Hydroxocobalamin ABM

Hydroxoxcobalamin Injection 1 mg/mL

Presentation

Ampoules of 1 mL containing a clear, red solution containing 1 mg (1,000 micrograms) Hydroxocobalamin Acetate per mL equivalent to 0.96 mg Hydroxocobalamin per mL.

Other ingredients: Sodium Chloride, Sodium Acetate, Acetic Acid, Water for Injections.

Uses

Actions

Hydroxocobalamin may be regarded as a precursor of two co-enzymes, which are involved in various biological systems in man. Co-enzyme B12 is required for the conversion of methylmalonate to succinate. Deficiency of this enzyme could therefore interfere with the production of lipoprotein in myelin sheath tissue and so give rise neurological lesions. Methylcobalamin is necessary for the conversion of homocysteine to methionine, which is essential for the metabolism of folic acid. Deficiency of tetrahydrafolate leads to reduced synthesis of thymidylate resulting in reduced synthesis of DNA, which is essential for cell maturation. Vitamin B12 is also concerned in the maintenance of sulphydryl groups in reduced form, deficiency leading to decreased amounts of reduced SH content of erythrocytes and liver cells.

Pharmacokinetics

Vitamin B12 exists in four major forms referred to collectively as cobalamins; deoxyadenosylcobalamin, methylcobalamin, hydroxocobalamin, and cyanocobalamin. Cobalamins are absorbed in the ileum and stored in the liver. They continuously undergo enterohepatic recycling via secretion in the bile. Part of a dose is excreted in the urine, most of it in the first 8 hours. As many as five different forms of cobalamin have been identified in the urine. The proportion of the dose excreted in the urine increases with the size of the dose, rising from 8% of 100 microgram dose to 29% of a 1000 microgram dose. In a normal person, following injection of hydroxocobalamin, the half life in the serum depends on the glomerular filtration rate, whereas in a patient with deficient stores the removal from the plasma will depend on the rate of absorption into the body stores as well as the renal excretion.

Cobalamins are extensively bound to two specific plasma proteins called transcobalamin 1 and 2; 70% to transcobalamin 1, 5% to transcobalamin 2. The normal average blood level of vitamin B12 is 472 pg/mL. Range is 163-925 pg/mL. A vitamin B12 below 160 pg/mL indicates a deficiency state.

Cobalamins diffuse across the placenta. No information has been found regarding the effect of age, renal hepatic dysfunction on the kinetics of hydroxocobalamin.

During therapy with weekly intramuscular doses of 500 mcg, serum vitamin B12 concentration of over 0.8ng/mL are attained in 2 weeks and of 5ng/mL in 8 weeks, rising in some cases to 15ng/mL.

Indications

Addisonian pernicious anaemia. Prophylaxis and treatment of other macrocytic anaemias associated with vitamin B12 deficiency. Tobacco amblyopia and Leber’s optic atrophy.

Dosage and Administration

The following dosage schemes are suitable for adults and children.

Addisonian pernicious anaemia and other macrocytic anaemias without neurological involvement

Initially, 250 to 1000 micrograms intramuscularly on alternate days for one to two weeks, then 250 micrograms weekly until the blood count is normal.

Maintenance: 1000 micrograms every two or three months.

Addisonian pernicious anaemia and other macrocytic anaemias with neurological involvement

Initially: 1000 micrograms on alternate days as long as improvement is occurring.

Maintenance: 1000 micrograms every two months.

Prophylaxis of macrocytic anaemia associated with vitamin B12 deficiency resulting from gastrectomy, some malabsorption syndromes and strict vegetarianism

1000 micrograms every two or three months.

Tobacco amblyopia and Leber's optic atrophy

Initially: 1000 micrograms or more daily by intramuscular injection for two weeks then twice weekly as long as improvement is occurring.

Maintenance: 1000 micrograms monthly.

Contraindications

Hypersensitivity to any ingredient of the preparation.

Warnings and Precautions

Hydroxocobalamin should only be used in properly diagnosed cases of deficiency.

The dosage schemes given above are usually satisfactory, but regular examination of the blood is advisable. If megaloblastic anaemia fails to respond to Hydroxocobalamin ABM, folate metabolism should be investigated. Doses in excess of 10 micrograms daily may product a haematological response in patients with folate deficiency. Indiscriminate administration may mask the true diagnosis.

Before commencing treatment of pernicious anaemia it is important to establish baseline levels for haematological parameters and plasma levels of cobalamin and to monitor response at frequent intervals particularly in the first few weeks of treatment and thereafter at less frequent intervals.

Cardiac arrhythmias secondary to hypokalaemia during initial therapy have been reported. Plasma potassium should therefore be monitored during this period.

Pregnancy and Lactation

Hydroxocobalamin ABM should not be used for the treatment of megaloblastic anaemia in pregnancy.

It is not known whether cobalamin is excreted in breast milk. Therefore, if a mother is receiving Hydroxocobalamin ABM injections the decision has to be taken whether to discontinue treatment or discontinue breast feeding, bearing in mind the risk benefit ratio to both mother and baby.

Adverse Effects

Sensitisation to hydroxocobalamin is rare but may manifest itself as itching exanthema, chills, fever, hot flushes, nausea, dizziness, and exceptionally, anaphylaxis. Acneiform and bullous eruptions have been reported rarely.

Interactions

Chloramphenicol-treated patients may respond poorly to hydroxocobalamin. Serum concentrations of hydroxocobalamin may be lowered by oral contraceptives.

These interactions are unlikely to have clinical significance.

Antimetabolites and most antibiotics invalidate vitamin B12 assays by microbiological techniques.

Overdosage

Treatment is unlikely to be needed in cases of overdosage.

Pharmaceutical Precautions

Store below 25° C. Protect from light.

Any portion of the contents remaining should be discarded.

Medicines Classification

General Sales Medicine

Package Quantities

Ampoules of 1mL in boxes of 3.

Further Information

An intramuscular injection of hydroxocobalamin produces higher serum levels than the same dose of cyanocobalamin, and these levels are well maintained.

As single dose ampoules, no preservatives are required.

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