Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:
FEVASTIN ET 500

2. Qualitative and quantitative composition
Each Effervescent Tablet Contains
Paracetamol BP.....500 mg
Excipients.....QS

For the full list of excipients, see section 6.1.

3. Pharmaceutical form
Effervescent Tablet

4. Clinical particulars

4.1 Therapeutic indications
Paracetamol 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
This presentation is reserved for use only in adults and in adolescents aged 12 years and above.
Doses depend on body weight and age; a single dose ranges from 10 to 15 mg/kg body weight (b.w.) to a maximum of 60 mg/kg
b.w. for total daily dose.

Pediatric Patients:
• Children below 12 years of age: Paracetamol effervescent Tablet is not recommended in children aged less than 12 years.
• Adolescents of 12 to 15 years and weighing 41 to 50 kg the posology is one tablet per dose, repeated if necessary 6-4 hours later, without exceeding 4 tablets daily.
• Adolescents of 16 to 18 years and weighing more than 50 kg: as adults.

Adults:
The usual adults' dose is one to two tablets of 500mg, repeated if necessary 4 hours later, without exceeding 4g of Paracetamol a day (i.e. 8 tablets).

Maximum daily dose:
• The maximum daily dose of Paracetamol must not exceed 4g.
• Maximum single dose is 1g (2 effervescent tablets)
Paracetamol 500 mg Effervescent Tablets are for oral administration. The tablets should be placed in a full tumbler of water and allowed to dissolve completely before swallowing.

Frequency of administration:
The specific dose interval depends on the symptoms and the maximum daily dose. Systematic administration enables to avoid pain or fever oscillation. Depending on the reoccurrence of symptoms (fever and/or pain), repeated administration is allowed. It should, however, preferably never fall below 6 hours and in no case fall below 4 hours. In adolescent's administration should be regularly spaced, including night-time, preferably at 6-hour intervals, otherwise at intervals of a minimum of 4 hours. If the pain persists for more than 5 days or the fever lasts for more than 3 days, or gets worse or other symptoms appear, you should stop the treatment and consult a doctor.

Renal Insufficiency:
In case of renal insufficiency the dose should be reduced:

Glomerular filtration	Dose
10 – 50 ml/min	500 mg every 6 hours
< 10 ml/min	500 mg every 8 hours

Impaired liver function:
In patients with impaired hepatic function or Gilbert's syndrome, the dose must be reduced or the dosing interval prolonged. The daily effective dose should not exceed 60 mg/kg/day (up to maximum 2g/day) in the following situations:

- Adults weighing less than 50 kg
- Mild to moderate hepatic insufficiency, Gilbert's syndrome (familial non-haemolytic jaundice)
- Dehydration
- Chronic malnutrition
- Chronic alcoholism.

Intake of paracetamol with food and drink does not affect the efficacy of the medicinal product.

4.3 Contraindications

Hypersensitivity to Paracetamol or any of the excipients used in formulation.

4.4 Special warnings and precautions for use

Prolonged or frequent use is discouraged. Patients should be advised not to take other Paracetamol containing products concurrently. Taking multiple daily doses in one administration can severely damage the liver; in such case unconsciousness does not occur. However, medical assistance should be sought immediately. Prolonged use except under medical supervision may be harmful. In adolescents treated with 60mg/kg daily of Paracetamol, the combination with another antipyretic is not justified except in the case of ineffectiveness.

Caution is advised in the administration of Paracetamol to patients with moderate and severe renal insufficiency, mild to moderate hepatic insufficiency (including Gilbert's syndrome), severe hepatic insufficiency (child-pugh>9), acute hepatitis, concomitant treatment with medicinal products affecting hepatic functions, glucose-6-phosphatedehydrogenase deficiency, hemolytic anemia, alcohol abuse dehydration and chronic malnutrition.
The hazards of overdose are greater in those with non- cirrhotic alcoholic liver disease. Caution should be exercised in cases of chronic alcoholism. The daily dose should not exceed 2 grams in such case. Alcohol should not be used during the treatment with Paracetamol.
Caution is advised in asthmatic patients sensitive to aspirin, because light reaction bronchospasm with paracetamol (cross-reaction) has been reported in less than 5% of the patients tested.
This medicinal product contains sorbitol. Patients with rare hereditary problems of fructose intolerance should not take this medicine.
This medicinal product contains 503 mg of sodium per effervescent tablet, equivalent to 25.15% of the WHO recommended maximum daily intake of sodium. The maximum daily dose of this product is equivalent to 201.2% of the WHO recommended maximum daily intake for sodium. Paracetamol 500 mg Effervescent Tablet is considered high in sodium. Paracetamol 500 mg Effervescent Tablet should be taken into account for those on a low salt diet.
In the case of high fever, or signs of secondary infection or persistence of symptoms a doctor should be consulted.
Immediate medical advice should be sought in the event of overdosage even if the patient feels well because of the risk of irreversible liver damage.

4.5 Interaction with other medicinal products and other forms of interaction

Hepatotoxic substances may increase the possibility of Paracetamol accumulation and overdose. The risk of hepatotoxicity of paracetamol may be increased by drugs which induce liver microsomal enzymes such as barbiturates, tricyclic antidepressants, and alcohol.
Probenecid causes an almost 2-fold reduction in clearance of Paracetamol by inhibiting its conjugation with glucuronid acid. A reduction of the Paracetamol dose should be considered for concomitant treatment with probenecid.

- Salicylamide may prolong the elimination t1/2 of Paracetamol
- Metoclopramide and Domperidone: accelerate absorption of Paracetamol
- Cholestyramine: reduces absorption of Paracetamol
- Concomitant use of Paracetamol (4 g per day for at least 4 days) with oral anticoagulants may lead to slight variations of INR values. In this case, increased monitoring of INR values should be done during the duration of the combination and after its discontinuation. 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.

- Isoniazid: Reduction of paracetamol clearance, with possible potentiation of its action and/or toxicity, by inhibiting its metabolism in the liver.
- Lamotrigine: Decrease in the bioavailability of lamotrigine, with possible reduction of its effect, due to possible induction of its metabolism in the liver.

Interference with laboratory tests: Paracetamol may affect uric acid tests by wolframatop phosphoric acid, and blood sugar tests by glucose-oxidase-peroxidase.

4.6 Pregnancy and Lactation

Pregnant women:

Epidemiological data on the oral administration of therapeutic doses of Paracetamol indicate no adverse effects on pregnancy or on the health of the fetus/new-born child. Prospective data on overdose during pregnancy showed no increased risk of malformations. Reproduction studies investigating oral administration did not indicate any signs of malformation or fetotoxicity. Paracetamol is considered to be safe in normal therapeutic doses for short-term use as a minor analgesic/antipyretic in pregnancy.

Lactating women:

Following oral administration, Paracetamol is excreted into breast milk in small quantities. To date, no adverse reactions or undesirable effects are known in association with lactation. Therapeutic doses of Paracetamol can be administered during breast-feeding.

4.7 Effects on ability to drive and use machines

None.

4.8 Undesirable effects

The frequency using the following convention: very common (> 1/10); common (>1/100 to < 1/10); uncommon (>1/1000 to < 1/100); rare (>1/10000 to < 1/1000); very rare (< 1/10000), including isolated reports; not known: frequency cannot be estimated from the available data. Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Frequency	**System**	**Symptoms**
Rare >1/10000 - < 1/1000	Blood and lymphatic system	Platelet disorders stem cell
	Immune system disorders	Allergies (excluding angioedema).
	Psychiatric disorders	Depression NOS, confusion,
	Nervous system disorders	Tremor NOS, headache NOS.
	Eye disorders	Abnormal vision.

	Cardiac disorders	Oedema.
	Gastrointestinal disorders	Haemorrhage NOS, abdominal NOS, nausea, vomiting.
	Hepato-biliary disorders	Hepatic function abnormal, necrosis, jaundice.
	Skin and subcutaneous tissue	Pruritus, rash, sweating, purpura,
	General disorders and conditions	Dizziness (excluding vertigo), drug interaction NOS.
	Injury, poisoning and	Overdose and poisoning
Very Rare (< 10 000)	Hepato-biliary disorders	Hepatotoxicity
	General disorders and administration site conditions	hypersensitivity reaction (requiring discontinuation of treatment)
	Blood and lymphatic system disorders	Thrombocytopenia, leukopenia, neutropenia, hemolytic anemia, agranulocytosis
	Metabolism and nutrition disorders	Hypoglycemia
	Renal and urinary disorders	Sterile pyuria (cloudy urine) and renal side effects
	Skin and subcutaneous disorders	Serious skin reactions have been reported.

Not known: Edema of the larynx, anaphylactic shock, anemia, bronchospasm*, liver alteration and hepatitis, renal alteration (severe renal impairment, nephrite interstitial, haematuria, anuresis), gastrointestinal effects and vertigo have been reported.

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

Reporting of suspected adverse reactions:

Reporting of suspected adverse reactions: Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org.

4.9 Overdose

There is a risk of poisoning, particularly in elderly subjects, in young adolescents, in patients with liver disease, in cases of chronic alcoholism, in patients with chronic malnutrition. Overdosing may be fatal.
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 depleted, e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia.
d)

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. Simultaneously, increased levels of hepatic transaminases (AST, ALT), lactate dehydrogenase and bilirubin are observed together with increased prothrombin levels that may appear 12 to 48 hours after administration.

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 follow 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.

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 hypernatremia; electrolytes should be monitored and patients managed accordingly.

5. Pharmacological properties

5.1 Pharmacodynamic properties

i. **Pharmacotherapeutic group:** Analgesics and Antipyretics; Anilides
ii. **ATC code**: N02BE01

5.2 Pharmacokinetic properties

Ascorbic acid is absorbed in the proximal small intestine in a dose-dependent manner. The bioavailability drops with increasing dosage to 60 - 75% after 1 g, to approx. 40% after 3 g and approx. 16% after 12 g. The portion which is not absorbed is broken down by the large intestinal flora into CO2 and organic acids. The maximal metabolic turnover of 40 to 50 mg/day in healthy adults is reached at plasma concentrations of 0.8 to 1.0 mg/dl. The total daily turnover is about 1 mg/kg BW. Brief plasma concentrations of up to 4.2 mg/dl are achieved about three hours after applying extremely high oral doses. Under these circumstances ascorbic acid is eliminated in the urine by up to 80%. The half-life constitutes 2.9 hours on average. Renal elimination ensues via glomerular filtration and subsequent reabsorption in the proximal tubule. The upper limits given for healthy adults are 1.34 ± 0.21 mg ascorbic acid/dl plasma in men and 1.46 ± 0.22 mg in women, respectively. The total body content of ascorbic acid is at least 1.5 g following a high dose of about 180 mg daily. Ascorbic acid is concentrated in the pituitary gland, adrenal glands, lenses of the eye and white blood cells.

5.3 Preclinical safety data

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

Citric acid (Anhydrous)
Sodium bicarbonate (Anhydrous)
Sodium saccharin
PVP-K 30
Sodium Bicarbonate
Simethicone 100 %
Tween-80
Sodium Carbonate
Aspartame
Sodium Benzoate
Flavour Orange
Purified Water
Isopropyl Alcohol

6.2 Incompatibilities

Not applicable

6.3 Shelf-Life

36 Months

6.4 Special Precautions for storage

Store below 30°C. Protect from light.

6.5 Nature and Content of container

10 tablets packed in plastic tube and it's packed in a carton

6.6 Special precautions for disposal and other handling

Not applicable.

7. Marketing Authorization Holder

Manufacturer:

Vovantis Laboratories Private Limited
Survey no. 546/1/1, Opp. Ranoli Railway station,Near GACL plant, Ranoli, Vadodara, Gujarat - 391 350, India

Marketed by:

TIL HEALTHCARE PVT LTD
"Jhaver Centre", Rajah Annamalai Building, 72, Marshalls Road, Egmore, Chennai – 600008, India

8. Marketing Authorization Number

H2022/CTD9221/20333

9. Date of first authorization/renewal of the authorization

04/July/2022

10. Date of revision of the text

04/July/2022