IRISH MEDICINES BOARD ACTS 1995 AND 2006

MEDICINAL PRODUCTS(CONTROL OF PLACING ON THE MARKET)REGULATIONS,2007

(S.I. No.540 of 2007)

PA0167/097/002
Case No: 2068802

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

Baxter Healthcare Limited

Caxton Way, **Thetford**, **Norfolk IP24 3SE**, **United Kingdom**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

Cernevit, Bioset,Powder for Solution for Injection or Infusion

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **09/04/2010**.

Signed on behalf of the Irish Medicines Board this

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A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Cernevit, Bioset,Powder for Solution for Injection or Infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial of powder contains:

Retinol Palmitate (Vit A)	3500	IU
Colecalciferol (Vit D_3)	220	IU
DL α tocopherol (Vit E)	10.20	mg
- corresponding to α-tocopherol	11.200	IU
Ascorbic acid (Vit C)	125	mg
Cocarboxylase tetrahydrate	5.80	mg
- corresponding to Thiamine (Vit B_1)	3.510	mg
Riboflavin dihydratedsodium phosphate (Vit B_2)	5.67	mg
- corresponding to Riboflavin	4.14	mg
Pyridoxine hydrochloride (Vit B_6)	5.50	mg
- corresponding to Pyridoxine	4.53	mg
Cyanocobalamin (Vit B_{12})	6	micrograms
Folic acid	414	micrograms
Dexpanthenol	16.15	mg
- corresponding to pantothenic acid	17.25	mg
D-Biotin	69	micrograms
Nicotinamide	46	mg

Excipients: Each vial contains 24mg sodium and less than 112.5mg soya oil.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Powder for Solution for injection or infusion.
Orange-yellow sterile cake of lyophilised powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Supply of vitamins corresponding to the daily needs of adults and children over 11 years requiring multi-vitamin supplementation by the parenteral route when oral nutrition is contraindicated, impossible or insufficient (e.g. due to malnutrition, gastrointestinal malabsorption, parenteral nutrition, etc).

4.2 Posology and method of administration

Adults and children aged over 11 years: 1 vial/day.

Method of reconstitution

See 6.6 Instruction for use and handling

Method of administration

Intravenous route- By slow intravenous injection (at least 10 minutes) or by infusion in, for example, isotonic saline or glucose solution.

Cernevit may be included in the composition of nutritive mixtures combining carbohydrates, lipids, amino, acids electrolytes provided that compatibility and stability have been confirmed for each nutritive mixture.

4.3 Contraindications

Pre-existing hyper-vitaminosis or known hypersensitivity to any of the ingredients, in particular patients with hypersensitivity to thiamine (Vitamin B_1), soya or peanuts.

4.4 Special warnings and precautions for use

Anaphylactic reactions may occur in allergic subjects because of the presence of vitamin B_1 and soybean phosphatides.
Mild allergic reactions such as sneezing or mild asthma are warning signs that a further injection may give rise to anaphylactic shock.

Due to glycocholic acid content, repeated and prolonged administration in patients with jaundice of hepatic origin or severe biochemical evidence of cholestasis requires careful monitoring of liver function.

Caution should be exercised when administering Cernevit to patients who may be receiving vitamin A from other sources.

Following IV bolus injection, a moderate rise only in SGPT transaminases has been noted in some patients with active inflammatory enterocolitis. Increased levels are rapidly reversible following the interruption of administration. It is advisable to monitor transaminase levels in patients of this type. Also in the case of impaired kidney function, lipid-soluble vitamin levels should be carefully monitored.

Cernevit does not contain Vitamin K. Vitamin K must be administered separately if necessary.

This medicinal product contains 1.04 mmol sodium per dose. To be taken into consideration by patients on a controlled diet.

4.5 Interaction with other medicinal products and other forms of interaction

The content of pyridoxine may interfere with the effects of concurrent levodopa therapy.
The dosage of drugs known to be influenced by folic acid, for example phenytoin, must be carefully monitored.

4.6 Pregnancy and lactation

This product should not be used in pregnancy or in women breast feeding infants.
Vitamins are excreted in breast milk.

4.7 Effects on ability to drive and use machines

Not applicable

4.8 Undesirable effects

Because of the presence of Vitamin B, and soybean phosphatides, anaphylactic reactions may occur in subjects with underlying allergy (see section 4.3).

Elevation of SGPT transaminases following IV bolus injections in some patients (c.f. special precautions).

4.9 Overdose

Manifestations of Vitamin A hypervitaminosis and Vitamin D hypervitaminosis (symtomatology related to hypercalcaemia) are possible in case of prolonged administration of significant doses of these vitamins.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Balanced association of all water soluble and fat soluble, vitamins essential for the metabolism of the adult and the child aged over 11 years, with the exception of Vitamin K.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Not applicable

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glycine
Glycocholic acid
Soybean phosphatides
Sodium hydroxide (for pH adjustment)
Hydrochloric Acid (for pH adjustment)

6.2 Incompatibilities

None.

6.3 Shelf Life

Unopened: 2 years

Once reconstituted: Chemical and Physical in-use stability has been demonstrated for Cernevit for 24 hours at 25°C when reconstituted with 5ml of Water for Injections.

From a microbiological point of view, the product should be used immediately. If not used immediately, in use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8°C, unless reconstitution/dilution etc has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

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

6.5 Nature and contents of container

Type I Ph.Eur. brown glass vial with a BIO-SET, containing an orange-yellow sterile cake of powder;

Box of 1, 10 or 20 vials of lyophilised powder

Not all pack sizes may be marketed

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

Do not use unless solution is clear and the container is undamaged.

For single use only. Discard any unused content.

Cernevit BIO-SET allows a direct reconstitution in containers (both single or multi-compartment plastic bags) equipped with an injection port.

Mono-bag:

1. Remove the cap by twisting and then pulling to break the security ring.

2. Connect directly the BIO-SET to the bag injection port.

3. Activate the BIO-SET by applying a pressure on the transparent mobile part of the Bio-set. This action punctures the rubber stopper of the vial.

4. Hold vertically the connected system (Cernevit BIO-SET and infusion bag), the bag being on top of it. Gently squeeze the infusion bag several times to transfer the solution into the vial (about 5ml). Agiatte thevila to reconstitute Cernevit.

5. Upturn the connected system and hold it vetically upside down. Gently squeeze the infusion bag several times to move the headspace gas volume into the vial, thus allowing reverse transfer of the solution into the infusion bag.

6. Repeat instructions 4 and 5 until the vial is empty.

7. Remove and discard the Cernevit BIO-SET vial.

Multi-compartment bag:

Reconstitution of CERNEVIT BIO-SET has to be made before activation of the multi-chamber bag (before opening the non-permanent seals and before mixing the content of each department).

1. Place the multi-chamber bag on a bench

2. Remove the cap of Cernevit by twisting and then puling to break the security ring.

3. Connect directly the BIO-SET to the muli-chamber bag injection port.

4. Activate the BIO-SET by applying pressure on the transparent mobile part of the BIO-SET. This action punctures the rubber stopper of the vial.

5. Hold the vial vertically. Gently squeeze the compartment several times to transfer the solution into the vial (about 5ml). Agitate the vial to reconstitute Cernevit.

6. Upturn the connected system, holding the vial vertically upside down. Gently Squeeze the compartment several times to move the headspace gas volume into the vial, thus allowing reverse transfer of the solution into the infusion bag.

7. Repeat step 5 & 6 until the vial is empty.

8. Remove and discard the Cernevit BIO-SET

9. Finally, activate the multi-chamber bag.

Warning:

Take care that there is no disconnection of the BIO-SET fron the injection port during all the reconstitution process.

7 MARKETING AUTHORISATION HOLDER

Baxter Healthcare Ltd.,
Caxton Way,
Thetford,
Norfolk,
IP24 3SE, United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA 167/97/2

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of First Authorisation: 22nd June 2007

Date of last renewal: 4th January 2008

10 DATE OF REVISION OF THE TEXT

April 2010