IDAMAN PHARMA MANUFACTURING

FEPRIL TABLET 500MG

PRODUCT DESCRIPTION
Round and biconvex tablets with one side scored. White to off white in colour.

Each tablet contains: Paracetamol 500mg

Preservative:-
Potassium Sorbate: 0.58mg

ROUTE OF ADMINISTRATION
Oral

PHARMACODYNAMICS
Paracetamol is a centrally acting analgesic and antipyretic with minimal anti-inflammatory properties.

Analgesic
The mechanism of analgesic action has not been fully determined. Paracetamol may act predominantly by inhibiting prostaglandin synthesis in the central nervous system (specifically cyclooxygenase (COX)-2) and, to a lesser extent, through a peripheral action by blocking pain impulse generation.

The peripheral action may also be due to inhibition of prostaglandin synthesis or to inhibition of the synthesis or actions of other substances that sensitize pain receptors to mechanical or chemical stimulation.

Antipyretic
Paracetamol act centrally on the hypothalamic heat-regulating center to produce peripheral vasodilatation resulting in increased blood flow through the skin, sweating and heat loss.

Paracetamol reduces fever by inhibiting the formulation and release of prostaglandins in the CNS and by inhibiting endogenous pyrogens at the hypothalamic thermoregulator center.

PHARMACOKINETICS
Absorption
After oral administration Paracetamol is rapidly and almost completely absorbed. Peak plasma concentrations are reached after 30 minutes to 2 hours.

Distribution
Paracetamol is distributed rapidly throughout all tissues. Concentrations are comparable in blood, saliva and plasma.
The volume of distribution of Paracetamol is approximately 1 L/kg bodyweight. At therapeutic doses protein binding is negligible.

Metabolism
In adults, paracetamol is conjugated in the liver with glucuronic acid (~60%), sulphate (~35%) conjugates. The latter route is rapidly saturated at doses higher than the therapeutic dose. A minor route, catalyzed by the cytochrome P450, results in the formation of an intermediate reagent (N acetyl-p-benzoquinoneimine) which under normal conditions of use is rapidly detoxified by glutathione and eliminated in the urine, after conjugation with cysteine (~3%) and mercaptopuric acid.

In neonates and children <12 years sulphate conjugation is the main elimination route and glucuronidation is lower than in adults. Total elimination in children is comparable to that in adults, due to an increased capacity for sulphate conjugation.

Elimination
Elimination of Paracetamol is essentially through the urine. 90% of the ingested dose is eliminated via the kidneys within 24 hours, predominantly as the glucuronide (60 to 80%) and the sulphate (20 to 30%) conjugates. Less than 5% is eliminated in unchanged form. The elimination half-life is about 2 hours.

In cases of renal or hepatic insufficiency, after overdose, and in neonates the elimination half-life of paracetamol is delayed. The maximum effect is equivalent with plasma concentrations. For elderly patients, the capacity for conjugation is not modified.

INDICATIONS
Mild to moderate pain and pyrexia.

RECOMMENDED DOSAGE
Adults and children aged 12 years and over:-
500mg to 1g paracetamol, taken every 4-6 hours as required up to a maximum of 4 g daily.

Children:-
7 to 12 years:
250mg -500mg every 4 to 6 hours as required.

CONTRAINDICATIONS
Hypersensitivity to paracetamol or any of the other ingredients/components of the product. Severe and active hepatic impairment.

WARNING & PRECAUTIONS

This preparation contains PARACETAMOL. Do not take any other paracetamol containing medicines at the same time.

Allergy Alert: Paracetamol may cause severe skin reactions. Symptoms may include skin reddening, blisters or rash. These could be signs of a serious condition. If these reactions occur, stop use and seek medical assistance right away.

Paracetamol should be given with care to patients with impaired kidney or liver function. Large doses should be avoided in patients with hepatic impairment. Paracetamol overdose may harm the liver. Do not exceed recommended dose.

For paediatric population, the hazard of overdose is greater in those with non-cirrhotic alcoholic liver disease. Do not take paracetamol for more than 3 days without consulting a doctor. Immediate medical advice should be sought in the event of an overdose even if you feel well, because of the risk of delayed, serious liver damage.

Paracetamol provides symptomatic relief only, additional therapy to treat the cause of the pain or fever should be instituted when necessary. It should be given with care to patients with alcohol dependence.

Paracetamol must also be used in cautions in patient with known G6PD deficiency, chronic malnutrition or dehydration, weight <50kg, children, pregnancy and lactation.

Do not take if allergic to paracetamol. Patients should contact their health care provider if symptoms persist (if the pain lasts for more than 10 days, if there is redness or fever lasts more than 3 days).

INTERACTIONS WITH OTHER MEDICAMENTS

The speed of absorption of paracetamol may be increased by metoclopramide or domperidone and absorption reduced by cholestyramine. The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular daily use of paracetamol with increased risk of bleeding; occasional doses have no significant effect.

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. 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.

Lactation

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

SIDE/ADVERSE EFFECTS

Cutaneous hypersensitivity reactions including skin rashes, angioedema, Stevens Johnson Syndrome/Toxic Epidermal Necrolysis have been reported.

Adverse effects of paracetamol are rare and usually mild, although haematological reactions have been reported.

Hypotension and tachycardia were rarely reported.

Immune system disorders: Hypersensitivity including skin rash may occur such as anaphylactic shock and angioedema.

Blood and lymphatic system disorders: Blood dyscrasias including thrombocytopenia, leucopenia, neutropenia, pancytopenia, methaemoglobinaemia and agranulocytosis.

Skin and subcutaneous disorders: Very rare cases of serious skin reactions such as Toxic Epidermal Necrolysis (TEN), Stevens-Johnson syndrome (SJS), acute generalised exanthematous pustulosis, fixed drug eruption have been reported.

Gastrointestinal disorders: Nausea, vomiting, constipation.

Nervous system disorders: Headache.

Psychiatric disorders: Insomnia.

Skin and subcutaneous tissue disorders: Erythema, flushing, pruritus.

Potentially Fatal: Hepatotoxicity, acute renal tubular necrosis.

SYMPTOMS & TREATMENT OVERDOSE

Symptoms

Acute Paracetamol intoxication can progress in several phases.

The symptoms of Paracetamol over dosage in the first two days are nausea, vomiting, anorexia, pallor and abdominal pain. Slight intoxication is limited to these symptoms.

When intoxication is more severe, subclinical symptoms as increased liver enzymes appear. From 2 to 4 days after exposure, clinical symptoms of liver damage are manifest, such as painful hepatomegaly, jaundice, encephalopathy, coma and disturbed blood clotting, all secondary to liver insufficiency. Insufficient kidney functioning (tubule necrosis) is rare. Severe intoxication may result in metabolic acidosis may occur.

Treatment

Local treatment guidelines for Paracetamol overdose should be followed. Directly after intake of a Paracetamol overdose, possibly leading to severe intoxication, absorption decreasing therapy can be applied such as gastric lavage within one hour of intake or administration of activated charcoal.

N-acetyl cysteine (NAC) can be administered as antidote. For administration of NAC and further treatment, the concentration of paracetamol in blood should be determined. In general, intravenous administration of NAC is preferred and should be continued until paracetamol is no longer detectable. It is important to realize that intake of NAC up to 36 hours after intake can improve prognosis. Oral administration of NAC should not be combined with oral activated charcoal

Liver tests have to be performed at the start of treatment and need to be repeated each 24 hours after treatment. In most cases, hepatic transaminases will return to normal levels within two weeks after intake of overdose with complete recovery of liver function. In rare cases, liver transplantation may be required.

EFFECTS ON ABILITY TO DRIVE & USE MACHINE

It is unlikely to impair a patient's ability to drive or use machinery.

PACK SIZES

Blister pack of 10 tablets:
i) 10 strips of 10 tablets
ii)100 strips of 10 tablets

STORAGE CONDITION

Keep in a dry place, below 30°C; Protect from light.

INSTRUCTIONS FOR USE

Not Applicable.

SHELF LIFE

2 years from the date of manufacture

REGISTRATION NUMBER

MAL19912157XZ

KEEP MEDICINES OUT OF REACH OF CHILDREN
JAUHI UBAT-UBATAN DARI KANAK-KANAK

For further information, please consult your doctor or your pharmacist.

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Lt-032.01 PRODUCT REGISTRATION HOLDER AND MANUFACTURER
IDAMAN PHARMA MANUFACTURING SDN BHD (661901-P)
LOT 24 & 25, JALAN PERUSAHAAN LAPAN,
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KEDAH DARUL AMAN, MALAYSIA.