Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Paracetamol Banner 500 mg soft capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each soft capsule contains 500 mg paracetamol.

Excipients with known effect
Every capsule contains 58.2 mg of sorbitol and 6.0 mg of propylene glycol.
The capsules may contain trace amounts of soya lecithin.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Capsules, soft.

White, oblong soft gelatin capsule

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Symptomatic treatmentof mild to moderate pain and/or fever.

4.2 Posology and method of administration

Posology

Paediatric population

Children weighing less than 30 kg (approximately below 9 years old):

- Paracetamol Banner should not be used in children weighing less than 30 kg (approximately below the age of 9 years). For those children other formulations and dosage strengths are available which may be more appropriate.

Children weighing between 31 and 55 kg (aged approximately 9 to 15 years):

- For children weighing 31 to 40 kg (approximately 9 to 12 years), take 1 capsule (500 mg) at a time, without exceeding 4 capsules (2000 mg) per day.
- For children weighing 41 to 55 kg (approximately 12 to 15 years), take 1 capsule (500 mg) at a time, without exceeding 6 capsules per day.

The lower frequency of administration is intended for the youngest children in the relevant age group.
For children weighing less than 50 kg (approximately below 12 years of age) the daily dose should not be higher than 60 mg/kg body weight.

For adults and children weighing more than 55 kg (from about 15 years old):
The usual dosage is 1 to 2 capsules (500-1,000 mg) at a time, with a maximum of 6 capsules (3,000 mg) every 24 hours.

Instructions for use:

- The administration interval must be at least 4 hours.
- Do not use in combination with other paracetamol-containing products.

- Do not exceed the stated dose on account of the risk of severe hepatic damage (see section 4.4 and 4.9).
- Depending on the recurrence of symptoms (fever and pain), repeated administration is allowed.
- If pain lasts for longer than 5 days or fever lasts for longer than 3 days or these symptoms become worse or if other symptoms occur, the treatment must be stopped, and a doctor must be consulted.

Renal impairment:

In case of unsatisfactory activity of the kidneys (renal insufficiency) (creatinine clearance <10 ml / min), the dose must be reduced:

Glomerular filtration rate	Dose
10 - 50 ml/min	500 mg/6 hours
< 10 ml/min	500 mg/8 hours

Hepatic impairment:

For patients with unsatisfactory activity of the liver (hepatic insufficiency) or Gilbert's syndrome, the dose must be reduced, or the administration intervals must be prolonged.

The effective daily dose should also not exceed 60 mg/kg/day (up to 2000 mg/day) in the following situations:

- Adults under 50 kg
- Mild hepatic insufficiency to moderate
- Chronic alcoholism
- Chronic malnutrition
- Dehydration

Method of administration

Paracetamol Banner is administered orally.

4.3 Contraindications

Hypersensitivity to paracetamol, peanut or soya, or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

- Long-term or frequent use is not advised.
- Caution is required in the case of hepatic and renal impairment.
- Patients must be advised not to use any other paracetamol-containing products at the same time.
- The taking of several daily doses at once can cause severe damage to the liver. In such cases, a loss of consciousness will not occur. However, immediate medical help must be sought even if the patient feels well because of the risk of irreversible damage to the liver (see section 4.9).
- Long-term use can be harmful except under medical supervision. In young people who are treated with 60 mg/kg/day of paracetamol, combination with another antipyretic is not allowed except where there is a lack of efficacy.
- Caution is required when administering paracetamol to patients with moderate to severe renal insufficiency, mild to moderate hepatic insufficiency (incl. Gilbert's syndrome), severe hepatic insufficiency (Child-Pugh > 9), acute hepatitis, the concomitant administration of medicinal products which have an influence on hepatic function, glucose-6-phosphate dehydrogenase deficiency, haemolytic anaemia, alcohol abuse, dehydration and chronic malnutrition.
- The risk of an overdose is greater in patients with non-cirrhotic alcoholic liver conditions. Caution is required in the case of chronic alcoholism. The daily dose may not exceed 2 grams in this case. No alcohol may be used during treatment with paracetamol.
- In the case of a high fever, symptoms of secondary infection or the persistence of symptoms, it will be necessary to reconsider the treatment.
- After the long-term use (> 3 months) of analgesics with intake every other day or more frequently, headache can occur or become worse. Headache which is caused by the excessive use of analgesics (drug-dependent headache) must not be treated by lowering the dose. In these cases, the use of analgesics must be stopped in consultation with a doctor.
- Caution is required in the case of asthmatic patients who are sensitive to acetylsalicylic acid as mild bronchospasms have been reported as a cross-reaction after the use of paracetamol.
- Patients with rare hereditary problems of fructose intolerance should not take this medicine.

- The capsules contain sorbitol. Patients with rare hereditary problems of fructose intolerance should not take this medicine.
- Paracetamol Banner contains lecithin originating from soya oil. Patients who are allergic to peanut or soya should not use this medicinal product.
- Caution is advised ifparacetamol is administered concomitantly with flucloxacillin due to increasedrisk of high anion gap metabolic acidosis (HAGMA), particularly in patientswith severe renal impairment, sepsis, malnutrition and other sources ofglutathione deficiency (e.g. chronic alcoholism), as well as those using maximumdaily doses of paracetamol. Close monitoring, including measurement of urinary5 oxoproline, is recommended.

4.5 Interaction with other medicinal products and other forms of interaction

- Paracetamol is metabolised in the liver and can consequently enter into interactions with other medicinal products which follow the same metabolic route, or which are able to inhibit or induce the route. In the case of chronic alcohol abuse and the use of drugs which induce hepatic enzymes such as barbiturates and tricyclic antidepressants, an overdose of paracetamol can take a more severe course as a result of the increased and more rapid formation of toxic metabolites.
- Caution is required with the concomitant intake of enzyme-inducing drugs (see section 4.9 Overdose).
- In the case of concomitant treatment with probenecid, the dose of paracetamol must be reduced as probenecid reduces the clearance of paracetamol by 50% since it prevents the conjugation of paracetamol with glucuronic.
- Paracetamol can cause an increase in the half-life of chloramphenicol.
- The rate of absorption of paracetamol can be increased by metoclopramide or domperidone and absorption can be reduced by colestyramine.
- The anticoagulatory effect of warfarin and other coumarins can increase during the long-term, regular use of paracetamol with an increase in the risk of bleeding as a result. There is no significant effect with the occasional taking of a dose.
- With the concomitant chronic use of paracetamol and zidovudine, neutropenia often occurs, probably as a result of the reduced metabolism of zidovudine because of the competitive prevention of conjugation. Concomitant intake of paracetamol and zidovudine should, therefore, only take place on medical advice.
- Salicylamide can prolong the half-life of paracetamol.
- Isoniazid ensures a reduction in the clearance of paracetamol, which possibly increases the activity and/or toxicity of paracetamol by preventing metabolism in the liver.
- The concomitant intake of paracetamol with lamotrigine ensures a reduction in the bioavailability of lamotrigine, as a result of which there is possibly a decrease in activity as a result of the possible induction of metabolism in the liver.
- Effect on laboratory tests: paracetamol can have an influence on the urine test with wolfram phosphoric acid as well as the blood sugar test with glucose oxidase peroxidase.
- Caution should be taken when paracetamol is used concomitantly with flucloxacillin as concurrent intake has been associated with high anion gap metabolic acidosis, especially in patients with risks factors (see section 4.4).

4.6 Fertility, pregnancy and lactation

Pregnancy
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 at the lowest effective dose for the shortest possible time and at the lowest possible frequency.

Breastfeeding
After oral administration, paracetamol is excreted into breast milk in small quantities. No undesirable effects on nursing infants have been reported. Consequently, Paracetamol Banner may be used in breast-feeding women.

Fertility
There are insufficient fertility data available to indicate paracetamol has any effect on fertility.

4.7 Effects on ability to drive and use machines

Paracetamol Banner 500 mg capsules, soft has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The following side-effects can occur when using Paracetamol 500 mg capsules.
The side-effects are listed below per system/organ class and frequency.
The following frequencies are taken as a basis when evaluating side effects: 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) and not known frequency (cannot be estimated from the available data).

System organ class	Side effect	Frequency
Blood and lymphatic system disorders	Agranulocytosis (after long-term use), thrombocytopenia, thrombocytopenic purpura, leukopenia, haemolytic anaemia	Rare
	Pancytopenia	Very rare
Immune system disorders	Allergies (exclusive of angioedema)	Rare
	Hypersensitivity reactions, (angioedema, breathing difficulties, perspiration, nausea, hypotension, shock, anaphylaxis), as a result of which treatment has to be stopped	Very rare
Respiratory, thoracic and mediastinal disorders	Bronchospasm in patients sensitive to aspirin or other NSAIDs (analgesic asthma)	Very rare
Metabolism and nutrition disorders	Hypoglycaemia	Very rare
Psychiatric disorders	Depression, confusion, hallucinations	Rare
Nervous system disorders	Tremor, headache	Rare
Ophthalmological abnormalities	Visual abnormalities	Rare
Cardiac disorders	Oedema	Rare
Gastrointestinal disorders	Bleeding, abdominal pain, diarrhoea, nausea, vomiting	Rare
Hepatobiliary disorders*	Abnormal hepatic function, hepatic failure, hepatic necrosis, jaundice	Rare
	Hepatotoxicity	Very rare
Skin and subcutaneous tissue disorders	Pruritus, rash, perspiration, purpura, urticaria	Rare
	Exanthema, severe skin reactions	Very rare
	Acute generalised exanthematous pustulosis (AGEP), toxic necrolysis (TEN), drug induced dermatosis, Stevens-Johnson syndrome	Not known
Renal and urinary disorders	Sterile pyuria (cloudy urine) and renal side effects (severe renal impairment, interstitial nephritis, haematuria and anuresis)	Very rare
General disorders and administration site conditions	Dizziness (excluding vertigo), malaise, pyrexia, sedation, a drug interaction which is not specified in any more detail	Rare
Injury, poisoning and procedural complications	Overdose and intoxication	Rare

* Quantities of even 6 grams of paracetamol can cause liver damage (in children weighing more than 140 mg/kg); larger quantities cause irreversible hepatic necrosis. Liver damage has been reported after the chronic use of 3-4 grams of paracetamol per day.

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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

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:

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

Or

- Regularly consumes ethanol in excess of recommended amounts.

Or

- 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.

Treatment
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.
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.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Analgesics and antipyretics. Anilides, ATC code: N02BE01.

Paracetamol has both analgesic as well as antipyretic activity. However, it does not have anti-inflammatory activity. The mechanism of action of paracetamol has so far not been fully explained. The effect appears to be based on inhibition of the enzyme prostaglandin synthetase, but the lack of an anti-inflammatory effect cannot be explained by this. It is possible that the distribution of paracetamol over the body and hence the site of the inhibition of prostaglandin synthetase plays a role.
Paracetamol has the advantage that number of side effects which are characteristic of NSAIDs are completely or largely absent in the case of paracetamol.
Paracetamol is, therefore, a good alternative to NSAIDs for combating pain and fever.
In an acute pain study with paracetamol, there was no difference in the onset of pain relief between fasting and feeding people.

5.2 Pharmacokinetic properties

Absorption
Paracetamol is rapidly and almost completely absorbed from the gastrointestinal tract after oral administration. The maximum plasma concentration is reached 15 minutes to 1.5 hours after intake. The maximum concentration is reached 30 minutes to 2 hours after the intake of regular paracetamol capsules. The concentration in plasma reaches a peak in 30 to 60 minutes and the plasma half-life is 1 - 4 hours after therapeutic doses.

Distribution
The distribution volume of paracetamol is about 1 l/kg of body weight. The amount of plasma protein binding is negligible at therapeutic doses. The concentration in saliva and maternal milk is related to the plasma concentration.

Biotransformation

Paracetamol is conjugated with glucuronic acid (around 60 %), sulphate (around 35 %) and cysteine (around 3 %) in the liver of adults. With the help of cytochrome P-450, a small proportion of paracetamol is converted in the body into a very reactive metabolite which is normally quickly inactivated by conjugation with glutathione. Overdose can deplete glutathione stocks and thus result in acute hepatic damage.
In neonates and children up to 12 years of age, sulphate conjugation is the main elimination route and glucuronidation takes place to a lesser extent than is the case in adults. However, the total elimination capacity in children is overall similar to that of adults because of the increased sulphation capacity.

Elimination
Paracetamol is mainly excreted in the urine. 90% of the dose taken is excreted via the kidneys within 24 hours, mainly in the form of the glucuronide (60-80 %) and the sulphate conjugate (20-30 %) and with around 5% unchanged.

5.3 Preclinical safety data

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

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Macrogol
Purified water
Propylene glycol
Povidone
Silica, colloidal anhydrous

Capsule shell
Gelatin
Sorbitol, liquid, partially dehydrated
Purified water
Glycerol
Titanium dioxide (E171)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

30 months

6.4 Special precautions for storage

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

6.5 Nature and contents of container

Blister formed of PVDC/PVC//Alu/PET, packed into carton.

Pack sizes of 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30 or 32 capsules in blister.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Any ususued medicinal product or waste material should be disposed of in accordance with local requirments.

7 MARKETING AUTHORISATION HOLDER

Banner Pharmacaps Europe B.V.
De Posthoornstraat 7
5048 AS Tilburg
Netherlands

8 MARKETING AUTHORISATION NUMBER

PA1121/003/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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