SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

1. NAME OF THE MEDICINAL PRODUCT

Dolo-Meta B® Tablet (Vitamins B1+B6+B12+Diclofenac Sodium)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains:

Vitamin B1 50mg

Vitamin B6 100mg

Vitamin B12 100mcg

Diclofenac Sodium 50mg

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Tablet

4. Clinical particulars

4.1 Therapeutic indications

Musculoskeletal and joint disorder, inflammation, pain, neuralgia and neuritis (Neuropathies).

4.2 Posology and method of administration

Posology

Adults and children over 12 years of age:

10 mg once daily. The tablet may be taken without regard to mealtime.

Children 2 to 12 years of age with:

Body weight more than 30 kg: 10 mg once daily.

Body weight 30 kg or less: These tablets are not suitable in children with a body weight less than 30 kg.

Efficacy and safety of Loratadine Tablets in children under 2 years of age has not been established.

Patients with severe liver impairment should be administered a lower initial dose because they may have reduced clearance of loratadine. An initial dose of 10 mg every other day is

recommended for adults and children weighing more than 30 kg, and for children weighing 30 kg or less, 5 ml (5 mg) every other day is recommended.

No dosage adjustments are required in the elderly or in patients with renal insufficiency.

Method of administration

For oral administration.

4.3 Contraindications

Dolo-Meta B® is contra-indicated in patients with hypersensitivity to any of its components.

Aviod use in the presence of peptic ulcer, pregnancy, lactation hypersensitivity (e.g. asthma attacks) to acetylsalicylic acid or other NSAID agent, severe disorders of liver function in haemopoietic disorders.

4.4 Special warnings and precautions for use

Should be use with caution in patients with evidence of peptic ulcer, those with unexplained gastrointestinal disorders, those with liver of kidney damage and those with high blood pressure, elderly.

4.5 Interaction with other medicinal products and other forms of interaction

Because of Diclofenac Sodium as an active ingredient, avoid concomitant administration with other NSAID. Anticoagulants, probenecid, diuretic, Beta-blocker, Codicosleroids, Oral anti-diabetics, cyclosporine, digoxin.

4.6 Pregnancy and Lactation

Pregnancy:

Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/foetal development. Data from epidemiological studies suggest an increased risk of miscarriage and of cardiac malformation and gastroschisis after use of a prostaglandin synthesis inhibitor in early pregnancy. The absolute risk for cardiovascular malformation was increased from less than 1%, up to approximately 1.5 %.

The risk is believed to increase with dose and duration of therapy. In animals, administration of a prostaglandin synthesis inhibitor has been shown to result in increased pre- and post-implantation loss and embryo-foetal lethality.

In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period. If diclofenac is used by a woman attempting to conceive, or during the first and second trimester of

pregnancy, the dose should be kept as low and duration of treatment as short as possible.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the foetus to:

- cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension);

- renal dysfunction, which may progress to renal failure with oligo-hydroamniosis;

the mother and the neonate, at the end of pregnancy, to:

- possible prolongation of bleeding time, an anti-aggregating effect which may occur even at very low doses.

- inhibition of uterine contractions resulting in delayed or prolonged labour.

Consequently, diclofenac sodium tablets are contraindicated during the third trimester of pregnancy.

Breast-feeding:

Like other NSAIDs, diclofenac passes into the breast milk in small amounts. Therefore, diclofenac should not be administered during breast feeding in order to avoid undesirable effects in the infant (see section 5.2).

Femaile Fertility

As with other NSAIDs, the use of diclofenac may impair female fertility and is not recommended in women attempting to conceive. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of diclofenac should be considered (see also section 4.4 regarding female fertility).

4.7 Effects on ability to drive and use machines

In clinical trials that assessed driving ability, no impairment occurred in patients receiving loratadine. Loratadine tablets has no or negligible influence on the ability to drive and use machines. However, patients should be informed that very rarely some people experienced drowsiness, which may affect their ability to drive or use machines.

4.8 Undesirable effects

Gastrointestinal upsets upper abdominal pain, nausea, diarrhea, light headedness of headaches at the start of treatment. These effects are generally mild and usually regress after a few days.

Hypersensitivity reaction such as skin rash and pruritus, asthma attacks and a tendency to oedema may arise.

4.9 Overdose

Overdosage with loratadine increased the occurrence of anticholinergic symptoms. Somnolence, tachycardia, and headache have been reported with overdoses.

In the event of overdose, general symptomatic and supportive measures are to be instituted and

maintained for as long as necessary. Administration of activated charcoal as a slurry with water may be attempted. Gastric lavage may be considered. Loratadine is not removed by haemodialysis and it is not known if loratadine is removed by peritoneal dialysis. Medical monitoring of the patient is to be continued after emergency treatment.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

Pharmacotherapeutic group

Non-steroidal anti-inflammatory drugs (NSAlDs).

Mechanism of action:

Diclofenac sodium is a non-steroidal agent with marked analgesic/anti inflammatory properties. It is an inhibitor of prostaglandin synthetase, (cyclo-oxygenase).

Diclofenac sodium in vitro does not suppress proteoglycan biosynthesis in cartilage at concentrations equivalent to the concentrations reached in human beings.

5.2 Pharmacokinetic properties

Absorption

Absorption is complete but onset is delayed until passage through the stomach, which may be affected by food which delays stomach emptying. The mean peak plasma diclofenac concentration reached at about 2 hours (50mg dose produces 1511± 466 ng/ml).

Bioavailability:

About half of the administered diclofenac is metabolised during its first passage through the liver ("first-pass" effect), the area under the concentrations curve (AUC) following oral administration is about half that following an equivalent parenteral dose.

Pharmacokinetic behaviour does not change on repeated administration. Accumulation does not occur, provided the recommended dosage intervals are observed.

Distribution

The active substance is 99.7% protein bound, mainly to albumin (99.4%).

Diclofenac enters the synovial fluid, where maximum concentrations are measured 2-4 hours after

the peak plasma values have been attained. The apparent half-life for elimination from the synovial fluid is 3-6 hours. Two hours after reaching the peak plasma values, concentrations of the active substance are already higher in the synovial fluid than they are in the plasma and remain higher for up to 12 hours.

Diclofenac was detected in a low concentration (100 ng/mL) in breast milk in one nursing mother. The estimated amount ingested by an infant consuming breast milk is equivalent to a 0.03 mg/kg/day dose (see section 4.6).

Metabolism

Biotransformation of diclofenac takes place partly by glucuronidation of the intact molecule, but mainly by single and multiple hydroxylation and methoxylation, resulting in several phenolic metabolites, most of which are converted to glucuronide conjugates. Two phenolic metabolites are biologically active, but to a much lesser extent than diclofenac.

Elimination

The total systemic clearance of diclofenac in plasma is 263 ± 56 mL/min (mean value ± SD). The terminal half-life in plasma is 1-2 hours. Four of the metabolites, including the two active ones, also have short plasma half-lives of 1-3 hours.

About 60% of the administered dose is excreted in the urine in the form of the glucuronide conjugate of the intact molecule and as metabolites, most of which are also converted to glucuronide conjugates. Less than 1% is excreted as unchanged substance. The rest of the dose is eliminated as metabolites through the bile in the faeces.

Characteristics in patients

Elderly: No relevant age-dependent differences in the drug's absorption, metabolism, or excretion have been observed, other than the finding that in five elderly patients, a 15 minute iv infusion resulted in 50% higher plasma concentrations than expected with young healthy subjects.

Patients with renal impairment: In patients suffering from renal impairment, no accumulation of the unchanged active substance can be inferred from the single-dose kinetics when applying the usual dosage schedule. At a creatinine clearance of less than 10 mL/min, the calculated steady-state plasma levels of the hydroxy metabolites are about 4 times higher than in normal subjects.

However, the metabolites are ultimately cleared through the bile.

Patients with hepatic impairment: In patients with chronic hepatitis or non-decompensated cirrhosis, the kinetics and metabolism of diclofenac are the same as in patients without liver disease.

5.3 Preclinical safety data

Non stated.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hypromellose, Microcrystalline Cellulose, Sodium Starch Glycolate, Magnesium Stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store in a cool dry place below 30°C and protect from light.

KEEP MEDICINES OUT OF REACH OF CHILDREN

6.5 Nature and contents of container

Primary package is aluminum foil/PVC panel

100 tablets per box

6.6 Special precautions for disposal

Any unused product or waste material should be disposed of in accordance with local requirements.

7. APPLICANT/MANUFACTURER

Name: Jiangsu Ruinian Qianjin Pharmaceutical Co., Ltd.

Address: Chuanbu Village, Dingshu Town, Yixing City, Jiangsu Province, China

Tel: +86-0510-7155090

Fax: +86-0510-7155086

Email: wuzhijuan@hotmail.com