HAUTE AUTORITÉ DE SANTÉ

The legally binding text is the original French version

TRANSPARENCY COMMITTEE

Opinion

26 November 2008

Examination of the dossier of the medicinal product included on the reimbursement list for a limited duration in accordance with the decree of 27 October 1999 (OJ of 30 October 1999) and with the order of 1 December 2006 (OJ of 21 December 2006).

MAGNE B6, coated tablet
Pack of 50 tablets (CIP: 312 500-9)

MAGNE B6, oral solution
Pack of 30 ampoules of 10 ml (CIP: 324 304-5)

Applicant: SANOFI AVENTIS FRANCE

Magnesium lactate dihydrate
Magnesium pidolate (oral solution alone)
Pyridoxine hydrochloride (vitamin B6)

Marketing authorisation (MA) date:
- coated tablets: MA validated on 21 January 1997, initial MA of 11 October 1973
- ampoules: MA validated on 21 January 1997, initial MA of 17 December 1975

Reason for request: Renewal of inclusion on the list of reimbursable medicinal products.

The provisional opinion issued on 11 June 2008 by the Transparency Committee was modified following the reassessment of the IAB of proprietary medicines containing magnesium in combination with another active ingredient.

Medical and Economic Evaluation and Public Health Division

1 CHARACTERISTICS OF THE MEDICINAL PRODUCT

1.1. Active ingredient

Magnesium lactate dihydrate
Magnesium pidolate
Pyridoxine hydrochloride (vitamin B6)

1.2. Indications

"Established magnesium deficiencies, whether isolated or associated with other deficiencies."

1.3. Dosage

In adults: 3 to 4 ampoules per day or 6 to 8 tablets per day
In the child: 10 to 30 mg/kg/day i.e. 1 to 4 ampoules per day or in children over 6 years (approximately 20kg), 4 to 6 tablets per day.

2 PREVIOUS COMMITTEE OPINIONS AND LISTING CONDITIONS

Opinion of 19 November 1999

The actual benefit is insufficient taking into account other available therapies or medicinal products to justify its reimbursement.

Opinion of 11 May 2005

The Actual Benefit of these proprietary drugs is moderate in their indication.

Opinion of 11 June 2008

The actual benefit of the proprietary medicines MAGNE B6 is:
- moderate only in established deficiencies secondary to severe enteropathy, tubulopathy or a nephrotic syndrome.
- insufficient in the other cases.

Provisional opinion pending the reassessment of proprietary medicines containing magnesium in combination with another active ingredient.

3 SIMILAR MEDICINAL PRODUCTS

3.1. ATC Classification (2008)

A	Alimentary tract and metabolism
A12	Mineral supplement
A12C	Other mineral supplements
A12CC	Magnesium
A12CC06	Magnesium lactate

3.2. Medicines in the same therapeutic category

These are preparations combining magnesium with vitamin B6:
- UVIMAG B6, ampoule (magnesium hydrogen glycerophosphate, pyridoxine hydrochloride)
- MAGNESIUM VITAMIN B6 BIOGARAN, tablet

3.3. Medicines with a similar therapeutic aim

These are proprietary medicines containing magnesium salts alone:
- EFIMAG, sachets (magnesium pidolate)
- MAG 2 (magnesium pidolate)
- MEGAMAG 45mg, capsule (magnesium aspartate)

4 UPDATING WITH DATA OBTAINED SINCE THE PREVIOUS OPINION

Efficacy

Within the scope of the reassessment of proprietary medicines containing a combination of magnesium with another active ingredient, the company was asked to justify the therapeutic use of the combination of a magnesium salt with vitamin B6.

None of the studies presented demonstrated the clinical benefit of combining a magnesium salt with vitamin B6.

5 DRUG USAGE DATA

IMS data (CMA August 2008) showed that there were 1.92 million prescriptions of MAGNE B6. The most frequent reasons for prescription were: malaise and fatigue (32%), anxiety disorders (12%), nervous and bone and muscle symptoms (8%), depressive episodes (3%), abnormal involuntary movements (3.5%). The mean daily dosage was 4.2 units per day. These were therefore usually off-label prescriptions.

6 TRANSPARENCY COMMITTEE CONCLUSIONS

6.1. Reassessment of actual benefit

Established magnesium deficiencies, confirmed by laboratory tests, mainly occur during chronic gastrointestinal (severe enteropathy) or renal disorders (tubulopathy or nephrotic syndrome). These disturbances must be treated by long-term administration of a magnesium salt.
Overt magnesium deficiency may cause mental, cardiovascular, neuromuscular or electrolyte disorders. In certain cases, these may progress and cause an impairment in quality of life or a disability.

There is no evidence that the combination of a magnesium salt and vitamin B6 is more effective than magnesium alone. The efficacy/safety ratio has not been established.

This proprietary drug is intended for symptomatic treatment.

There is no therapeutic use for combinations of a magnesium salt and vitamin B6 in magnesium deficiency.

> The public health burden of overt magnesium deficiency is low. These clinical situations do not constitute a public health need.

An assessment of the available data on overt magnesium deficiencies suggests that these medicines will not impact population health outcomes in terms of morbidity and mortality or quality of life.
Accordingly, these products are not expected to benefit public health.

The actual benefit of the proprietary medicines MAGNE B6 for oral administration, is insufficient to be reimbursed by national solidarity.

6.2. Therapeutic use

Apart from in overt deficiencies of gastrointestinal or renal origin, there is no need to prescribe magnesium.

There is no evidence that products containing magnesium combined with vitamin B6 have any clinical benefit compared to magnesium alone.

6.3. Transparency Committee recommendations

The Transparency Committee recommends that MAGNE B6 to be removed from the list of products reimbursed by National Insurance.