National Agency for Food & Drug Administration & Control (NAFDAC)

Registration & Regulatory Affairs (R & R) Directorate

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

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1. NAME OF THE MEDICINAL PRODUCT

DOLOWELL TABLTS

(Vitamins B_1 + B_6 + B_{12} + Diclofenac Potassium)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

COMPOSITION:

Each film-coated tablet contains:
Vitamins B_1:……..50mg
Vitamin B_6:……..100mg
Vitamin B_{12}:……..100µg
Diclofenac Potassium BP:……50mg
Excipients:…….q.s.

BP : British Pharmacopoeia

3. PHARMACEUTICAL FORM

Film Coated Tablet

Blue colour caplet

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Diclofenac Tablets is indicated:

1. For relief of the signs and symptoms of osteoarthritis
2. For relief of the signs and symptoms of rheumatoid arthritis
3. For acute or long-term use in the relief of signs and symptoms of ankylosing spondylitis

Systemic neurological disease with demonstrated deficiency of vitamins B1, B6 and B12, which cannot be resolved by correction of diet.

4.2 Posology and Method of Administration

Route of administration: Oral

Adults

One tablet, thrice daily, or as directed by a physician.

4.3 Contraindications

Hypersensitivity to the active substances or to any of the excipients listed in section 6.1. The medicinal product must not be used in severe conduction defects and in acute congestive heart failure. Pregnancy and lactation There are no objections to daily vitamin B6 doses up to 25 mg in pregnancy and lactation. As this medicinal product contains 100 mg/2 ml vial, it should not be used during pregnancy and lactation. Children and elderly Dolowell must not be used in children under 12 years due to the high dose of vitamins and the presence of benzyl alcohol. No special precautions are required in the elderly.

4.4 Special Warnings and Precautions for use

i) Do not exceed the stated dose.

This medicine contains potassium; however, this is less than 1 mmol (39 mg) per dose (2 mL). i.e. essentially “potassium-free”

4.5 Interaction with other medicinal products and other forms of interaction

Thiamine is completely degraded by sulfite-containing solutions. Other vitamins may be inactivated in the presence of vitamin B1 degradation products. Therapeutic doses of vitamin B6 may reduce the effect of L-dopa. Other interactions occur with isonicotinic acid hydrazide (INH) D-penicillamine and cycloserine. After parenteral administration of lidocaine, concurrent administration of epinephrine or norepinephrine increase the incidence of cardiac adverse effects. In case of overdose of local anesthetics, epinephrine and norepinephrine must not used in addition. Other interactions occur with sulfonamides

4.6 Pregnancy and Lactation

Pregnancy There are only insufficient animal studies on the effect of this medicinal product on pregnancy, embryo-fetal, prenatal and post natal development. The possible risk for human beings is not known. The recommended daily allowance (RDA) for thiamine (Vitamin B1) during pregnancy is 1.4mg/day. For pyridoxine (Vitamin B6) the RDA is 1.9 mg/day, the recommended upper limits for pregnant and lactating women are 80 mg/d for women 18 years and younger and 100 mg/d for women over 18 years of age. These doses may only be exceeded during pregnancy if vitamin B1 and B6 deficiency has been confirmed as the safety of administration of higher than the daily recommended doses is not established. The treating physician should decide about the use of this product during pregnancy after carefully weighing the risk-to-benefit ratio. Lactation Vitamins B1, B6 and B12 are secreted into human breast milk. High concentrations of vitamin B6 can inhibit the production of breast milk. Data on the extent of secretion into breast milk from animal studies are not available. Therefore a decision must be made whether to discontinue breast-feeding or to discontinue/abstain from Dolowell solution for injection therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman. Fertility No specific studies with Dolowell solution for injection in humans have been conducted to evaluate effects on fertility.In male rats the administration of very high doses of vitamin B6 induced damage to spermatogenesis (see section 5.3).

4.7 Effects on ability to drive and use machines

Dolowell Tablets has no or negligible influence on the ability to drive and use machines

4.8 Undesirable Effects

Very common: (≥1/10)
Common (≥1/100 to
Uncommon: (≥1/1,000 to

Immune system disorders

Rare: benzyl alcohol may rarely cause anaphylactoid reactions. Not known: hypersensitivity reactions (eg, exanthem, shortness of breath, shock, angioedema)

Nervous system disorders
Not known: dizziness, drowsiness

Cardiac disorders
Not known: bradycardia, arrhythmia, tachycardia

Gastrointestinal disorders
Not known: vomiting

Skin and subcutaneous tissue disorders
Not known: sweating, acne, skin reactions with itching and urticaria have been reported

Musculoskeletal and connective tissue disorders
Not known cramps

4.9 Overdose

If signs of overdose occur, symptomatic treatment by a doctor is required

5.1 Pharmacodynamic Properties

Pharmacodynamic properties Pharmacotherapeutic group: Vitamin preparation / neuropathy preparation ATC code: A11DB01/N07XB52 The neurotropic vitamins of the B complex have a beneficial effect on inflammatory and degenerative diseases of the nervous and musculoskeletal system. They are not used to resolve deficiencies, but have further pharmacological properties at high doses, which explain the analgesic effects achieved by Dolowell. Vitamin B1 has anti-neuritis properties. In the phosphorylated form (TPP) as cocarboxylase it regulates carbohydrate degradation and is used against acidotic metabolic disorders. Vitamin B6 regulates the degradation of protein, fat and carbohydrates. Its neurotropic effect can be used to reduce the inflammation of nerve fibers during therapy with isonicotinic acid hydrazide. It also reduces extrapyramidal symptoms by acting on brain stem. Vitamin B12 is essential for cell metabolism, normal hematopoiesis, and the function of the nervous system. It catalyzes nucleic acid synthesis and hence the construction of new cell nuclei. High doses of vitamin B12 also show analgesic properties.

5.2 Pharmacokinetic Properties

Thiamine is absorbed by an active transport process from the intestinal lumen. Absorption is limited to 8-15 mg daily. Approx. 1 mg Thiamine is degraded in the organism daily: excess thiamine is excreted in the urine. For the determination of vitamin B6 status, the tryptophan load test may be used. After an oral load of 0.1 g / kg body weight of L-Tryptophan the excretion of xanthurenic acid is generally less than 30 mg/24 hours. A higher excretion of xanthurenic acid indicates the presence of vitamin B6 deficiency. Pyridoxine, pyridoxal, and pyridoxamine are absorbed very rapidly and oxidation occurs by phosphorylation to pyridoxal-5-phosphate (PALP) and pyridoxal. The main excreted metabolite is 4- pyridoxic acid. Vitamin B12 released from the food during digestion binds to intrinsic factor (IF). IF is a glycoprotein produced by the parietal cells of the fundus and body of the stomach. The vitamin B12 - IF complex is resistant to proteolytic enzymes, and reaches the terminal ileum, where it binds to specific epithelial cell receptors to ensure the absorption of the vitamin. Vitamin B12 is transported through the mucosa to the capillary circulation, where it is bound to a transport protein. This complex is rapidly taken up by the liver, bone marrow and other proliferating cells. Absorption is impaired in patients with lack of intrinsic factor, in patients with malabsorption or with diseases or changes in intestine after gastrectomy, or in the presence of autoimmune antibodies. From food only 1.5 to 3.5 micrograms of vitamin B12 are usually absorbed. Vitamin B12 is excreted in the bile and enters the enterohepatic circulation. Vitamin B12 is excreted in placenta.

5.3 Preclinical Safety Data

In animals very high doses of vitamin B1 cause bradycardia. In addition, symptoms of blockade of the autonomic ganglia and muscle end plate occurs. The oral administration of 150-200 mg of vitamin B6 (pyridoxine hydrochloride) / kg / bw / day over a period of 100-107 days caused ataxia, muscle weakness, balance problems, and degenerative changes of the axons and myelin sheaths in dogs. In addition, convulsions and ataxia occurred in animals after high doses of vitamin B6. High doses of vitamin B12 (cyanocobalamin) in rats, administered intravenously three times per week at the doses 1, 5, 25 or 100 mg / kg/ bw for 26 weeks did not result in clinical symptoms of toxicity. No gross pathology and no pathohistology of the organs were conducted. Mutagenicity, Carcinogenicity: Under the conditions of clinical vitamin B1, B6 and B12 are not considered to pose any relevant genotoxic potential. Long-term studies in animals to the cancerogenic potential of vitamin B1, B6 and B12 are not available. Lidocaine was not genotoxic and the carcinogenic potential of lidocaine has not been studied. The lidocaine metabolite 2,6-xylidine has genotoxic potential in vitro. In a carcinogenicity study of rats exposed to 2,6-xylidine in utero, postnatally and throughout their lifetime, tumours in the nasal cavity, subcutaneous tumours and liver tumours

were observed. The clinical relevance of tumour findings in relation to short-term/intermittent use of lidocaine in humans is unknown. 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 B1at doses exceeding the stated daily requirements are not available. Vitamin B6 is insufficiently investigated in animal studies. An embryo toxicity 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. There are no data on possible adverse effects of excess of vitamin B12 intake on reproduction, development or lactation in animals or humans.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Starch 135mg

Dextrin 142mg

Microcrystalline Cellulose 35mg

Sodium Starch Glycolate 14mg

Low-Substituted Hydroxypropyl Cellulose 35mg

6.2 Incompatibilities

Thiamine is incompatible with oxidizing and reducing substances, mercury chloride, iodide, carbonate, acetate, ferrous sulfate, tannic acid, ferric ammonium citrate, as well as phenobarbital sodium, riboflavin, benzylpenicillin, glucose and metabisulfite. Copper advances the degradation of thiamine; furthermore, increasing pH values (> pH 3) reduce the activity of thiamine. Vitamin B12 is incompatible with oxidizing and reducing substances, and with heavy metal salts. In solutions containing thiamine, vitamin B12 as well as other components of the B-complex is quickly destroyed by decomposition products of thiamine (low concentrations of iron ions may prevent this degradation). Riboflavin also has a destructive effect, especially with concomitant light exposure. Nicotinamide accelerates the photolysis, while antioxidants inhibit it.

6.3 Shelf Life

36 months

6.4 Special Precautions for Storage

Do not store above 30°C. Protect from light & moisture.

6.5 Nature and contents of container

Pack of 10 Tablets (Alu-Alu blister)

6.6 Special precautions for disposal and other handling

No special requirement

Keep out of the reach of children.

7.0 MARKETING AUTHORIZATION HOLDER

MANUFACTURED BY:
Jiansgu Ruinian Qianjin Pharm. Co., Ltd.
Chuanbu Village, Dingshu Town, Yixing City.
Jiangsu Province, China.

MARKETED BY:
Freshborn Industries Limited, Lagos, Nigeria.