PROFESSIONAL INFORMATION FOR HUMAN MEDICINES

SCHEDULING STATUS

S3

1 NAME OF THE MEDICINE

NEUROBION AMPOULES

Solution for Injection; multicomponent

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 3 ml ampoule contains:

Thiamine hydrochloride (Vitamin B1) 100,0 mg

Pyridoxine hydrochloride (Vitamin B6) 100,0 mg

Cyanocobalamin (Vitamin B12) 1,0 mg

Sugar free

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Clear, red solution with no visible particles.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

NEUROBION AMPOULES are indicated for:

- Restoring Vitamin B_1, B_6 and/or B_{12} levels.
- The prevention and treatment of deficiencies in vitamin B_1, B_6 and B_{12}.

NEUROBION AMPOULES assist with the management of neuropathies.

4.2 Posology and method of administration

NEUROBION AMPOULES are preferably injected intramuscularly (deep intragluteal).

4.3 Contraindications

- Hypersensitivity to Vitamin B_1, B_6 and/or B_{12} or any of the excipients of NEUROBION AMPOULES (see section 6.1).
- Children below the age of 14 years (due to the high doses of the active ingredients).

NEUROBION AMPOULES should not be used in patients on Levodopa therapy.

4.4 Special warnings and precautions for use

NEUROBION AMPOULES should not be given for Vitamin B_{12} deficiency before a diagnosis has been fully established, because of the possibility of masking symptoms of subacute degeneration of the spinal cord. NEUROBION AMPOULES are not a suitable form of Vitamin B_{12} for the treatment of optic neuropathies associated with raised plasma concentrations of Vitamin B_{12}.

Neuropathies are described in the literature following long-term intake (6 - 12 months) of more than 50 mg mean daily dose of vitamin B_6. Therefore, regular monitoring is recommended if NEUROBION AMPOULES are given over longer periods of time.

4.5 Interactions with other medicines and other forms of interaction

- Vitamin B_6 (pyridoxine) may decrease the effect of L-DOPA.
- Pyridoxine antagonists such as isoniazide, cycloserine, penicillamine, or hydralazine may decrease the efficacy of Vitamin B_6 (pyridoxine).
- Long-term use of loop diuretics such as furosemide may accelerate the elimination and thus decrease the serum levels of Vitamin B_1 (thiamine).
- Long term use of acid-lowering agents may lead to Vitamin B_{12} deficiency.

4.6 Fertility, pregnancy and lactation

The safety of this preparation in pregnancy and lactation has not been established.

Vitamins B_1, B_6 and B_{12} (the components of NEUROBION AMPOULES) are secreted into human breast milk, but risks of overdose for the infant are not known. High doses of Vitamin B_6, i.e. > 600 mg daily, may inhibit the production of breast milk. Mothers on NEUROBION AMPOULES should not breastfeed their infants.

4.7 Effects on ability to drive and use machines

No effects of the product on the ability to drive or use machines are known.

4.8 Undesirable effects

As most undesirable effects are based on post-marketing spontaneous reporting, frequency estimation is not possible.

Immune system disorders

Frequency not known: Hypersensitivity reactions, such as sweating, tachycardia, and skin reactions with itching and urticaria.

Gastrointestinal disorders

Less frequent: Gastrointestinal complaints, such as nausea, vomiting, diarrhoea and abdominal pain.

Skin and subcutaneous tissue disorders

Less frequent: Cases of acne or eczema have been reported after high doses of Vitamin B12.

General disorders and administration site conditions

Frequency not known: Injection site reactions.

Renal and urinary disorders

Less frequent: Chromaturia (“reddish urine”, appeared during the first 8 hours after an administration and typically resolves within 48 hours).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications:

https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

Sensorial neuropathy and other sensorial neuropathy syndromes which can be caused by long-term administration of high doses of pyridoxine improve gradually upon vitamin discontinuation.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A.22.2 – Vitamins: Others

Vitamins B_1, B_6 and B_{12} act as coenzymes and accordingly constitute substances essential for metabolism.

5.2 Pharmacokinetic properties

Combined administration of vitamins B1, B6 and B12 is not expected to have a negative effect on the pharmacokinetics of the individual vitamins.

Thiamine (Vitamin B1)

The biological half-life of thiamine in humans is about 9,5 to 18,5 days, with an elimination half-life of approximately 4 hours. The reserve capacity is 4 to 10 days. The high turnover rate and limited storage of thiamine (20 – 30 mg, mainly in the heart, brain, liver, and kidneys) require an adequate daily thiamine intake to meet requirements. Deficiency can

present within 2 - 3 weeks of intake ceasing.

Pyridoxine (Vitamin B6)

Vitamin B6 is phosphorylated mainly in the liver, forming the biologically active pyridoxal phosphate. To cross cell membranes, phosphorylated Vitamin B6 must be hydrolysed by alkaline phosphatase to free Vitamin B6. Transport into the cells is by simple diffusion followed by rephosphorylation. Peak concentrations are reached after 3,5 to 4 hours. The biological half-life of pyridoxal phosphate is about 15 - 25 days with an elimination half-life of approximately 3 hours.

Cyanocobalamin (Vitamin B12)

About 90 % of plasma cobalamin is bound to proteins (transcobalamins). Most of the vitamin B12 not circulating in the plasma is stored in the liver.

Vitamin B12 is predominantly excreted via the bile and is largely reabsorbed via the enterohepatic circulation. If the body's storage capacity is exceeded as a result of high-dose and, in particular, parenteral administration, the portion not retained is excreted in the urine.

5.3 Preclinical safety data

Not Applicable

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Potassium cyanide, Sodium hydroxide solution

6.2 Incompatibilities

Not Applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store between 2 - 8 °C in a refrigerator.

Keep out of reach and sight of children.

6.5 Nature and contents of container

Boxes of 3 ampoules of 3 ml each.

6.6 Special precautions for disposal and other handling

No special requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION

P&G South African Trading (Pty) Ltd

10th Floor, Alice Lane Towers, 15 Alice Lane, Sandton, 2196

South Africa

8 REFERENCE NUMBER

H2488 (Act 101/1965)

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

11 March 1988

10 DATE OF REVISION OF THE TEXT

02/02/2023