Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Hydroxocobalamin 1mg/ml solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1ml of solution for injection contains 1.045 mg hydroxocobalamin acetate equivalent to 1 mg hydroxocobalamin (vitamin B_{12}).
1mg/ml of hydroxocobalamin equals 1000 micrograms/ml.
Excipients with known effect
Each ml of solution contains 0.5 mg sodium hydroxide and 8mg sodium chloride
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for Injection (injection)
Red, clear solution
pH 4.3 to 4.7

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 Posology and method of administration

Intramuscular injection

Posology
Adults and Children

Addisonian pernicious anaemias and other macrocytic anaemias without neurological involvement.
Initially: 250 to 1000 micrograms intramuscularly on alternate days *for* one or two weeks, then 250 micrograms weekly until the blood count is normal
Maintenance: 1000 micrograms every two to 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 of three 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 daily by intramuscular injection for two weeks then twice weekly as long as improvement is occurring.
Maintenance: 1000 micrograms every one to three months as required.

4.3 Contraindications

Hypersensitivity to Hydroxocobalamin or to any of the ingredients in this preparation.

Hydroxocobalamin Injection 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 normally satisfactory, but regular examination of the blood is advisable.
If megaloblastic anaemia fails to respondto 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.
Cardiac arrhythmias secondary to hypokalaemia during initial therapy have been reported. Plasma potassium should therefore be monitored during this period.
The haematological and neurological state should be monitored regularly to ensure adequacy of therapy.
Platelet count should be monitored during the first weeks of use in megaloblastic anaemia due to the possible occurrence of reactive thrombocytosis.
This injection contains less than 1mmol (23mg) of sodium per 1ml (essentially 'sodium-free').

4.5 Interaction with other medicinal products and other forms of interaction

Chloramphenicol-treated patients may respond poorly to Hydroxocobalamin injection.
Serum concentrations of hydroxocobalamin may be lowered by oral contraceptives.
The above interactions are unlikely to have clinical significance. Antimetabolites and most antibiotics invalidate Vitamin B12 assays by microbiological techniques.

4.6 Fertility, pregnancy and lactation

Hydroxocobalamin injection should not be used for the treatment of megaloblastic anaemia of pregnancy unless vitamin B12 deficiency has been demonstrated.
Hydroxocobalamin injection is secreted into the breast milk but is unlikely to harm the infant, and may be beneficial if the mother and infant are vitamin B12 deficient.

No studies on fertility have been performed.

4.7 Effects on ability to drive and use machines

None known

4.8 Undesirable effects

The following effects have been reported and are listed below by body system:

Blood and lymphatic system disorders:	
Frequency not known	Reactive thrombocytosis can occur during the first weeks of use in megaloblastic anaemia
Disorders of the immune system:	
Frequency not known:	Itching, exanthema
Rare:	Allergic hypersensitivity reactionsincluding skin reactions (e.g. rash, itching),,
Very rare:	Anaphylaxis
Cardiovascular disorders:	
Frequency unknown	Arrhythmias secondary to hypokalaemia
Gastro intestinal disorders:	
Frequency not known:	Nausea, vomiting, diarrhoea
General disorders:	
Frequency not known:	Fever, dizziness, Injection site reactions including injection site pain, injection site erythema, injection site pruritus, injection site induration and injection site swelling, hot flushes, chills, malaise, pain
Neurological disorders:	
Frequency not known:	Headache, sensory abnormalities such as paraesthesia, tremor
Renal and urinary disorders:	
Frequency unknown	Chromaturia
Skin and subcutaneous tissue disorders:	
Frequency unknown	Acneiform and bullous eruptions

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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL – Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; Email: medsafety@hpra.ie.

4.9 Overdose

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

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Vitamin B_{12}
ATC classification: B03BA03
An intramuscular injection of hydroxocobalamin produces higher serum levels than the same dose of cyanocobalamin and these levels are well maintained

5.2 Pharmacokinetic properties

Vitamin B_{12} is extensively bound to specific plasma proteins called transcobalamins; transcobalamin II appears to be involved in the rapid transport of the cobalamins to tissues. It is stored in the liver, excreted in the bile, and undergoes enterohepatic recycling; part of a dose is excreted in the urine, most of it in the first 8 hours. Vitamin B12 diffuses across the placenta and appears in breast milk.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the Summary of Product Characteristics.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium hydroxide
Glacial acetic acid
Sodium chloride
Water for injection

6.2 Incompatibilities

In the absence of compatibility studies, this product must not be mixed with other medicinal products.

6.3 Shelf life

18 months.

6.4 Special precautions for storage

Do not store above 30°C
Do not freeze.
Store in the original package.

6.5 Nature and contents of container

Clear glass ampoules, 5 x 1 ml

6.6 Special precautions for disposal and other handling

Single use only, discard any unused content.

7 MARKETING AUTHORISATION HOLDER

G.L. Pharma GmbH
Schlossplatz 1
8502 Lannach
Austria

8 MARKETING AUTHORISATION NUMBER

PA1770/002/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 3rd August 2018

Date of last renewal: 21st Day of May 2023

10 DATE OF REVISION OF THE TEXT

September 2022