

NEW ZEALAND DATA SHEET

1. PRODUCT NAME

Neo-B12™ Injection Hydroxocobalamin 1000 microgram/1 mL

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Neo-B12™ Injection ampoule contains hydroxocobalamin chloride equivalent to hydroxocobalamin anhydrous 1000 micrograms sodium chloride 9.0 milligrams and 1N acetic acid for pH adjustment and Water for Injections.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection

Neo-B12™ Injection is a clear, dark red coloured sterile solution, free from visible particles supplied in colourless glass ampoules of 1 mL.

The pH of the solution is approximately 4.6.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Neo-B12™ Injection is indicated for: the prophylaxis and treatment of pernicious (Addisonian) anaemia and other macrocytic anaemias associated with vitamin B₁₂ deficiency; Treatment of optic neuropathies such as tobacco amblyopia and Leber's optic atrophy.

4.2 Dose and method of administration

This product contains no antimicrobial agent. It is for single use in one patient only. Discard any residue.

Neo-B12™ Injection is to be administered intramuscularly. The following dosage schemes are suitable for adults and children:

Addisonian pernicious anaemia and other macrocytic anaemias without neurological involvement:

Initially: 250 to 1,000 micrograms intramuscularly on alternate days for one to two weeks, then 250 micrograms weekly until the blood count is normal.

Maintenance: 1,000 micrograms every two or three months.

Addisonian pernicious anaemia and other macrocytic anaemias with neurological involvement:

Initially: 1,000 micrograms on alternate days for one to two weeks.

Maintenance: 1,000 micrograms every two months.

Prophylaxis of macrocytic anaemia associated with vitamin B₁₂ deficiency resulting from gastrectomy, some malabsorption syndromes and nutritional deficiencies:

1,000 micrograms every two or three months.

Tobacco amblyopia and Leber's optic atrophy:

Initially: 1,000 micrograms daily by intramuscular injection for two weeks then twice weekly for four weeks.

Maintenance: 1,000 micrograms monthly.

4.3 Contraindications

Known sensitivity to hydroxocobalamin, or any other ingredient in Neo-B12™ Injection.

Known sensitivity to cobalt.

Neo-B12™ Injection should not be used for the treatment of megaloblastic anaemia of pregnancy (see section 4.6)

4.4 Special warnings and precautions for use

DO NOT USE INTRAVENOUSLY.

A sensitivity history should be obtained from the patient prior to administration of Vitamin B₁₂. An intradermal test dose is recommended before Vitamin B₁₂ is administered to patients who may be sensitive to cobalamins.

Hypokalaemia and cardiac arrest have been reported when megaloblastic anaemia is treated intensively.

Serum potassium is to be carefully monitored during the initial phase of treatment in pernicious anaemia.

Diagnosis of vitamin B₁₂ deficiency should be confirmed by laboratory investigation before institution of hydroxocobalamin (vitamin B₁₂) therapy. Do not use hydroxocobalamin until diagnosis is fully established, as it may mask symptoms of subacute degeneration of the spinal cord, or of the true diagnosis of pernicious anaemia. Folic acid may potentiate the neurological complications of vitamin B₁₂ deficiency, so should not be administered to patients with pernicious anaemia (see section 4.5).

Regular blood tests to determine vitamin B12 levels are advisable during treatment.

Administration of hydroxocobalamin doses in excess of 10 micrograms daily may improve folate deficient megaloblastic anaemia, and obscure the true diagnosis.

The therapeutic response to hydroxocobalamin may be impaired by concurrent infection, uraemia, folic acid or iron deficiency, or by drugs with bone marrow suppressing effects, such as chloramphenicol (see section 4.5).

Treatment with hydroxocobalamin may unmask polycythaemia vera, because vitamin B₁₂ deficiency may suppress the symptoms of this condition.

4.5 Interaction with other medicines and other forms of interaction

Concurrent administration of chloramphenicol and hydroxocobalamin may impair the therapeutic response to hydroxocobalamin in vitamin B₁₂ deficient patients. The haematological response should be carefully monitored in patients receiving both these drugs.

Serum concentrations of hydroxocobalamin may be lowered by oral contraceptives.

Vitamin B₁₂ concentrations in the blood may be reduced following administration of large and continuous doses of folic acid. Folic acid administration may impair the therapeutic response to hydroxocobalamin.

Most antibiotics, methotrexate and pyrimethane invalidate folic acid and vitamin B₁₂ microbiological blood analysis.

4.6 Fertility, pregnancy and lactation

Fertility

No data available.

Pregnancy

Problems in humans have not been documented with intake of normal daily amounts. Vitamin B₁₂ crosses the placental barrier. There are no studies establishing the safety of this drug during pregnancy. It is not recommended for pregnancy unless the expected benefits outweigh any potential risk to the infant.

Megaloblastic anaemia occurring during pregnancy is usually due to folic acid deficiency rather than vitamin B₁₂ deficiency. Hydroxocobalamin should not be used for the treatment of megaloblastic anaemia of pregnancy caused by folic acid deficiency.

Lactation

Hydroxocobalamin is distributed into breast milk. Therefore it is not recommended for breastfeeding mothers unless the expected benefits to the mother outweigh any potential risk to the infant.

4.7 Effects on ability to drive and use machinery

No data available.

4.8 Undesirable effects

Sensitisation to hydroxocobalamin is rare, but may manifest itself as itching exanthema and rarely, anaphylaxis.

Antibodies to hydroxocobalamin-transcobalamin II complex may develop during hydroxocobalamin therapy.

Other reported adverse effects include diarrhoea, nausea, vomiting, headache, dizziness, peripheral vascular thrombosis, chest pain/discomfort, cardiac arrest, injection site reactions, sensation of heat and cold, malaise, urticaria or a feeling of swelling of the whole body, eczematous skin lesions, acne and folliculitis.

Pulmonary oedema and congestive heart failure have been reported during early vitamin B₁₂ treatment, possibly as a result of an increase in blood volume induced by the medicine.

Polycythaemia vera may occur (see section 4.4).

Arrhythmias secondary to hypokalaemia have appeared at the beginning of parenteral treatment with hydroxocobalamin.

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. Healthcare professionals are asked to report any suspected adverse reactions <https://nzphvc.otago.ac.nz/reporting/>.

4.9 Overdose

Treatment is unlikely to be needed in cases of overdose.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Mechanism of action

Several chemically related forms of vitamin B₁₂, differing in slight modification of a side chain attached to the cobalamin nucleus have been isolated. Two such variants of vitamin B₁₂ are cyanocobalamin and hydroxocobalamin.

Vitamin B₁₂ is essential for normal growth, haematopoiesis, and production of all epithelial cells and maintenance of myelin throughout the nervous system. Whenever nucleic acid synthesis occurs and therefore whenever cell reproduction occurs, vitamin B₁₂ is required.

The amounts of vitamin B₁₂ needed to maintain normal blood forming functions are small and low doses are sufficient to correct the usual symptoms of vitamin B₁₂ deficiency.

Vitamin B₁₂ acts as an enzyme or co-enzyme in a number of metabolic processes and is transformed in the body to at least two compounds which possess enzymatic properties.

- (i) Co-enzyme B₁₂ is required for conversion of propionate to succinate, thus involving vitamin B₁₂ in both fat and carbohydrate metabolism.

(ii) Methylcobalamin acts in a transmethylation process converting homocysteine to methionine, thus involving vitamin B₁₂ in fat and protein metabolism.

In some cases of vitamin B₁₂ deficiency, severe neurological symptoms develop, as vitamin B₁₂ is necessary for the formation of protein structures required for the integrity of the nerve cell and myelin sheath.

5.2 Pharmacokinetic properties

Hydroxocobalamin produces higher and more prolonged serum levels of vitamin B₁₂ than cyanocobalamin when given by intramuscular injection in the same dosage. Hydroxocobalamin disperses more slowly from the site of injection than cyanocobalamin, is more strongly bound to plasma proteins and accumulated in the liver to a greater extent.

Hydroxocobalamin is excreted in the bile and urine, but more slowly than cyanocobalamin.

Hydroxocobalamin combines with cyanide and thus acts as a cyanide antagonist in vivo resulting in the formation of cyanocobalamin.

5.3 Preclinical safety data

Genotoxicity

No data available.

Carcinogenicity

No data available.

Reproductive and developmental toxicity

No data available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Acetic acid
- Sodium chloride
- Water for injections

6.2 Incompatibilities

No data available.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Store below 25°C

6.5 Nature and contents of container

Boxes of 3 x 1 mL clear glass ampoules

6.6 Special precautions for disposal

Any unused medicine or waste material should be disposed of in accordance with local requirements.

7. MEDICINE SCHEDULE

General Sale Medicine

8. SPONSOR

Pfizer New Zealand Limited

P O Box 3998

Auckland, New Zealand, 1140

Toll Free Number: 0800 736 363

9. DATE OF FIRST APPROVAL

26 Oct 2006

10. DATE OF REVISION OF THE TEXT

5 February 2019

Summary table of changes

Section changed	Summary of new information
All	Reformat to MedSafe Data Sheet guidance