SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Hydroxocobalamin 1mg in 1ml, solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Hydroxocobalamin (as acetate) 1.0 mg/ml

Hydroxocobalamin contains cobalt

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of Addisonian Pernicious anaemia.
Prophylaxis and treatment of other macrocytic anaemias associated with Vitamin B_{12} deficiency.
Treatment of Tobacco amblyopia.
Treatment of Leber's optic atrophy.

4.2 Posology and method of administration

Posology

Dosage - Adults (all ages) and children:

Addisonian pernicious anaemia and other macrocytic anaemias without neurological involvement.

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

Maintenance: 1mg every two or three months.

Addisonian pernicious anaemia and other macrocytic anaemias with neurological involvement.

Initially, 1mg on alternate days as long as improvement is occurring.

Maintenance: 1mg every 2 months.

Prophylaxis of macrocytic anaemia associated with Vitamin B_{12} deficiency resulting from gastrectomy, ileal resection, some malabsorption syndromes and strict vegetarianism

1mg every two to three months.

Tobacco amblyopia and Leber's optic atrophy

Initially, 1mg or more daily by intramuscular injection for 2 weeks. Then twice weekly as long as improvement is occurring.

Maintenance: 1mg monthly.

Method of administration
Intramuscular injection.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
Hydroxocobalamin should not be used for the treatment of megaloblastic anaemia of pregnancy unless vitamin B12 deficiency has been demonstrated.

4.4. Special warnings and precautions for use

The dosage schemes given above are usually satisfactory, but regular examination of the blood is advisable.

If megaloblastic anaemia fails to respond to hydroxocobalamin, folate metabolism should be investigated.

Doses in excess of 10 micrograms daily may produce a haematological response in patients with folate deficiency. Indiscriminate administration may mask the true diagnosis. The haematological and neurological state should be monitored regularly to ensure adequacy of therapy.

Cardiac arrythmias secondary to hypokalaemia during initial therapy have been reported. Plasma potassium should therefore be monitored during this period. Platelet count should be monitored during the first weeks of use in megaloblastic anaemia due to the possible occurrence of reactive thrombocytosis.

Hydroxocobalamin solution for injection contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per ampule, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Chloramphenicol
Parenteral chloramphenicol may attenuate the effect of hydroxocobalamin in anaemia.

Oral contraceptives
The serum concentration of hydroxocobalamin may be lowered.

The above interactions are unlikely to be of clinical significance but should be taken into account when performing assays for blood concentrations.

Vitamin B12 assays by microbiological techniques are invalidated by antimetabolites and most antibiotics.

4.6 Fertility, pregnancy and lactation

Pregnancy
Hydroxocobalamin injection should not be used for the treatment of megaloblastic anaemia of pregnancy unless vitamin B12 deficiency has been demonstrated.

Breast-feeding
Hydroxocobalamin is secreted into breast milk but this is unlikely to harm the infant, and may be beneficial if the mother and infant are vitamin B12 deficient.

Fertility
No data available

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

The following undesirable effects may occur with the use of hydroxocobalamin in the following frequencies:
Very common (> 1/10)
Common (> 1/100, <1/10)
Uncommon (> 1/1,000, <1/100)
Rare (> 1/10,000, <1/1,000)
Very rare (<1/10,000)
Not known (cannot be estimated from the available data).

There are no modern clinical studies available that can be used to determine the frequency of undesirable effects.
Therefore, all the undesirable effects listed are classed as “frequency unknown”.
The following effects have been reported and are listed below by body system:

System organ class	Frequency	Undesirable effects
Blood and lymphatic system disorders	Not Known	Reactive thrombocytosis can occur during the first weeks of use in megaloblastic anaemia.
Immune system disorders	Not Known	Hypersensitivity reactions including rash; itching; exanthema. Antibodies to hydroxocobalamin-transcobalamin II complex have developed during hydroxocobalamin therapy. Anaphylaxis
Metabolism and nutrition disorders	Not Known	Initial hypokalaemia
Nervous system disorders	Not Known	Headache, paraesthesia, tremor.
Cardiac disorders	Not Known	Arrhythmias secondary to hypokalaemia.
Gastrointestinal	Not Known	Nausea, vomiting,

disorders		diarrhoea.
General disorders and administration site conditions	Not Known	Fever, chills, hot flushes; dizziness; malaise; pain; Injection site reactions including injection site pain, injection site erythema, injection site pruritus, injection site` induration, and injection site swelling.
Skin and subcutaneous tissue disorders	Not Known	Acneiform and bullous eruptions
Renal and urinary disorders	Not Known	Chromaturia

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme (Website: www.mhra.gov.uk/yellowcard) or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Treatment is unlikely to be required in the case of overdose.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antianaemic preparations – Vitamin B_{12}. ATC code: B03BA03

Hydroxocobalamin is used in the treatment and prevention of Vitamin B_{12} deficiency. For adults, the daily requirement of Vitamin B_{12} is probably about 1 to 2 micrograms and this amount is present in most normal diets. However, Vitamin B_{12} only occurs in animal products, not in vegetables, and therefore strict vegetarian or vegan diets that exclude dairy products may provide an inadequate amount, although a deficiency may not be apparent for many years.

Deficiency is more likely in patients with malabasorption syndromes or metabolic disorders, nitrous-oxide induced megalobastosis, or following gastrectomy or extensive ileal resection. Deficiency leads to megaloblastic anaemias and demyelination and other neurological damage.

On oral intake, Vitamin B_{12} substances bind to intrinsic factor, a glycoprotein secreted by the gastric mucosa, and are then actively absorbed from the gastrointestinal tract. A specific anaemia known as pernicious anaemia develops in patients with an absence of intrinsic factor. Absorption is also impaired in patients with disease or abnormality of the gut.

Treatment usually results in rapid haematological improvement and a striking clinical response. However, neurological symptoms respond more slowly.

5.2 Pharmacokinetic properties

Distribution
Hydroxocobalamin is extensively bound to specific plasma proteins (transcobalamins); transcobalamin II appears to be involved in the rapid transport of the cobalamins to tissues.

Elimination
Hydroxocobalamin is stored in the liver, excreted in the bile, and undergoes extensive enterohepatic recycling; part of the dose is excreted in the urine, most of it in the first 8 hours.
Hydroxocobalamin diffuses across the placenta and also appears in breast milk. Hydroxocobalamin is better retained than cyanocobalamin; 90% of a 100 microgram dose and 30% of a 1000 microgram dose are retained, a range believed to be sufficient for body requirements for 2 to 10 months.

5.3 Preclinical safety data

There is no additional information relevant to the prescriber.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Acetic acid
Sodium chloride
Sodium hydroxide
Water for injections

6.2 Incompatibilities

None known.

6.3 Shelf life

18 months.

6.4 Special precautions for storage

Do not store above 25°C.
Keep container in the outer carton.

6.5. Nature and contents of container

1ml colourless glass (Ph. Eur. Type I) ampoules containing 1ml solution for injection.

Pack size: 5 ampoules per carton.

6.6 Special precautions for disposal

None.

7 MARKETING AUTHORISATION HOLDER

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