1.4 Product Information

1.4.1 Prescribing Information

1. NAME OF MEDICINAL PRODUCT

Product name
Dilconeurine Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Qualitative Declaration
Vitamin B1 (Thiamine Hydrochloride)
Vitamin-B6 (Pyridoxine Hydrochloride)
Vitamin B12 (Cyanocobalamine)

Quantitative Declaration
Each Film coated tablet contains:
Vitamin B1 B.P..... 100mg
Vitamin B6 B.P 100mg
Vitamin B12 B.P..... 100mcg

3. PHARMACEUTICAL FORM

Light orange colored Capsular Shaped Film coated tablet

4. CLINICAL PARTICULARS:

4.1 Therapeutic indications

- Vitamin B1, B6 & B12 deficiency leading to mono & polyneuropathy, peripheralneuropathy, Dementia, Beri-Beri etc.
- Alcoholic Polyneuropathy & Wernicke ’s encephalopathy
- Supportive treatment in trigeminal neuralgia

4.2 Posology and Method of Administration

Posology
The recommended dose of Dilconeurine Tablet is one tablet per day.
For treatment during Pregnancy, 1 Tablet daily

Method of administration
Oral use.

4.3 Contra Indications
Hypersensitivity to cobalt, vitamin B12 or any component of this medication.

4.4 Special Warning and Precautions for Use
Pregnancy
Category A: (Category C if used in doses greater than the RDA)

Lactation:
Vitamin B12 is excreted during lactation. Data is not available whether Thiamine is excreted in milk or not.

Deficiency:
Single Vitamin B1 deficiency is rare; suspect multiple vitamin deficiencies.

Wernicke's encephalopathy:
May occur or worsen suddenly in Thiamine-deficient patients given glucose. If deficiency is suspected, give Thiamine before or with dextrose containing fluids.

4.5 Interaction with other medicinal products and other forms of interaction
Interactions common to the combination

Some medicines may interact with Pyridoxine (Vitamin B6).

Hydantoins or Levodopa:
The effectiveness of hydantoins (eg Phenytoin) or Levodopa may be decreased by using Pyridoxine (Vitamin B6).

4.6 Fertility, Pregnancy and Lactation

Pregnancy
Category A: (Category C if used in doses greater than the RDA)

Lactation:
Vitamin B12 is excreted during lactation. Data is not available whether Thiamine is excreted in milk or not.

Fertility
There are no clinical studies on fertility with Dilconeurine.

4.7 Effects on ability to drive and use machines

N/A

4.8 Undesirable Effects

In the following, the undesirable effects are classified by organ system and frequency. The assessment of undesirable effects is based on the following frequency grouping:

- Very common (≥1/10)
- Common (≥1/100, <1/10)
- Uncommon (≥1/1.000, <1/00)
- Rare (≥1/10.000, <1/1.000)
- Very rare (<1/10.000),
- Unknown (frequency not estimatable on the basis of the data available)

Nervous system disorders:

- Unknown: Long-term intake (> 6-12 months) of a daily dosage > 50 mg vitamin B6 may cause peripheral sensory neuropathy.

Gastrointestinal disorders:

- Unknown: Gastrointestinal complaints such as nausea, vomiting, diarrhoea and abdominal pain.

Immune system disorders:

- Very rare: Hypersensitivity reactions such as sweating, tachycardia and skin reactions like itching and urticaria.

4.9 Overdoses:

High doses of B6 can cause nerve damage, light sensitivity and painful skin lesions.

Symptoms:
The symptoms of over dose may include Excessive thirst, Skin conditions, Blurry vision, Abdominal cramp, Nausea, Vomiting, Increased urination, Diarrhea, Skin flushing

5. Pharmacological properties

5.1 Pharmacodynamic properties:

Pharmacotherapeutic group: Vitamin B1 in combination with vitamin B6 and/or vitamin B12

ATC code: A11DB

Mechanism of action: Dilconeurine coated tablets contain a combination of neurotropic active substances of the vitamin B complex. The vitamins thiamine (B1), pyridoxine (B6) and cobalamin (B12) contained play a particular role as coenzymes in the intermediary metabolism of the central and peripheral nervous system. Like all other vitamins, they are essential nutrients which the body cannot synthesize itself. Therapeutic supply of vitamins B1, B6 and B12 may supplement inadequate nutritive vitamin intake and thus ensure the availability of the required quantities of coenzymes. The therapeutic use of these vitamins in diseases of the nervous system serves, on the one hand, to compensate for concomitant deficiencies (possibly due to an increased requirement induced by the disease) and, on the other, to stimulate natural repair mechanisms.
Models used in animal studies have indicated analgetic activity for vitamin B1.

5.2 Pharmacokinetic properties

Thiamine:
Has after oral administration a dose-dependent dual transport mechanism:
Active absorption up to concentrations of 2 µmol and passive diffusion in concentrations over 2 µmol).

The elimination half-life is approx. 4 hours.
The human body can store approx. 30 mg thiamine. On account of the rapid metabolisation, the reserve capacity, at 4-10 days, is very limited.

Pyridoxine:
Pyridoxine is absorbed very rapidly, mainly in the upper gastrointestinal tract, and is excreted with a maximum between 2 and 5 hours.
Approx. 40 to 150 mg can be stored, 1.7 to 3.6 mg is excreted in the urine per day.

Cobalamin:
Cobalamin is absorbed from the gastrointestinal tract by means of 2 mechanisms:

- Release through gastric acid and immediate binding to the intrinsic factor
- Independently of the intrinsic factor through passive influx in the blood

At doses over 1.5 µg the latter mechanism increases in significance.
Patients with pernicious anaemia absorb approx. 1% of oral doses of 100 µg and over.
Vitamin B12 is stored predominantly in the liver, the daily requirement is 1 µg.
The turnover rate is 2.5 µg B12 per day, or 0.05% of the stored quantity.
Vitamin B12 is mainly secreted into bile and largely reabsorbed during the enterohepatic circulation.

5.3 Pre-clinical safety data

The toxicity of vitamins B1, B6 and B12 is very low. The data available to date do not suggest any potential risk for humans.
The literature available on the subject does not contain any findings indicating that vitamins B1, B6 and B12 have carcinogenic, mutagenic or teratogenic properties.
Chronic toxicity: In animals, very high doses of vitamin B1 cause bradycardia. Other symptoms are blockade of vegetative ganglia and motor end plates. The oral administration of 150–200 mg of vitamin B6/kg body weight/day over a period of 100-107 days caused ataxia, muscular asthenia, disorders of balance, as well as degenerative changes of axons and myelin sheaths in dogs. Animal studies also showed incidences of convulsions and impaired coordination after high doses of vitamin B6.
Mutagenic and tumorigenic potential: Mutagenic effects of vitamin B1 and vitamin B6 are not to be expected under the conditions of clinical use.
There are no long-term animal studies available on the tumorigenic potential of thiamine and vitamin B6.
Reproduction toxicity: Thiamine is transported actively to the foetus. Concentrations in the foetus and the newborn exceed maternal concentrations of vitamin B1. Systematic investigations on human embryonal and foetal development in connection with the use of Vitamin B1 at doses exceeding the stated daily requirements are not available.
Vitamin B6 is insufficiently investigated in animal studies. An embryotoxicity study in rats gave no indications of a teratogenic potential. In male rats the administration of very high doses of vitamin B6 induced damage to spermatogenesis.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients:

For Core

- Vitamin B1 (Thiamine) Hydrochloride
- Vitamin-B6 (Pyridoxine Hydrochloride)
- Vitamin B12 (Cyanocobalamine)
- Avecil pH 102 (Microcrystalline Cellulose)
- Lactose
- Kollidon K-30 (Polyvinylpyrrolidone/Povidone)
- Magnesium Stearate
- Sodium Starch Glycollate (Primogel)
- Isopropyl Alcohol

For Film coating:

- Opadry AMB (80 W53321) Orange Colorcon Limited England
- Opadry Clear OY-S 29019 (Colorcon Limited England)
- Eudragit E 100
- Isopropyl Alcohol

6.2 Incompatibilities

Not applicable.

6.3 Shelf-Life

2 years

6.4 Special Precautions for Storage

- Store at or below 30^{o}C.
- Protect from heat, sunlight and moisture
- Keep out of the reach of children

6.5 Nature and Contents of Container

10 x 10’s tablets packed in ALU-PVDC blister, in bleach board unit carton with leaflet

6.6 Special Precautions for Disposal and other Handling

Not applicable

7 Marketing Authorization Holder and Manufacturing Site Address

Name: CCL Pharmaceuticals (Pvt.) Ltd.
Address: 62-Industrial Estate, Kot Lakhpat, Lahore-54770, Pakistan.
Telephone: +92-42-5114753
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8 Marketing Authorization Number

000739

9 Date of First Authorization / Renewal of Authorization

Date of first authorization	15-08-1976
Date of first renewal	15-08-1981
Date of second renewal	15-08-1986
Date of third renewal	15-08-1991
Date of fourth renewal	15-08-1996
Date of fifth renewal	15-08-2001
Date of sixth renewal	15-08-2006
Date of seventh renewal	15-08-2011
Date of Last renewal	15-08-2016
Date of next renewal	15-08-2021

10 Date of Revision Of The Text

01-01-2021