SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Paracetamol Tablets 500mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 500 mg of paracetamol. Each tablet also contains sodium metabisulphite 0.56 mg.

For a list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet.
White to off white, circular flat bevelled edge tablet with breakline on one side and plain on other.
The tablet can be divided into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of mild to moderate pain, including headache, neuralgia, toothache, period pains, aches and pains.

Symptomatic relief of rheumatic aches and pains.

Symptomatic relief of influenza, feverishness, feverish colds.

4.2. Posology and Method of Administration

These tablets are for oral administration.
Adults, the elderly and children 16 years or older:

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Age	500mg tablet	How Often
16 years and over	One – Two	Every 3 hours when necessary to a maximum of 8 doses in 24 hours

Children:

Age	500mg tablet dose	How Often
6-8 years	Half	Every 4-6 hours when necessary to a maximum of 4 doses in 24 hours
8-10 years	Half	Every 4-6 hours when necessary to a maximum of 4 doses in 24 hours
10-12 years	One	Every 4-6 hours when necessary to a maximum of 4 doses in 24 hours
12-15 years	One – One & half	Every 4-6 hours when necessary to a maximum of 4 doses in 24 hours

Dosage instruction:

Take every 4 to 6 hours, as required. Do not take more frequently than every 4 hours. Not more than 4 doses should be administered in any 24 hour period.

4.3 Contraindications

Hypersensitivity to paracetamol or any other ingredients.
If you are taking any other medicines that contain Paracetamol

4.4 Special warnings and precautions for use

i) Do not exceed the stated dose.

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

iii) Consult a doctor if symptoms persist or worsen. Do not continue to use for longer than 3 days except on the advice of a doctor .

iv) Ask the doctor or pharmacist about taking the tablets if pregnant or already on a course of medication.

v) This product contains paracetamol.

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

vii) *The label shall say:* "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."
"Do not take more medicine than the label tells you to. If you do not get better, talk to your doctor."

viii) *The leaflet shall say:* "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.".

ix) 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.

x) Contains sodium metabisulphite which may rarely cause severe hypersensitivity reactions and bronchospasm.
xi) Keep out of the sight and reach of children.

4.5 Interaction with other medicinal products and other forms of interaction

Alcohol reduces liver capacity to deal with paracetamol.
Chronic use of paracetamol enhances effect of warfarin and other coumarins with increased risk of bleeding; occasional doses have no significant effect.
Colestyramine reduces absorption of paracetamol. Therefore, the colestyramine should not be taken within one hour if maximal analgesia is required.
Metoclopramide and Domperidone accelerate absorption of paracetamol. However concurrent use need not be avoided
May interact with Chloramphenicol causing increased plasma levels of Chloramphenicol.

4.6 Fertility, pregnancy and lactation

Epidemiological studies in human pregnancy have shown no ill effects due to paracetamol being used in the recommended dosage, but patients should follow the advice of their doctor regarding its use. Paracetamol is excreted in breast milk but not in clinically significant quantities. Available published data do not contraindicate breast-feeding.

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 however it should be used at the lowest effective dose for the shortest possible time and at the lowest possible frequency

4.7. Effects on Ability to Drive and Use Machines

None known.

4.8 Undesirable effects

Adverse events of paracetamol from historical clinical trial data are both infrequent and from small patient exposure.
Accordingly, events reported from extensive postmarketing experience at therapeutic/labelled dose and considered attributable are tabulated below by system class.

Due to limited clinical trial data, the frequency of these adverse events is not known (cannot be estimated from available data), but postmarketing experience indicates that adverse reactions to paracetamol are rare and serious reactions are very rare.

Immune system disorders
Hypersensitivity including skin rash may occur.
Not known: anaphylactic shock, angioedema

Blood and lymphatic system disorders
Not known: blood dyscrasias including thrombocytopenia and agranulocytosis.
Respiratory, thoracic and mediastinal disorders
Bronchospasm*
Hepatobiliary disorders
Hepatic dysfunction

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

Gastrointestinal
Not known: acute pancreatitis

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.

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

4.9. Overdose

Liver damage is possible in adults who have taken 10 g or more of paracetamol. Ingestion of 5 g 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 overdosage in the first 24 hours are pallor, nausea, vomiting,
anorexia and abdominal pain. 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, 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 hour. 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 hours after ingestion of paracetamol, however, the maximum protective effect is obtained up to 8 hours post-ingestion. The effectiveness of the antidote declines sharply after this time. 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 24h from ingestion should be discussed with the NPIS or a liver unit.

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.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code: N02BE01, Other analgesics and antipyretics

Paracetamol is an effective analgesic and antipyretic agent but has only weak antiinflammatory properties. The mechanism of action is probably similar to that of aspirin. Paracetamol may act predominantly by inhibiting prostaglandin synthesis in the central nervous system and to a lesser extent, through a peripheral action by blocking pain-impulse generation. This

inhibition appears, however to be on a selective basis.

The peripheral action may also be due to inhibition of prostaglandin synthesis or to the 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

Paracetamol is readily absorbed from the gastrointestinal tract with peak plasma concentrations occurring in 30 to 60 minutes. It is metabolised in the liver and excreted in the urine mainly as the glucuronide and sulphate conjugates. The elimination half-life varies from about 1-4 hours after therapeutic doses. Paracetamol is relatively uniformly distributed throughout most body fluids. Binding of the drug to plasma proteins is variable; 20 to 30% may be bound at the concentrations encountered during acute intoxication.

Following therapeutic doses 90 - 100% of the drug may be recovered in the urine within the first day. However, practically no paracetamol is excreted unchanged and the bulk is excreted after hepatic conjugation.

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 overdosage and cause liver damage.

5.3 Preclinical safety data

There is no pre-clinical data of relevance to a prescriber, which is additional to that already included in other sections of the SPC.

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 starch (maize)

Sodium metabisulphite

Stearic acid (E570)

Magnesium stearate (E572)

6.2 Incompatibilities

None stated.

6.3 Shelf life

5 years.

6.4 Special Precautions for Storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Paracetamol 500mg Tablets are available in child-resistant packs (Glassine paper foil/ Aluminium or PVC *I* Aluminium foil) of 100 tablets.
Specification details of blister packs :

PVC/Aluminium foil
- PVC (white, rigid, opaque): 250 microns
- PVC/Aluminium foil (hard tempered): 15/20 microns
- Primer (nitrocellulose): 1.5 to 2.5 gsm
- Heat seal lacquer: 6.5 to 8.5 gsm

PVC/Glassine paper – Aluminium foil
- PVC (white, rigid, opaque): 250 microns
- Glassine paper/Aluminium foil :35±3.50/25±2.0 gsm

6.6 Special precautions for disposal

No special precautions required.

7 MARKETING AUTHORISATION HOLDER

Flamingo Pharma UK Ltd
1st Floor, Kirkland House,
11-15 Peterborough Road,
Harrow, Middlesex,
HA1 2AX,

United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 43461/0003

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

5th February 2011

Renewal: Pending

10 DATE OF REVISION OF THE TEXT

23/07/2019