

SUMMARY OF PRODUCT CHARACTERISTICS**APPROVED****By namita at 10:41 am, Dec 13, 2019****1 NAME OF THE MEDICINAL PRODUCT**

Paracetamol 500mg Tablets
Paracetamol 500mg Caplets
Boots Paracetamol 500mg Caplets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Paracetamol 500 mg.

Excipient with known effect: Also contains 0.56mg of Sodium metabisulfite.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet

White, capsule shaped tablet with a break-line on one face.

The break line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

4 CLINICAL PARTICULARS**4.1 Therapeutic indications**

For the treatment of most painful and febrile conditions for example headache including migraine and tension headaches neuralgia, toothache, sore throat, period pains, aches and pains. Also recommended for symptomatic relief of rheumatic aches and pains and the fever, aches and pains of cold and flu.

4.2 Posology and method of administration***Posology*****Adults, the elderly and children 16 years and over:**

Take one to two tablets every 4-6 hours, if you need to. Do not take more than 8 tablets in any 24 hours.

Children 10 to 15 years of age:

Take one tablet every 4-6 hours, if you need to. Do not take more than 4 tablets in any 24 hours.

Children under 10 years of age:

Do not give to children under 10 years of age.

Do not take more often than every 4 hours.

Children should not be given Paracetamol for more than 3 days without consulting a doctor.

Method of administration

For oral administration.

4.3. Contra-indications

Hypersensitivity to paracetamol or to any of the excipients listed in section 6.1

4.4 Special warnings and special precautions for use

Prolonged or frequent use is discouraged. Patients should be advised not to take other Paracetamol containing products concurrently. Taking multiple daily doses in one administration can severely damage the liver; in such case unconsciousness does not occur. However, medical assistance should be sought immediately. Prolonged use except under medical supervision may be harmful. In adolescents treated with 60mg/kg daily of Paracetamol, the combination with another antipyretic is not justified except in the case of ineffectiveness.

Caution is advised in the administration of Paracetamol to patients with moderate and severe renal insufficiency, mild to moderate hepatic insufficiency (including Gilbert's syndrome), severe hepatic insufficiency (child-pugh>9), acute hepatitis, concomitant treatment with medicinal products affecting hepatic functions, glucose-6-phosphatedehydrogenase deficiency, hemolytic anemia, alcohol abuse dehydration and chronic malnutrition (see section 4.2).

The hazards of overdose are greater in those with non-cirrhotic alcoholic liver disease. Caution should be exercised in cases of chronic alcoholism. The daily dose should not exceed 2 grams in such case. Alcohol should not be used during the treatment with Paracetamol.

Caution is advised in asthmatic patients sensitive to aspirin, because light reaction bronchospasm with paracetamol (cross-reaction) has been reported in less than 5% of the patients tested.

In the case of high fever, or signs of secondary infection or persistence of symptoms a doctor should be consulted.

Do not exceed the stated dose.

Patients should be advised to consult their doctor if their headaches become persistent.

Patients should be advised not to take other paracetamol-containing products concurrently.

Patients should be advised to consult a doctor if they suffer from non-serious arthritis and need to take painkillers every day.

If symptoms persist consult your doctor.

Keep out of the reach and sight of children.

Pack Label:

These words must appear in a prominent position.

“Do not take more medicine than the label tells you to. If you do not get better, talk to your doctor”. *This must appear adjacent to either the directions for use or the recommended dosage.*

“Talk to a doctor at once if you take too much of this medicine, even if you feel well”;

“Do not take anything else containing paracetamol while taking this medicine”.

Patient Information Leaflet:

Talk to a doctor at once if you take too much of this medicine even if you feel well. This is because too much paracetamol can cause delayed, serious liver damage”.

Important information regarding the ingredients of this medicine

This medicinal product contains sodium metabisulfite which may rarely cause severe hypersensitivity reactions and bronchospasm.

4.5 Interaction with other medicinal products and other forms of interaction

Hepatotoxic substances may increase the possibility of Paracetamol accumulation and overdose. The risk of hepatotoxicity of paracetamol may be increased by drugs which induce liver microsomal enzymes such as barbiturates, tricyclic antidepressants, and alcohol.

Probenecid causes an almost 2-fold reduction in clearance of Paracetamol by inhibiting its conjugation with glucuronid acid. A reduction of the Paracetamol dose should be considered for concomitant treatment with probenecid.

Salicylamide may prolong the elimination $t_{1/2}$ of Paracetamol

Colestyramine: The speed of absorption of paracetamol is reduced by colestyramine..

Metoclopramide and Domperidone: The speed of absorption of paracetamol is increased by metoclopramide and domperidone

Warfarin and other anticoagulants: Concomitant use of Paracetamol (4 g per day for at least 4 days) with oral anticoagulants may lead to slight variations of INR values. In this case, increased monitoring of INR values should be done during the duration of the combination and after its discontinuation. 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.

Isoniazid: Reduction of paracetamol clearance, with possible potentiation of its action and/or toxicity, by inhibiting its metabolism in the liver.

Lamotrigine: Decrease in the bioavailability of lamotrigine, with possible reduction of its effect, due to possible induction of its metabolism in the liver.

Interference with laboratory tests: Paracetamol may affect uric acid tests by wolframtop phosphoric acid, and blood sugar tests by glucose-oxydase-peroxydase.

4.6 Fertility, pregnancy and lactation

Pregnancy:

A large amount of data on pregnant women indicate neither malformative, nor fetoneonatal toxicity. Epidemiological studies on neurodevelopment in children exposed to paracetamol in utero show inconclusive results. If clinically needed, paracetamol can be used during pregnancy however it should be used at the lowest effective dose for the shortest possible time and at the lowest possible frequency.

Lactation:

Following oral administration, Paracetamol is excreted into breast milk in small quantities. To date, no adverse reactions or undesirable effects are known in association with lactation. Therapeutic doses of Paracetamol can be administered during 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

The frequency using the following convention: very common (> 1/10); common (>1/100 to < 1/10); uncommon (>1/1000 to < 1/100); rare (>1/10000 to < 1/1000); very rare (< 1/10000), including isolated reports; not known: frequency cannot be estimated from the available data. Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Frequency	System	Symptoms
Rare >1/10000 - < 1/1000	Blood and lymphatic system disorders	Platelet disorders, stem cell disorders.
	Immune system disorders	Allergies (excluding angioedema).
	Psychiatric disorders	Depression NOS, confusion, hallucinations.
	Nervous system disorders	Tremor NOS, headache NOS.
	Eye disorders	Abnormal vision.
	Cardiac disorders	Oedema.
	Gastrointestinal disorders	Haemorrhage NOS, abdominal pain NOS, diarrhoea NOS, nausea, vomiting.
	Hepato-biliary disorders	Hepatic function abnormal, hepatic failure, hepatic necrosis, jaundice.
	Skin and subcutaneous tissue disorders	Pruritus, rash, sweating, purpura, angioedema, urticaria. Very rare cases of serious skin reactions have been reported.
	General disorders and administration site conditions	Dizziness (excluding vertigo), malaise, pyrexia, sedation, drug interaction NOS.
Injury, poisoning and procedural complications	Overdose and poisoning	

Very Rare (< 10 000)	Hepato-biliary disorders	hepatotoxicity
	General disorders and administration site conditions	hypersensitivity reaction (requiring discontinuation of treatment)
	Blood and lymphatic system disorders	thrombocytopenia leukopenia neutropenia hemolytic anemia agranulocytosis
	Metabolism and nutrition disorders	Hypoglycaemia
	Renal and urinary disorders	Sterile pyuria (cloudy urine) and renal side effects

Not known: Some cases of edema of the larynx, anaphylactic shock, anaemia, bronchospasm*, liver alteration and hepatitis, renal alteration (severe renal impairment, nephrite interstitial, haematuria, anuresis), gastrointestinal effects and vertigo have been reported.

* There have been cases of bronchospasm with paracetamol, but these are more likely in asthmatics sensitive to aspirin or other NSAIDs.

Reporting of Suspected Adverse Reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for the MHRA yellow Card in the Google Play or Apple App Store..

4.9 Overdose

There is a risk of poisoning, particularly in elderly subjects, in young adolescents, in patients with liver disease, in cases of chronic alcoholism, in patients with chronic malnutrition. Overdosing may be fatal.

Liver damage is possible in adults who have taken 10g or more of paracetamol. Ingestion of 5g or more of paracetamol may lead to liver damage if the patient has risk factors (see below)

Risk Factors

If the patient

a) Is on long term treatment with carbamazepine, phenobarbitone, phenytoin, primidone, rifampicin, St. John's Wort or other drugs that induce liver enzymes.

Or

b) Regularly consumes ethanol in excess of recommended amounts.

Or

c) Is likely to be glutathione deplete e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia.

Symptoms

Symptoms of paracetamol overdose in the first 24 hours are pallor, nausea, vomiting, anorexia and abdominal pain. Liver damage may become apparent 12 to 48 hrs after ingestion. Abnormalities of glucose metabolism and metabolic acidosis may occur. In severe poisoning, hepatic failure may progress to encephalopathy, haemorrhage, hypoglycaemia, cerebral oedema, and death. Acute renal failure with acute tubular necrosis, strongly suggested by loin pain, haematuria and proteinuria, may develop even in the absence of severe liver damage. Cardiac arrhythmias and pancreatitis have been reported.

Management

Immediate treatment is essential in the management of paracetamol overdose. Despite a lack of significant early symptoms, patients should be referred to hospital urgently for immediate medical attention. Symptoms may be limited to nausea or vomiting and may not reflect the severity of overdose or the risk of organ damage. Management should be in accordance with established treatment guidelines, see BNF overdose section.

Treatment with activated charcoal should be considered if the overdose has been taken within 1 hr. Plasma paracetamol concentration should be measured at 4 hours or later after ingestion (earlier concentrations are unreliable)

Treatment with N-acetylcysteine may be used up to 24 hrs after ingestion of paracetamol however, the maximum protective effect is obtained upto 8 hours post ingestion.

If required the patient should be given intravenous – N-acetylcysteine, in line with the established dosage schedule. If vomiting is not a problem, oral methionine may be a suitable alternative for remote areas, outside hospital.

Management of patients who present with serious hepatic dysfunction beyond 24 hours from ingestion should be discussed with the NPIS or a liver unit.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code: N02B E01

Pharmacotherapeutic Group: Antipyretic analgesic

Mechanism of Action/ Effect

Analgesic – the mechanism of analgesic action has not been fully determined. Paracetamol may act predominantly by inhibiting prostaglandin synthesis in the central nervous system (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 synthesis or actions of other substances that sensitise pain receptors to mechanical or chemical stimulation.

Antipyretic- paracetamol probably produces antipyresis by acting centrally on the hypothalamic heat – regulation 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.

5.2. Pharmacokinetic Properties

Absorption

The absorption of paracetamol by the oral route is rapid and complete. Maximum plasma concentrations are reached 30 to 60 minutes following ingestion.

Distribution

Paracetamol is distributed rapidly throughout all tissues. Concentrations are comparable in blood, saliva and plasma. Protein binding is low.

Metabolism

Paracetamol is metabolized mainly in the liver following two major metabolic pathways: glucuronic acid and sulphuric acid 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 and mercaptopuric acid. Conversely, when massive intoxication occurs, the quantity of this toxic metabolite is increased.

Elimination

Elimination is essentially through the urine. 90% of the ingested dose is eliminated via the kidneys within 24 hours, principally as glucuronide (60 to 80%) and sulphate conjugates (20 to 30%). Less than 5% is eliminated in unchanged form.

Elimination half life is about 2 hours.

Physiopathological Variations

Renal Insufficiency: In cases of severe renal insufficiency (creatinine clearance lower than 10 ml/min) the elimination of paracetamol and its metabolites is delayed.

Elderly Subjects-The capacity for conjugation is not modified.

5.3. Preclinical Safety Data

Conventional studies using the currently accepted standards for the evaluation of toxicity to reproduction and development are not available.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Pregelatinised Maize Starch

Sodium Metabisulfite

Magnesium Stearate

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

5 years.

6.4. Special precautions for storage

Blisters: Do not store above 25°C. Store in the original package in order to protect from moisture.

Containers: Do not store above 25°C. Keep the container tightly closed in order to protect from moisture.

6.5. Nature and contents of container

Al/PVC child resistant blisters enclosed in an outer carton.

Pack sizes: 8, 12, 16, 24, 30, 32, 100 tablets

HDPE tablet containers.

OR

Child resistant and adult accessible PP container with HDPE lid

Pack sizes: 16, 1000 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Bristol Laboratories Ltd
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8. MARKETING AUTHORISATION NUMBER

PL 17907/0001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

02/12/2008

10 DATE OF REVISION OF THE TEXT

12/12/2019