DATA SHEET

1 PRODUCT NAME

Hydroxocobalamin ABM Solution for injection 1 mg/mL

2 QUALITATIVELY AND QUANTITATIVE COMPOSITION

Hydroxocobalamin acetate 1 mg/mL

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Solution for injection

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

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

4.2 Dose and method of administration

Hydroxocobalamin ABM 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 as long as improvement is occurring. Maintenance: 1,000 micrograms every two months.

Prophylaxis of macrocytic anaemia associated with vitamin B12 deficiency resulting from gastrectomy, some malabsorption syndromes and strict vegetarianism
1,000 micrograms every two or three months.

**Tobacco amblyopia and Leber’s optic atrophy**

Initially: 1,000 micrograms or more daily by intramuscular injection for two weeks then twice weekly as long as improvement is occurring.

Maintenance: 1,000 micrograms monthly.

### 4.3 Contraindications

Hypersensitivity to any ingredient of the preparation.

### 4.4 Special warnings and precautions for use

**DO NOT USE INTRAVENOUSLY.**

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

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 produce a haematological response in patients with folate deficiency. Indiscriminate administration may mask the true diagnosis. Folic acid may potentiate the neurological complications of vitamin B12 deficiency, so should not be administered to patients with pernicious anaemia (see *Interactions*).

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.

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.

The therapeutic response to hydroxocobalamin may be impaired by concurrent infection, uraemia, folic acid or iron deficiency.

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**

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.

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.

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

4.6 **Fertility, pregnancy and lactation**

**Use in pregnancy**

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

**Use in lactation**

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.

4.7 **Effects on ability to drive and operate machines**

Not relevant

4.8 **Undesirable 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.

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 Warnings and Precautions).

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

Treatment is unlikely to be needed in cases of overdosage.

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5 **PHARMACOLOGICAL PROPERTIES**

5.1 **Pharmacodynamic properties**

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 to 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 sulphhydryl groups in reduced form, deficiency leading to decreased amounts of reduced SH content of erythrocytes and liver cells.

5.2 **Pharmacokinetic properties**

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

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 1,000 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 0.8 ng/mL are attained in 2 weeks and of 5 ng/mL in 8 weeks, rising in some cases to 15 ng/mL.

5.3 **Preclinical safety data**

Not applicable
6 PHARMACEUTICAL PARTICULARS

6.1 **List of excipients**

sodium chloride,
sodium acetate,
acetic acid,
water for injections.

As single dose ampoules, no preservatives are required.

6.2 **Incompatibilities**

Not applicable

6.3 **Shelf life**

The proposed shelf life is 3 years

6.4 **Special precautions for storage**

Store below 25°C. Protect from light.
Any portion of the contents remaining should be discarded.

6.5 **Nature and contents of container**

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.

Ampoules of 1 mL in boxes of 3.

6.6 **Special precautions for disposal**

No special requirements for disposal

7 MEDICINE SCHEDULE

General Sales Medicine
8  SPONSOR

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9  DATE OF FIRST APPROVAL

31 May 2007

10  DATE OF REVISION OF TEXT

28 March 2017

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<td>“Do not use hydroxocobalamin until fully diagnosis; Additional warnings with concurrently used with folic acid, and others” added</td>
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<tr>
<td>4.5</td>
<td>Interaction with Folic acid added</td>
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