted Marketing Authorisation for the medicinal product Sodium Bicarbonate 500 mg Capsules, Hard (PL 30464/0063) on 6th September 2012. This Prescription-only medicine (POM) is intended for the treatment of dyspepsia. It may also be used to treat metabolic acidosis.

This is a national abridged application for Sodium Bicarbonate 500 mg Capsules, Hard submitted under article 10 (1) of Directive 2001/83/EC, as amended. The applicant cross-refers to Sodium Bicarbonate 500 mg Capsules, originally granted to H N Norton and Company Limited on 14th April 1975. The reference licence has gone under a Change of Ownership (CoA) procedure and was authorised to the current Marketing Authorisation Holder, TEVA UK Limited (PL 00289/1423) on 26th January 2010.

Sodium Bicarbonate is an antacid. It acts by a simple neutralization reaction in the stomach between sodium bicarbonate and hydrochloric acid. The normal concentration range of bicarbonate in plasma is 22 to 32 mmol per litre. The average intake of bicarbonate in the diet is negligible and very little is excreted in the urine under normal conditions; bicarbonate ions formed in the body are excreted in biliary, intestinal, pancreatic and salivary fluids. If bicarbonate is administered therapeutically thus increasing the plasma-bicarbonate concentration above the normal range then compensatory renal mechanisms comes to play and bicarbonate is excreted in the urine.

No new data were submitted nor were they necessary for this application, as the data are identical to those of the previously granted cross-reference product. As the cross-reference product was granted prior to the introduction of current legislation, no PAR was generated.

A pharmacovigilance system has been provided with this application and is satisfactory. A suitable justification for non-submission of the Risk Management Plan has been provided.
**PHARMACEUTICAL ASSESSMENT**

**DRUG SUBSTANCE**

Nomenclature

rINN: Sodium Bicarbonate

Chemical names: Sodium Bicarbonate, Sodium Hydrogen Carbonate

Structure

\[
\begin{array}{c}
\text{Na}^+ \\
\text{O}^-
\end{array}
\begin{array}{c}
\text{O} \\
\text{C} \\
\text{O}
\end{array}
\]

Molecular formula: NaHCO₃

Molecular Mass: 84.0

Physical Description: A white or almost white, crystalline powder.

Solubility: Soluble in water, practically insoluble in alcohol

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

**DRUG PRODUCT**

Other ingredients

Other ingredients consist of pharmaceutical excipients, namely microcrystalline cellulose and magnesium stearate making up the capsule core, and the capsule shell: was made of gelatine and titanium dioxide (E171). The printing ink is consisting of shellac resins, isopropyl alcohol, propylene glycol, black iron oxide and sodium lauryl sulphate.

All excipients used comply with their respective European Pharmacopoeia monograph with the exception of printing ink which complies with an in-house specification. Satisfactory Certificates of Analysis have been provided for all excipients.

None of the excipients are sourced from animal or human origin. The magnesium stearate used in the manufacture of the finished product is a vegetable origin. It had also been confirmed that the gelatin used is free of TSE/BSE and the corresponding certificate was issued by the supplier. This is acceptable.

**Pharmaceutical development**

The objective of the development programme was to formulate robust, stable capsules that contain the same active ingredient as Sodium Bicarbonate 500 mg Capsules (Teva UK Limited).
Comparative dissolution profile has been presented for test and reference product.

**Manufacture**
A description and flow-chart of the manufacturing method have been provided. In-process controls are satisfactory based on process validation data and controls on the finished product. Process validation has been carried out on batches of the product. The results appear satisfactory.

**Finished product specification**
The finished product specification is satisfactory. Test methods have been described and adequately validated, as appropriate. Batch data have been provided and comply with the release specification. Certificates of Analysis have been provided for any working standards used.

**Container Closure System**
The product is packaged in opaque Polyvinylchloride/polyvinylidichloride/Aluminium blisters with packs of 56 capsules.

Specifications and Certificates of Analysis for all packaging types used have been provided. These are satisfactory. All primary product packaging complies with EU legislation regarding contact with food.

**Stability**
Finished product stability studies have been conducted in accordance with current guidelines. Based on the results, a shelf-life of 36 months with a storage condition of “Store in the original package” is set and this is acceptable.

**Summary of Product Characteristics (SPC), Patient Information Leaflet (PIL) and Labelling**
The SPC, PIL and labelling are pharmaceutically satisfactory.

User testing of the package leaflet has been accepted, based on a bridging report provided by the applicant making reference to the user-testing of the PIL for Sodium Bicarbonate 500 mg Capsules (Focus Pharmaceuticals Limited). The products are from the same therapeutic class and have similar indications. A critical analysis demonstrated that the key messages for safe and effective use for both leaflets were similar. The justification of the rationale for bridging is accepted.

**Marketing Authorisation Application (MAA) Form**
The MAA form is pharmaceutically satisfactory.

**Expert Report**
The pharmaceutical expert report is written by an appropriately qualified person and is a suitable summary of the pharmaceutical aspects of the dossier.

**Conclusion**
There are no objections to the approval of this product from a pharmaceutical point of view.
NON-CLINICAL ASSESSMENT

The pharmacodynamic, pharmacokinetic and toxicological properties of sodium bicarbonate are well-known. Thus, the applicant has not provided additional studies and further studies are not required.

A non-clinical expert report has been provided, written by an appropriately qualified person. This is satisfactory.

A suitable justification has been provided for non-submission of an environmental risk assessment.

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

Clinical Pharmacology
Pharmacokinetics
In support of this application, the following justification for a bio-waiver has been submitted by the applicant.

“The product is a simple 500 mg capsule presentation of sodium bicarbonate intended for treatment of dyspepsia via local acid neutralisation and it is essentially similar to an already authorized product. There are no additional bio-pharmaceutics issues. A bioavailability study is not relevant. Any absorbed sodium or bicarbonate ion will enter the relevant body pools. Dissolution studies are provided as a surrogate for in vivo bioequivalence studies in accordance with the CPMP Note for Guidance on the investigation of bioavailability and bioequivalence.”

The bio-waiver is acceptable.

Pharmacodynamics
No new data have been submitted and none are required for this generic application.

Clinical Efficacy
No new data have been submitted and none are required for this generic application.

Clinical Safety
No new data have been submitted and none are required for this generic application.

Expert Report
A clinical overall summary, written by an appropriately qualified physician, has been provided. This is satisfactory.

Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and labelling
The SmPC, PIL and labelling are medically satisfactory and consistent with those for the reference product.

Marketing Authorisation Application (MAA) Forms
The MAA form is medically satisfactory.

Clinical Conclusion
There are no objections to the approval of this product from a clinical point of view.
IV. OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

QUALITY
The important quality characteristics of Sodium Bicarbonate 500 mg Capsules, Hard are well-defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

NON-CLINICAL
No new non-clinical data were submitted and none are required for applications of this type.

EFFICACY
A bioavailability study is not relevant. Any absorbed sodium or bicarbonate ion will enter the relevant body pools. Dissolution studies are provided as a surrogate for in vivo bioequivalence studies in accordance with the CPMP Note for Guidance on the investigation of bioavailability and bioequivalence.

No new or unexpected safety concerns arise from this application.

The SmPC and PIL are satisfactory and consistent with those of the reference product. Satisfactory labelling has also been submitted.

RISK-BENEFIT ASSESSMENT
The quality of the product is acceptable and no new non-clinical or clinical safety concerns have been identified. Extensive clinical experience with sodium bicarbonate is considered to have demonstrated the therapeutic value of the compound. The risk-benefit is, therefore, considered to be positive.
## STEPS TAKEN FOR ASSESSMENT

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<td>1</td>
<td>The MHRA received the marketing authorisation application on 5(^{th}) November 2010</td>
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<td>2</td>
<td>Following standard checks and communication with the applicant the MHRA considered the application valid on 1(^{st}) December 2010</td>
</tr>
<tr>
<td>3</td>
<td>Following assessment of the application the MHRA requested further information relating to the quality dossier on 25(^{th}) March 2011, 13(^{th}) January 2012 and on the clinical dossier 25(^{th}) March 2011</td>
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<tr>
<td>4</td>
<td>The applicant responded to the MHRA’s requests, providing further information to the quality section on 6(^{th}) December 2011 and 27(^{th}) March 2012 and on the clinical dossier 6(^{th}) December 2011</td>
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<td>5</td>
<td>The application was determined on 6(^{th}) September 2012</td>
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SUMMARY OF PRODUCT CHARACTERISTICS

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

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