DIZPHARM PARACETAMOL TABLETS 500MG

1. **Name of the medicinal product**
Dizpharm Paracetamol 500mg Tablets

2. Qualitative and quantitative composition
Each uncoated tablet contains Paracetamol BP 500mg
For the full list of excipients, see section 6.1

3. Pharmaceutical form
Tablet.
White, circular, flat beveled-edge, uncoated tablets de-bossed **"P", "Break line" and 500"** on one side and **"DIZPHARM"** in circular form on the other side.

4. Clinical particulars
4.1 Therapeutic indications
Dizpharm Paracetamol has analgesic and antipyretic properties similar to those of Aspirin, and is recommended for the treatment of most painful and febrile conditions, for example, headache including migraine, toothache, neuralgia, colds and influenza, sore throat, backache, rheumatic pain and dysmenorrhoea.

4.2 Posology and method of administration
4.2.1 Posology
- Adults: 1 to 2 tablets up to 3 times daily.
- Children 12 years and older: 1 tablet up to 3 times daily.
- Children from 6 to 12 years old: 1/2 to 1 tablet up to 3 times a day

Method of administration
Oral administration

4.3 Contraindications
Hypersensitivity to the active substance or to any of the excipients listed in section 6.1

4.4 Special warnings and precautions for use
Paediatric population
Not recommended for children under the age of 10 years.
Care is advised in the administration of paracetamol to patients with severe renal or severe hepatic impairment. The hazard of overdose is greater in those with non-cirrhotic alcoholic liver disease.
Do not exceed the recommended dose.
Do not take for more than 3 days without consulting a doctor.
Do not take with any other paracetamol-containing products.
If symptoms persist consult your doctor.
Keep out of the reach of children.

4.5 Interaction with other medicinal products and other forms of interaction
• Colestyramine – may reduce absorption if given within one hour of Paracetamol.

• Anticoagulants - the effect of warfarin and other coumarins may be enhanced by prolonged regular use of Paracetamol with increased risk of bleeding. Occasional doses have no significant effect.
• Metoclopramide – may increase speed of absorption of Paracetamol.
• Domperidone – may increase speed of absorption of Paracetamol.
• Imatinib - restriction or avoidance of concomitant regular Paracetamol use should be taken with imatinib.

4.6 Fertility, pregnancy and lactation

Pregnancy

Epidemiological studies in human pregnancy have shown no ill effects due to paracetamol used in the recommended dosage, but patients should follow the advice of their doctor regarding its use. A large amount of data on pregnant women indicate neither malformative, nor feto/neonatal toxicity. Epidemiological studies on neurodevelopment in children exposed to paracetamol in utero show inconclusive results. If clinically needed, paracetamol can be used during pregnancy if clinically needed however it should be used at the lowest effective dose for the shortest possible time and at the lowest possible frequency.

Breastfeeding

Paracetamol is excreted in breast milk but not in a clinically significant amount. Available published data do not contraindicate breast feeding.

4.7 Effects on ability to drive and use machines

Paracetamol has no influence on the ability to drive and use machines.

4.8 Undesirable effects

In therapeutic doses, paracetamol has only few undesirable effects

The frequencies of adverse reactions reported with paracetamol are defined as:

- very common (≥ 1/10)
- common (≥ 1/100 to < 1/10)
- uncommon (≥ 1/1,000 to < 1/100)
- rare (≥ 1/10,000 to < 1/1,000)
- very rare (< 1/10,000)
- not known (cannot be estimated from the available data)

System organ class	Frequency	Undesirable effects
Blood and lymphatic system disorders	Rare:	Thrombocytopenia, leukopenia, pancytopenia, neutropenia, haemolytic anaemia, agranulocytosis
	Not known	Anaemia
Immune system disorders	Rare	Allergic reactions
	Very rare	Allergic reactions requiring treatment stop
	Not known	Anaphylactic choc
Metabolism and nutrition disorders	Very rare	Hypoglycaemia

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System organ class	Frequency	Undesirable effects
Psychiatric disorders	Rare	Depression*, confusion, hallucinations
Nervous system disorders	Rare	Tremor *, headache *
Eye disorders	Rare	Abnormal vision
Cardiac disorders	Rare	Oedema
Respiratory, thoracic and mediastinal disorders	Not reported	Not reported
Gastrointestinal disorders	Rare	Haemorrhage *, abdominal pain *, diarrhoea *, nausea, vomiting, constipation
Hepatobiliary disorders	Rare	Decreased hepatic function, liver failure, hepatic necrosis, jaundice
	Very rare:	Hepatotoxicity
	Not known	Hepatitis
Skin and subcutaneous tissue disorders	Rare	Pruritus, rash, sweating, purpura, angioedema, urticaria
	Very rare	Severe skin reactions
Renal and urinary disorders	Very rare	Sterile pyuria (cloudy urine) and renal adverse events
	Not Known	Neuropathies (interstitial nephritis, tubular necrosis) with long-term use of high doses
General disorders and administration site conditions	Rare	Dizziness (except vertigo), malaise, pyrexia, sedation, drug interaction*
Injury, poisoning and procedural complications	Rare	Overdose and intoxication

*Without specifications

4.9 Overdose

An overdose with paracetamol may be fatal.

- Symptoms of paracetamol intoxication include nausea, vomiting, anorexia, pallor, and abdominal pain. These symptoms usually appear within 24 hours of taking the overdose.
- A paracetamol overdose of 10 g or more in a single dose in adults or 150 mg / kg body weight in a single dose in children results in hepatic cytolysis that may result in complete and irreversible necrosis resulting in hepatocellular insufficiency, metabolic acidosis, and encephalopathy may lead to coma and death.
- At the same time, hepatic transaminases (ASAT, ALT), lactic dehydrogenase, and bilirubin levels were observed to increase, with prothrombin levels decreasing 12 to 48 hours after ingestion of the overdose.
- Clinical signs of liver injury usually appear after two days and peak after 4-6 days. Even in the absence of severe hepatic injury, acute renal failure with acute tubular necrosis may occur.
- Other non-hepatic symptoms of paracetamol overdose may be myocardial alterations and pancreatitis.

Emergency treatment

- Immediate hospitalization.
- After an overdose, a blood sample should be taken to determine the paracetamol level as soon as possible before starting treatment.
- Rapid evacuation of the ingested product by gastric lavage, then administration of active charcoal (adsorbent) and sodium sulphate (laxative).
- Dialysis may reduce the plasma concentration of paracetamol.
- The treatment consists of the administration of the antidote N-acetylcysteine (NAC), intravenously or orally, if possible before the tenth hour after ingestion of the overdose. NAC treatment may result a protective effect even after 10 hours when given as a prolonged treatment.
- Symptomatic treatment.
- Liver tests should be performed at the beginning of treatment and repeated every 24 hours. In most cases, hepatic transaminases will return to normal levels within one to two weeks, and liver function will be fully restored. However, in very rare cases, liver transplantation may be indicated.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other analgesics and antipyretics, Anilides ATC code N02B E01
Paracetamol has both analgesic and antipyretic effect. However, it has no anti-inflammatory effect. The mechanism of analgesic action has not been fully determined. The main action of paracetamol is the inhibition of cyclo-oxygenase, an important enzyme in the synthesis of prostaglandin. Cyclo-oxygenase in the central nervous system is more sensitive to paracetamol than peripheral cyclo-oxygenase, which is why paracetamol has antipyretic and analgesic efficacy. Paracetamol probably produces antipyretics by acting centrally on the hypothalamic centre of thermoregulation.

5.2 Pharmacokinetic properties

Absorption
Paracetamol is rapidly and completely absorbed after oral administration. Peak plasma concentration is reached within two hours.
Distribution
Paracetamol is poorly bound to plasma proteins (20 to 50%) and its diffusion is rapid.
Metabolism and elimination
Paracetamol is metabolized in the liver and is then eliminated in the urine, mainly in two forms: glucuronoconjugate (60 to 80%) and sulfoconjugate (20 to 40%). A small fraction (less than 4%) is transformed in the liver by cytochrome P 450 into a metabolite that is involved in the paracetamol hepatotoxicity. At therapeutic doses, this toxic metabolite is eliminated by conjugation with glutathione. The conjugation capacity is not modified in the elderly and the kinetics is linear for doses up to 7 g. In case of massive overdose, the conjugation capacity is exceeded, and the fraction of the hepatotoxic metabolite increases.

5.3 Preclinical safety data

- In toxicity studies in rats and mice, gastrointestinal lesions, changes in blood counts, degeneration of hepatic and renal parenchyma, and necrosis have been observed. These changes are attributed to both the mechanism of action and the metabolism of paracetamol.

- Extensive research has not shown any relevant genotoxic risk of paracetamol at therapeutic dose.
- Long-term studies in rats and mice showed no relevant carcinogenic effects at non-hepatotoxic doses of paracetamol.
- Paracetamol passes the placental barrier.
- Studies in animals have shown no reproductive toxicity.

6. Pharmaceutical particulars

6.1 List of excipients

Maize starch
Purified talc
Magnesium stearate
Gelatin 180 bloom
Methyl paraben
Propyl paraben
Purified water

6.2 Incompatibilities

None known

6.3 Shelf life

48 months.

6.4 Special precautions for storage

Store below 30°C, in original pack to protect from humidity.

6.5 Nature and contents of container

Polypropylene containers
Pack sizes: 1000

6.6 Special precautions for disposal and other handling

No special requirements for disposal. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing authorization holder

DIZPHARM NIGERIA LIMITED
Km 10, Ibusa Road, Ibusa, Delta State, Nigeria.

9. Date of first authorization/renewal of the authorization

Not Applicable

10. Date of revision of the text

Not Applicable