Summary of Product Characteristics
GACET – 125/250

(Acetaminophen Suppositories USP)

1. NAME OF THE MEDICINAL PRODUCT

GACET – 125/250 (Acetaminophen Suppositories USP 125/250)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each suppository contains.

Acetaminophen USP 125/250 mg

Excipients q.s

Colour: Titanium Dioxide

Excipient list is mentioned in Section 6.1

3. PHARMACEUTICAL FORM

Suppositories

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

GACET – 125/250 Suppositories:

Indicated for the treatment of mild to moderate pain and pyrexia in children.

4.2 Posology and method of administration

For rectal use only

GACET – 125

Use in Children aged 1 to 5 years **(**10 – 20 kg Body weight) – 1 -2 Suppositories

GACET – 250

Use in Children aged 6 to 12 years **(**20 – 40 kg Body weight) – 1 -2 Suppositories

Method of administration:

These doses may be repeated upto maximum of 4 times in 24 hours. The dose should not be repeated more frequently than every 4 hours. The recommended dose should not be exceeded. Higher doses do not produce any increase in analgesic effect. Only whole suppositories should be administered – do not break suppository before administration.

4.3 Contraindications

Hypersensitivity to Acetaminophen or any of the other constituents listed in section 6.1.

4.4 Special warnings and precautions

GACET – 125/250 suppositories should not be combined with other analgesic medications that contain acetaminophen. Acetaminophen should be given with care to patients with impaired kidney or liver function.

Doses higher than those recommended involve a risk of very severe liver damage. Liver damage is also associated with certain risk factors (see also Section 4.5 Interaction with other medicinal products and other forms of interaction, and Section 4.9 Overdose). If liver damage is suspected, then liver function tests should be performed.

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

4.5 Interaction with other medicinal products and other form of interactions:

Drugs which induce hepatic microsomal enzymes such as alcohol, barbiturates and other anticonvulsants, may increase the hepatotoxicity of acetaminophen, particularly after overdosage.

The anti-coagulant effect of warfarin and other coumarins may be enhanced by prolonged regular use of acetaminophen with increased risk of bleeding. The effect appears to increase as the dose of acetaminophen is increased, but can occur with doses as low as 1.5–2 g acetaminophen per day for at least 5–7 days. Occasional doses have no significant effect.

Probenicid inhibits the glucuronidation of acetaminophen which can affect the clearance of acetaminophen. This should be considered when these medicines are administered concomitantly.

Acetaminophen may affect the pharmacokinetics of chloramphenicol. This interaction should be considered when these medications are administered concomitantly, especially in malnourished patients.

Enzyme-inducing medicines, such as some antiepileptic drugs (phenytoin, phenobarbital, carbamazepine, primidone) have been shown in pharmacokinetic studies to reduce the plasma AUC of acetaminophen to approx. 60 %. Other substances with enzyme-inducing properties, e.g. rifampicin and St. John's wort (hypericum) are also suspected of causing lowered concentrations of Acetaminophen. In addition, the risk of liver damage during treatment with

maximum recommended doses of Acetaminophen will be higher in patients being treated with enzyme-inducing agents.

4.6 Fertility, Pregnancy and lactation:

A large amount of data on pregnant women indicate neither malformative, nor feto/neonatal toxicity. Epidemiological studies on neurodevelopment in children exposed to acetaminophen in utero show inconclusive results. If clinically needed, acetaminophen 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.

Acetaminophen is excreted in breast milk but not in clinically significant amounts.

4.7 Effects on Ability to Drive and Use Machines

None known.

4.8 Undesirable effects:

Frequency	**System Organ Class (SOC)**	**Event**
Common (≥1/100 to <1/10)	Gastrointestinal disorders	Redness of the rectal mucous membranes
Rare (≥1/10,000 to <1/1,000)	Immune system disorders	Allergic reaction
	Hepatobiliary disorders	Liver damage
	Skin and subcutaneous tissue disorders	Exanthema, urticaria, angioedema
	Investigations	Increase in creatinine (mostly secondary to hepatorenal syndrome)

Very rare cases of serious skin reactions have been reported.

There have been reports of blood dyscrasias including thrombocytopenia and agranulocytosis, but these were not necessarily causally related to acetaminophen.

Hepatic necrosis may occur after overdosage

4.9 Overdose

Toxicity:

Liver damage is possible in adults who have taken 10g or more of acetaminophen. Ingestion of 5g or more of acetaminophen may lead to liver damage if the patient has risk factors,

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) is likely glutathione depleted, e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia.

Symptoms

Symptoms of acetaminophen overdosage in the first 24 hours are pallor, nausea, vomiting, anorexia and abdominal pain. Liver damage may become apparent 12 to 48 hours after administration and clinical symptoms generally culminate after 4 to 6 days. 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 acetaminophen overdose. Despite a lack of significant early symptoms, patients should be referred to hospital urgently for immediate medical attention. This is because early 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.

As concentrations soon after acetaminophen ingestion are unreliable, plasma acetaminophen concentration should be measured at 4 hours or later after initial administration

Treatment with N-acetylcysteine may be used up to 24 hours after administration of acetaminophen; however, the maximum protective effect is obtained up to 8 hours post-administration. The effectiveness of the antidote declines sharply after this 8 hour time period. 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:

Analgesic, Antipyretic: N02 BE01

Acetaminophen is an aniline derivative with analgesic and antipyretic actions similar to those of aspirin but with no demonstrable anti-inflammatory activity. Acetaminophen is less irritant to the stomach than aspirin. It does not affect thrombocyte aggregation or bleeding time. Acetaminophen is generally well tolerated by patients hypersensitive to acetylsalicylic acid.

5.2 Pharmacokinetic properties:

Absorption

Acetaminophen is well absorbed by both oral and rectal routes. Peak plasma concentrations occur about 2 to 3 hours after rectal administration. The plasma half life is about 2 hours.

Biotransformation

Acetaminophen is primarily metabolised in the liver by conjugation to glucuronide and sulphate. A small amount (about 3-10% of a therapeutic dose) is metabolised by oxidation and the reactive intermediate metabolite thus formed is bound preferentially to the liver glutathione and excreted as cystein and mercapturic acid conjugates.

Elimination

Excretion occurs via the kidneys. 2-3% of a therapeutic dose is excreted unchanged; 80-90% as glucuronide and sulphate and a smaller amount as cystein and mercapturic acid derivatives.

5.3 Preclinical safety data

Not applicable

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Polyethylene Glycol -1500 (PEG-1500), Polyethylene Glycol-6000 (PEG-6000), Methyl Paraben, Propyl Paraben, Butylated Hydroxy Toluene, Titanium Dioxide

6.2 Incompatibilities

Not known

6.3 Shelf Life

Three years.

6.4 Special precaution for storage

Store in the original package below 30^0C.Keep out of reach of children.

6.5 Nature and content of container

GACET-125/250 polyvinylchloride foil coated with Polyethylene. (PVC/PE Foil)

2 strips each containing 5 Suppositories are packed in a carton along with pack insert.

6.6 Special precautions for disposal and other handling

Not Applicable

7.MARKETING AUTHORIZATION HOLDER

Bliss GVS Pharma Ltd.,
102, Hyde Park, Saki-Vihar road, Andheri (East) Mumbai 400 072, INDIA

8. NUMBER(S) IN THE NATIONAL REGISTER OF FINISHED PHARMACEUTICAL PRODUCTS

Not Applicable

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Not Applicable

10. DATE OF REVISION OF THE TEXT

Not Applicable