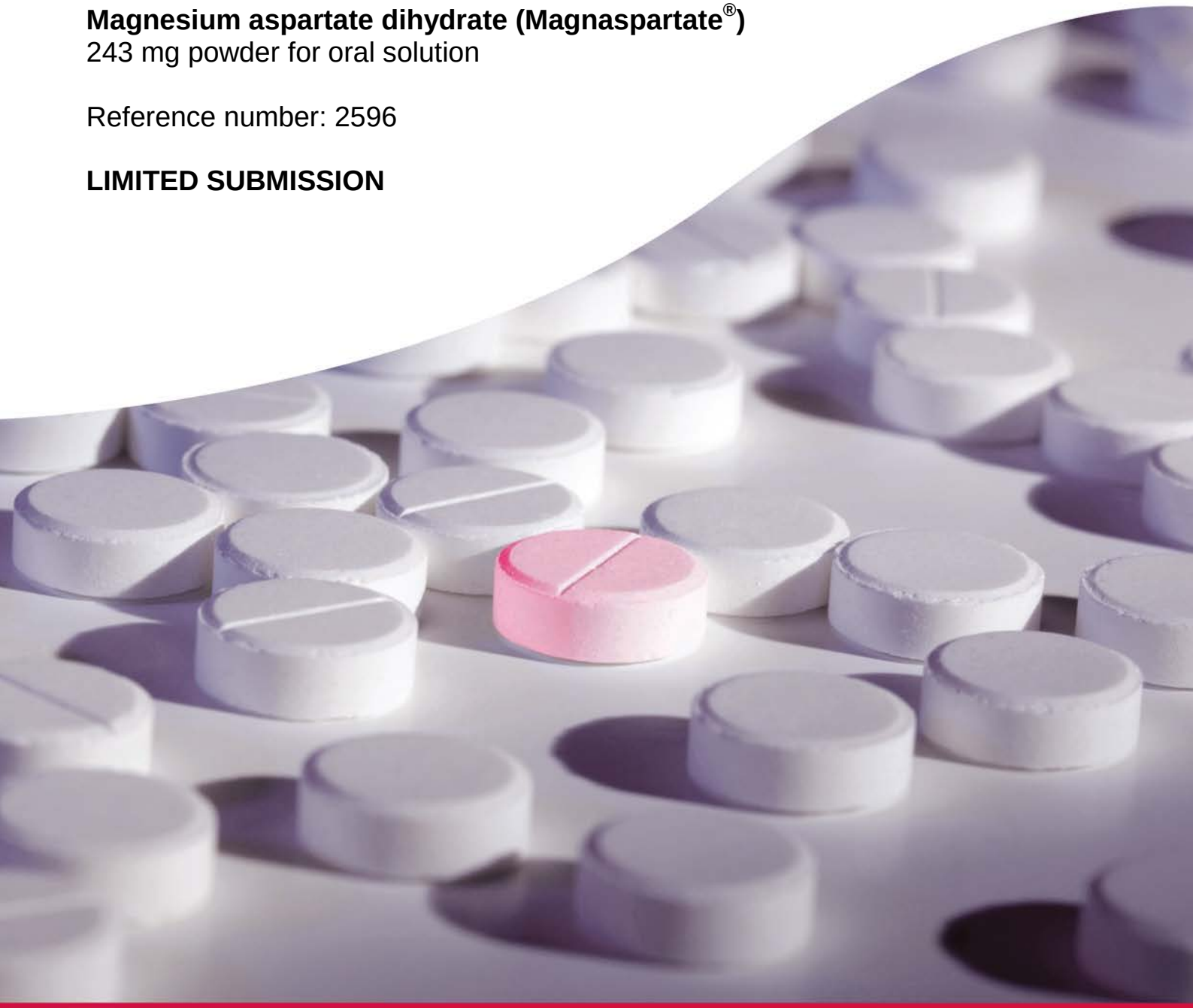
All Wales Therapeutics and Toxicology Centre
Canolfan Therapiwteg a Thocsicoleg Cymru Gyfan

AWMSG SECRETARIAT ASSESSMENT REPORT

Magnesium aspartate dihydrate (Magnaspartate®)
243 mg powder for oral solution

Reference number: 2596

LIMITED SUBMISSION



This report has been prepared by the All Wales Therapeutics and Toxicology Centre (AWTTC), in collaboration with the Centre for Health Economics & Medicines Evaluation, Bangor University.

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AWMSG Secretariat Assessment Report
Magnesium aspartate dihydrate (Magnaspartate®)
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This assessment report is based on evidence from a limited submission by Kora Healthcare on 9 March 2015[1].

1.0 PRODUCT AND APPRAISAL DETAILS

Licensed indication under consideration	Magnesium aspartate dihydrate (Magnaspartate®) for the treatment and prevention of magnesium deficiency, as diagnosed by a doctor, in adults, children and adolescents aged from two years[2].
Dosing	• Adults (> 18 years): one to two sachets daily • Children and adolescents (10–18 years): one sachet daily • Children (4–10 years): one level 5 ml spoon daily (109 mg magnesium) or one sachet daily • Children (2–4 years): one level 5 ml spoon daily (109 mg magnesium)[2].
Marketing authorisation date	7 November 2014[2]
Comparator	The main comparator included in the company submission was magnesium glycerophosphate (Magnaphate®)[1]. Magnaphate® is classed as a food supplement and is therefore not licensed for the indication under consideration.
Limited submission details	Magnesium aspartate dihydrate (Magnaspartate®) for the above indication met the following criteria for eligibility for a limited submission: • Anticipated usage in NHS Wales is considered to be of minimal budgetary impact • Estimated small difference in cost compared to comparator(s).

2.0 SUMMARY OF EVIDENCE ON CLINICAL EFFECTIVENESS

As the use of magnesium preparations for treatment and supplementation is well-established, the Marketing Authorisation for Magnaspartate® was granted under a bibliographic application[3]; as such no new clinical or non-clinical efficacy studies were required by the Medicines and Healthcare products Regulatory Agency (MHRA) to support the application for a licence. The applicant company submission included a literature-based assessment of several studies assessing the bioavailability and clinical efficacy of different magnesium salts for the treatment and prevention of magnesium deficiency[1].

2.1 Bioavailability

The bioavailability of magnesium from magnesium salts has been shown to be dependent on their water solubility[4]. Organic salts of magnesium such as magnesium aspartate dihydrate have been shown to have the greatest water solubility and demonstrate greater oral absorption and bioavailability compared to less soluble magnesium salts[4,5]. The applicant company additionally conducted a comparative aqueous solubility test comparing magnesium aspartate dihydrate to magnesium

glycerophosphate and magnesium oxide. Results indicated that magnesium aspartate dihydrate had greater solubility than magnesium glycerophosphate or magnesium oxide[1].

2.2 Clinical efficacy

The company submission included details of a number of studies demonstrating the efficacy of oral magnesium salts in raising magnesium levels. The majority of studies were conducted in healthy adult populations although studies for a range of clinical scenarios e.g. following cisplatin therapy, in short bowel syndrome, in type 2 diabetes mellitus, in children and adolescents were also included. In addition the company provided details of eight prevention studies of magnesium aspartate salt[6–13]. Results suggested that irrespective of aetiology, supplementation with oral magnesium salts may be effective in treating or preventing mild and moderate magnesium deficiency.

No comparative safety data for Magnaspartate® and other magnesium preparations are available. The most frequent adverse event associated with magnesium supplementation reported in the literature is mild diarrhoea[14].

2.3 Points to note

- As of April 2015, Magnaspartate® is the only UK licensed oral magnesium product for the treatment and prevention of magnesium deficiency[2]. There are no clinical efficacy or safety data available specifically for Magnaspartate®. Marketing authorisation was granted under the basis of well-established use of magnesium salts, including magnesium aspartate salt; there is a body of evidence which demonstrates that magnesium treatment and supplementation effectively raise magnesium stores in the body. The licensing authority were satisfied that bibliographic references demonstrated the favourable benefit-risk profile of magnaspartate® for the treatment and prevention of magnesium deficiency[3].
- Clinical experts contacted by the All Wales Therapeutics and Toxicology Centre (AWTTC) have confirmed that magnesium glycerophosphate is the predominant treatment in Wales; however, other magnesium salts are occasionally used on a case by case basis. There is no available evidence of clinical superiority of one oral magnesium preparation over another.
- In addition to Magnaspartate® which is available as a powder for oral solution there are a range of presentations that may be used for the treatment of hypomagnesaemia e.g. tablets, capsules, oral solutions. The availability of different presentations may impact on patient preference and compliance.
- Each 6.5 g sachet of Magnaspartate® contains 2.706 g sucrose which may be harmful to teeth with frequent or long-term use. In addition, patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrose-isomaltose insufficiency should not take this medicine[2].

3.0 SUMMARY OF EVIDENCE ON BUDGET IMPACT

3.1 Budget impact evidence

The company's budget impact analysis has been based on the assumption that Magnaspartate® will be prescribed in place of the top ten products by expenditure that are prescribed for the treatment of hypomagnesaemia.

Based on an extrapolation of English Prescription Cost Analysis (PCA) data to the Welsh population the company estimate an expenditure of £132,798 per annum for Magnaspartate® within NHS Wales with savings of £194,704 per annum from switching to Magnaspartate®.

3.1.1 AWTTC critique

- The company has based their budget impact estimates on PCA data extrapolated to a Welsh population. In the absence of Welsh specific prescribing data the company estimates of relative prescribing of products used to treat hypomagnesaemia within Wales is therefore subject to some uncertainty.
- In the absence of robust incidence and prevalence data, assumptions of expenditure based on current prescribing data of magnesium products would seem a reasonable approach. However, the applicant company has assumed that Magnaspartate® will displace all of the top ten hypomagnesaemia products that are currently prescribed. This is highly unlikely in clinical practice and therefore the estimate of savings anticipated by the company is subject to considerable uncertainty.

3.2 Comparative unit costs

Table 1 provides an example of the comparative annual acquisition costs for Magnaspartate® and the comparator for the treatment and prevention of magnesium deficiency, as diagnosed by a doctor, in adults, children and adolescents aged from two years.

Table 1. Examples of costs for Magnaspartate® and comparator for the treatment and prevention of magnesium deficiency[1].

Treatment	Pack size	Unit costs	Price per mmol of magnesium
Magnesium aspartate dihydrate powder 243 mg (10 mmol) (Magnaspartate®)	10	£8.95	8.95p
Magnesium glycerophosphate tablets 97.2 mg (4 mmol) (Magnaphate®)	50	£20.94	10.47p
This table does not imply therapeutic equivalence of medicines or the stated doses.			

4.0 ADDITIONAL INFORMATION

4.1 Prescribing and supply

AWTTC is of the opinion that, if recommended, magnesium aspartate dihydrate (Magnaspartate®) for the indication under consideration may be appropriate for use within NHS Wales prescribed under specialist recommendation.

The company do not anticipate that magnesium aspartate dihydrate (Magnaspartate®) will be supplied by a home healthcare provider.

4.2 AWMSG review

This assessment report will be considered for review three years from the date of the Final Appraisal Recommendation.

4.3 Evidence search

Date of evidence search: 7 and 13 April 2015.
Date range of evidence search: No date limits were applied to database searches.

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