PARAFAST Tablets (Paracetamol)

**Composition**

PARAFAST 500 Tablets
Each tablet contains Paracetamol 500 mg

**Dosage Form**

Tablet

**Pharmacology**

- **Pharmacodynamics**

Paracetamol is an effective analgesic and antipyretic agent but has only weak anti-inflammatory properties. Its mechanism of action is not fully understood.

It has been suggested that it may act predominantly by inhibiting prostaglandin synthesis in the CNS 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.

Paracetamol probably produces an antipyretic action by a central effect on the hypothalamic heat-regulating centre to produce peripheral vasodilation resulting in increased blood flow through the skin, sweating and heat loss. The central action probably involves inhibition of prostaglandin synthesis in the hypothalamus. The drug has no effect on the cardiovascular and respiratory systems, and unlike salicylates it does not cause gastric irritation or bleeding.

- **Pharmacokinetics**

Paracetamol is readily absorbed from the gastro-intestinal tract with peak plasma concentrations occurring about 30 minutes to 2 hours after ingestion. It is metabolized in the liver and excreted in the urine mainly as the glucuronide and sulphate conjugates. Less than 5% is excreted as unchanged paracetamol. The elimination half-life varies from about 1 to 4 hours. Plasma-protein binding is negligible at usual therapeutic concentrations but increases with increasing concentrations.

A minor hydroxylated metabolite which is usually produced in very small amounts by mixed-function oxidases in the liver and which is usually detoxified by conjugation with liver glutathione may accumulate following paracetamol overdose and cause liver damage.

**Indications**

For the treatment of mild to moderate pain including headache, migraine, neuralgia, toothache, sore throat and dysmenorrhea. For the symptomatic relief of rheumatic and muscular aches and pains sciatica, fibrositis, lumbago, joint
swelling and stiffness.
For symptomatic relief of influenza, feverish colds and feverishness

**Dosage And Administration**

Adults, the elderly and young person's over 12 years:
2 tablets every 4 hours to a maximum of 8 tablets in 24 hours

Children 6 - 12 years:
1/2 to 1 tablet every 4 hours to a maximum of 4 tablets in 24 hours.

*Do not give to children aged below 6 years*

The dose should not be repeated more frequently than every four hours, and not more than four doses should be taken in any 24 hour period.

Dosage should not be continued for longer than 3 days without consulting a doctor.

**Contraindications**

Hypersensitivity to paracetamol or any of the constituents

**Warnings And Precautions**

➤ **Drug Interactions**

Cholestyramine
The speed of absorption of paracetamol is reduced by cholestyramine. Therefore, the cholestyramine should not be taken within one hour if maximal analgesia is required.

Metoclopramide and Domperidone
The absorption of paracetamol is increased by metoclopramide and domperidone. However, concurrent use need not be avoided.

Warfarin
The anticoagulant 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.

Chloramphenicol
Increased plasma concentration of chloramphenicol.

➤ **General**

Care is advised in the administration of paracetamol to patients with severe renal or severe hepatic impairment. The hazards of overdose are greater in those with non-cirrhotic alcoholic liver disease.

Do not exceed the stated dose.

Do not take with any other paracetamol-containing products.

If symptoms persist for more than 3 days or get worse consult your doctor.

Immediate medical advice should be sought in the event of an overdose, even if you feel well.

➤ **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 the doctor regarding its use.
Lactation

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

Undesirable Effects

Adverse effects of paracetamol are rare but hypersensitivity including skin rash may occur. There have been reports of blood dyscrasias including thrombocytopenia purpura, methaemoglobinemia and agranulocytosis, but these were not necessarily causality related to paracetamol.

Overdosage

Potentially fatal liver damage is likely in adults who have taken 15g or more of paracetamol. As little as 10g may lead to liver necrosis. Patients taking enzyme-inducing drugs or with a history of alcoholism may have an increased susceptibility. It is considered that excess quantities of a toxic metabolite (usually adequately detoxified by glutathione when normal doses of paracetamol are employed); become irreversibly bound to liver tissue. Symptoms of paracetamol over dosage in the first 24 hours are pallor, nausea, vomiting, diarrhea, anorexia, abdominal pain and increased sweating. Liver damage may become apparent 12 to 48 hours after ingestion. Abnormalities of glucose metabolism and metabolic acidosis may occur. In severe poisoning, hepatic failure may progress to encephalopathy, coma, and death. Acute renal failure with acute tubular necrosis may develop even in the absence of severe liver damage. Cardiac arrhythmias have been reported. Prompt treatment is essential in the management of paracetamol over dosage. Any patient who has ingested about 7.5g or more of paracetamol in the preceding 4 hours should undergo gastric lavage or induced emesis. Specific therapy with an antidote such as acetyl cysteine or methionine may be necessary. Acetyl cysteine may be given either intravenously or by mouth or methionine may be given by mouth within 10 -12 hours of ingestion of the overdose. Generally treatment is required if the blood-paracetamol concentration is higher than a line (the ‘200’ line) drawn on semi-log/linear paper joining the points 200 mg/litre (1.32 mmol/litre) at 4 hours and 30 mg/litre (0.20 mmol/litre) at 15 hours following ingestion. Determination of the concentration before 4 hours is not considered to give a reliable measurement. Administration of oral methionine or intravenous N-acetyl cysteine which may have a beneficial effect up to at least 48 hours after the overdose may be required. General supportive measures must be available. Liver function tests should be performed at 24 hour intervals for at least 96 hours post-ingestion if the plasma paracetamol concentration indicates a potential for hepatotoxicity. Renal and cardiac function should be monitored and supportive treatment should be directed at maintaining fluid and electrolyte balance and correcting hypo-glycaemia. Haemodialysis and haemoperfusion have been used with some success but peritoneal dialysis is ineffective.

Packaging Information

PARAFAST: Strip of 10 tablets

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Last reviewed: November 2013

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