SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Paracetamol 120mg/5ml Elixir

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each 5ml contains:
Paracetamol 120mg
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Oral Solution
Clear red liquid with raspberry flavour.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
For the treatment of mild to moderate pain, including headache, migraine, neuralgia, toothache, pain in teething, sore throat, aches and pains
Symptomatic relief of influenza, feverishness, feverish colds.

4.2 Posology and method of administration
Children 3-12 months: 2.5ml to 5.0ml every four hours.
Children 1 year – under 6 years: 5.0 ml to 10.0ml every four hours
Children 6 years – 12 years: 10.0ml to 20.0ml every four hours
Dosage for children under 3 months is at Physicians discretion.
Not more than 4 doses should be administered in any 24-hour period.
4.3 **Contraindications**

Hypersensitivity to Paracetamol or any of the excipients.

Contains sorbitol: Patients with rare hereditary problems of fructose intolerance should not take this medicine.

4.4 **Special warnings and precautions for use**

Use with caution in patients with severe renal or hepatic impairment. The hazards of overdose are greater in those with non-cirrhotic alcoholic liver disease.

The risk of hepatotoxicity with single doses or prolonged administration of paracetamol may be increased in chronic alcoholics, or in patients regularly taking other hepatotoxic medications, or hepatic-enzyme inducing agents.

Do not exceed the recommended dose
If symptoms persist consult your doctor
Keep out of reach and sight of children

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 cholestyramine.

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.

Enzyme-inducing medicines, such as some antiepileptic drugs (phenytoin, phenobarbital, carbamazepine) have been shown in pharmacokinetic studies to reduce the plasma AUC of paracetamol to approx. 60%.

Other substances with enzyme-inducing properties, e.g. rifampicine and St. John's wort (hypericum) are also suspected of causing lowered concentrations of paracetamol. In addition, the risk of liver damage during treatment with maximum recommended doses of paracetamol will be higher in patients being treated with enzyme-inducing agents.

Acute alcohol intake may diminish an individual’s ability to metabolise large doses of paracetamol, the plasma half-life of which can be prolonged.

The risk of hepatotoxicity with single doses or prolonged administration of paracetamol may be increased in chronic alcoholics, or in patients regularly taking other hepatotoxic medications, or hepatic-enzyme inducing agents.
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 However, in one study, eight cases of constriction and complete occlusion of the ductus arteriosus associated with maternal use of paracetamol. All were recovered. Hence, patients should follow the advice of their doctors 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**

Not relevant.

4.8 **Undesirable effects**

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

Allergic reactions may include skin rashes, and urticaria, anaphylaxis, angioneurotic oedema, toxic epidermal necrosis, erythema multiforme, and vasculitis have been rarely reported.

There have been reports of blood dyscrasias including thrombocytopenia and agranulocytosis but these were not necessarily causality related to paracetamol.

Most reports of adverse reactions to paracetamol relate to overdosage with the drug.

Nephrotoxicity following therapeutic doses of paracetamol is very rare, but papillary necrosis has been reported after prolonged administration.

4.9 **Overdose**

Immediate medical advice should be sought in the event of an overdose, even if the patient feels well, because of the risk of delayed serious liver damage.

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

- Long-term treatment with enzyme-inducing drugs such as some antiepileptic drugs (phenytoin, phenobarbital, carbamazepine), rifampicin and St. John's wort (hypericum). Even subacute “therapeutic” overdose has resulted in severe intoxication with doses varying from 6 g/24 hours for a week, 20 g for 2-3 days, etc

- Regular consumption of ethanol in excess of recommended amounts

- The existence of conditions that may lead to glutathione depletion e.g. eating disorders, cystic fibrosis, HIV infection, starvation, and 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 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, coma and death. Acute renal failure with acute tubular necrosis may develop even in the absence of severe liver damage. This is strongly suggested by loin pain, haematuria, and Protenuria. Cardiac arrhythmias and pancreatitis have been reported.

It is considered that excess quantities of a toxic metabolite (usually adequately detoxified by glutathione when normal doses of paracetamol are ingested) become irreversibly bound to liver tissue.

**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 for overdose, or 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.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Analgesic and Antipyretic
ATC code: N02BE01
Paracetamol has analgesic and antipyretic effects but has only weak anti-inflammatory effects. These actions are considered to be due to inhibition of the Biosynthesis of Prostaglandins.

5.2 Pharmacokinetic properties
Paracetamol is readily absorbed from the gastro-intestinal tract with peak plasma concentrations occurring about 30minutes to 2 hours after ingestion. It is metabolised 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 1-4 hours. Plasma protein binding is negligible at usual therapeutic concentrations but increase with increasing concentrations. A minor hydroxylated metabolite, which is usually produced in very small amounts by mixed function, oxidises in the liver and which is usually detoxified by conjugation with liver glutathione may accumulate following Paracetamol overdosage and cause liver damage.

Particularly no Paracetamol is excreted unchanged, and the bulk is excreted after hepatic conjugation with glucuronic acid (about 60%) sulphuric acid (about 35%) or cysteine (about 3%)
Children have less capacity for glucuronidation of the drugs than do adults. When high doses are ingested Paracetamol undergoes N-Hydroxylation t form (for further details see product licence file).
5.3 Preclinical safety data
None stated.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Alcohol 96%,
Propylene Glycol,
Potassium Sorbate,
Sorbitol,
Glycerol,
Saccharin Sodium,
Raspberry Flavour (IFF 17.40.0478),
Citric Acid Hydrated,
Amaranth Ariavit 311801,
Purified Water.

6.2 Incompatibilities
None stated.

6.3 Shelf life
36 months.

6.4 Special precautions for storage
Do not store above 25°C. Keep the bottle tightly closed. Store in the original container.
6.5 Nature and contents of container
Amber glass bottle with plastic cap
Amber glass bottle with Aluminium ROPP cap

Pack sizes: 60ml, 100ml, and 200ml

Not all pack sizes may be marketed.

6.6 Special precautions for disposal
Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER
Activase Pharmaceuticals Limited,
11 Boumpoulinas, 3rd Floor,
P.C. 1060
Nicosia.
Cyprus

8 MARKETING AUTHORISATION NUMBER(S)
PL 28444/0068

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
10/03/2008

10 DATE OF REVISION OF THE TEXT
19/01/2012