SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Panadol ActiFast

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Panadol ActiFast tablet contains Paracetamol 500 mg.

For excipients see Section 6.

3 PHARMACEUTICAL FORM

Form
Tablet.

Description
White film-coated capsule shaped tablet with flat edges, debossed with the letter ‘P’.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Panadol ActiFast is a mild analgesic and antipyretic, and is recommended for the treatment of most painful and febrile conditions, for example, headache including migraine and tension headaches, toothache, backache, rheumatic and muscle pains, dysmenorrhoea, sore throat, and for relieving the fever, aches and pains of colds and flu.

4.2 Posology and method of administration

For oral administration.

Adults, including the elderly and children 16 years and over:
Two tablets to be taken with half a tumbler of water (100 ml).

To ensure fast onset of pain relief no less than two tablets must be taken with 100 ml of water. For maximum speed of action this should be on an empty stomach.

Two tablets up to four times daily as required. The dose should not be repeated more frequently than every four hours nor should more than four doses be taken in any 24 hour period.

Children aged 12-15 years:
One tablet to be taken with half a tumbler of water (100ml), up to four times daily as required. The dose should not be repeated more frequently than every four hours nor should more than 4 doses be given in any 24 hour period.

Children under 12 years of age:

Panadol ActiFast is not recommended for children under 12 years of age**.**

4.3 Contraindications

Hypersensitivity to paracetamol or any of the other constituents.

4.4 Special warnings and precautions for use

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

Do not exceed the stated dose.
Patients should be advised not to take other paracetamol-containing products concurrently.
Each Panadol ActiFast tablet contains 173 mg of sodium and should not be taken by patients on a low sodium diet.
Patients should be advised to consult their doctor if their headaches become persistent.
If symptoms persist consult your doctor.
Keep out of the reach and sight of children.

Pack Label:

Immediate medical advice should be sought in the event of an overdose, even if you feel well.
Do not take with any other paracetamol-containing products.

Patient Information Leaflet:

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.

4.5 Interaction with other medicinal products and other forms of interaction

The speed of absorption of paracetamol may be increased by metoclopramide or domperidone and absorption reduced by colestyramine. 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.

4.6 Fertility, Pregnancy and lactation

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

4.7 Effects on ability to drive and use machines

None.

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 post-marketing 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 post-marketing experience indicates that adverse reactions to paracetamol are rare and serious reactions are very rare.

Post marketing data

Body System	**Undesirable effect**
Blood and lymphatic system disorders	Thrombocytopenia Agranulocytosis
Immune system disorders	Anaphylaxis Cutaneous hypersensitivity reactions including skin rashes, angiodema and Stevens Johnson syndrome/toxic epidermal necrolysis
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.

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

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.

High doses of sodium bicarbonate may be expected to induce gastrointestinal symptoms including belching and nausea. In addition, high doses of sodium bicarbonate may cause hypernatraemia; electrolytes should be monitored and patients managed accordingly.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code N02B E01

Paracetamol has analgesic and antipyretic actions. The mechanism of action is based on the inhibition of prostaglandin biosynthesis.

Paracetamol is poorly absorbed in the stomach but well absorbed in the small intestine due to the greater surface area and hence adsorptive capacity.

Sodium bicarbonate is an excipient in the formulation which has a role in increasing the rates of gastric emptying and of paracetamol dissolution and hence the speed of absorption of paracetamol to provide faster onset of relief.

The amount of sodium bicarbonate contained in 2 tablets of Panadol ActiFast are required per dose to have such effects. Sodium bicarbonate influences the rate of gastric emptying in a concentration dependant manner with the maximal effect achieved at near isotonic concentrations (150 mmol/litre)(i.e. 150 millimolar) – equivalent to 2 Panadol ActiFast tablets in 100 ml water.

Hypertonic solutions (500-1,000 mmol/litre)(i.e. 500 to 1,000 millimolar – equivalent to the amount of sodium bicarbonate in 6-12 Panadol ActiFast tablets given with 100 ml water) appear to inhibit gastric emptying. The therapeutic application of enhanced gastric emptying has previously been demonstrated with significantly faster rate of absorption of paracetamol and significantly faster onset of pain relief from soluble tablets containing sodium bicarbonate compared to conventional tablets. Panadol ActiFast has been formulated with 630 mg sodium bicarbonate per tablet that results in near isotonicity at a 2-tablet dose in gastric fluid.

The role of the dissolution rate of Panadol ActiFast Tablets in vivo at gastric pH is unknown. Therefore the role of tablet dissolution in the speed of action of Panadol ActiFast Tablets is unclear.

It is likely that no single mode of action is responsible for the pharmacokinetic profile observed with Panadol ActiFast. The relative contributions of the different factors will vary depending on the circumstances under which the product is taken.

5.2 Pharmacokinetic properties

Paracetamol is rapidly and almost completely absorbed from the gastrointestinal tract. It is metabolised in the liver and excreted in the urine as the glucuronide and sulphate conjugates, - less than 5% is excreted unchanged in the urine as unmodified paracetamol. Binding to plasma proteins is minimal.

The mean elimination half-life of paracetamol following administration of Panadol ActiFast is 2 to 3 hours and is similar to that achieved following administration of standard paracetamol tablets in fasted and fed states.

Following administration of Panadol ActiFast, paracetamol has a median time to peak plasma concentrations (t_{max}) of 25 minutes in fasted subjects and 45 minutes in the fed subjects. Maximum plasma concentrations were reached at least twice as fast for Panadol ActiFast as for standard paracetamol tablets in both the fed and fasted state (p= 0.0002). Following administration of Panadol ActiFast, paracetamol is generally measurable in plasma within 10 minutes in both the fed and fasted state.

Two tablets of Panadol ActiFast are required to be taken with 100 ml of water to obtain this fast rate of absorption of paracetamol. The maximum rate of absorption is obtained on an empty stomach. When one tablet is taken the rate of absorption of paracetamol for Panadol ActiFast is the same as for standard paracetamol tablets. This is thought to be due to insufficient sodium bicarbonate present in the single tablet dose to increase the rate of paracetamol absorption. In addition, tablets taken with insufficient (<100 mls) water are unlikely to have increased speed of action. (See 5.1 Pharmacodynamic properties).

The extent of absorption of paracetamol from Panadol ActiFast tablets is equivalent to that of standard paracetamol tablets as shown by AUC in both fed and fasted states.

5.3 Preclinical safety data

Preclinical safety data on paracetamol in the literature have not revealed any findings which are of relevance to the recommended dosage and use of the product and which have not been mentioned in other sections of the SmPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium bicarbonate
Starch, pre-gelatinised
Povidone
Maize starch
Potassium sorbate (E 202)
Microcrystaline cellulose
Magnesium stearate
Carnauba wax
Titanium dioxide (E171)
Polydextrose
Hypromellose
Glycerol triacetate
Polyethylene glycol

6.2 Incompatibilities

None known.

6.3 Shelf life

Two years.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

Tablets are in:

- PVC 250µm or 300µm/aluminium foil 30µm blister packs
- Child resistant PVC 250µm or 300µm/ Aluminium foil/ polyethylene terephthalate blister packs

Filled blisters are packed into cardboard cartons/PVC wallets with 4, 6, 8, 10, 12, 14 or 16 tablets per pack.

6.6 Special precautions for disposal

Not applicable.

7 MARKETING AUTHORISATION HOLDER

GlaxoSmithKline Consumer Healthcare (UK) Trading Limited,
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Brentford
Middlesex
TW8 9GS
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