SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

1. Name of the medicinal product

FEVAGRIP

(Paracetamol, Caffeine, Phenylephrine Hydrochloride and Chlorpheniramine Maleate Tablets)

2. Qualitative and Quantitative Composition

Each uncoated tablet contains:

Paracetamol BP……325 mg

Caffeine (anhydrous) BP……30 mg

Phenylephrine Hydrochloride BP……5 mg

Chlorpheniramine Maleate BP……2 mg

Excipients ……q.s.

Colour: Sunset Yellow.

For the full list of excipients, see section 6.1.

3. Pharmaceutical Form

Uncoated tablets

Orange coloured, elongated, biconvex, uncoated tablets having breakline on one side & plain on other side of each tablet.

4. Clinical particulars

4.1 Therapeutic indications

Fevagrip is a cold preparation to prevent any Influenza symptoms such as sneezing, nasal hyper secretion, nasal congestion, sluggishness, weariness, muscle pain, headache/ dizziness, fever throat itches and dry mouth.

4.2 Posology and method of administration

Posology

Adults: 1-2 caplets 3-4 times daily.

Children: ½-1 caplet 3-4 times daily.

These doses should not be repeated more frequently than every four hours.

Do not take continuously for more than 7 days without medical advice.

Method of administration: For oral administration only.

4.3 Contraindications

Fevagrip is contraindicated in patients with known hypersensitivity to any components of the

drug or in individuals with a history of allergic manifestations to aspirin or other NSAIDs. Severe anaphylactic-like reactions to ibuprofen have been reported in such patients, some with fatal outcome. There is evidence that caffeine causes tachyarrhythmias in susceptible individuals. So use of Fevagrip should be avoided in patients with cardiac arrhythmias. Caffeine enhances gastric acid and pepsin secretion and should also be avoided in individuals with a history of peptic ulceration. Interestingly, decaffeinated coffee has a similar effect, indicating that components other than caffeine contribute to the increased gastric acid output. It is not recommended to be taken by patients with impaired liver function.

4.4 Special warnings and precautions for use

Warnings

Severe hypertensive episodes leading to intracranial haemorrhage have followed phenylephrine ingestion. Patients should be informed of the dangers of exceeding the recommended dose; in particular the increased risk of serious adverse effects such as hypertensive crisis. This medicine may lead to drowsiness and impaired concentration, which may be aggravated by the simultaneous intake of alcohol or other central nervous system depressant agents. Patients should be warned not to drive a motor vehicle, operate dangerous machinery or perform potentially dangerous tasks, as impaired decision making could lead to accidents. Dosages in excess of those recommended may cause severe liver damage.

Precautions for use

Use caution when driving, operating machinery, or performing other hazardous activities. Fevagrip may cause dizziness or drowsiness. If you experience dizziness or drowsiness, avoid these activities.
Use alcohol cautiously. Alcohol may increase drowsiness and dizziness while taking Fevagrip. Alcohol may also cause damage to the liver when taken with paracetamol.
Fevagrip may increase the effects of other drugs that cause drowsiness, including antidepressants, alcohol, other antihistamines, pain relievers, anxiety medicines, seizure medicines, and muscle relaxants. Dangerous sedation, dizziness, or drowsiness may occur if Fevagrip is taken with any of these medications. It is not recommended for children under 6 years old, nursing mothers and pregnant women except on doctor's prescription. Stop using this drug if insomnia & palpitation occurs.

4.5 Interaction with other medicinal products and other forms of interaction

Clinically significant drug interactions may occur on concomitant administration of Fevagrip with monoamine oxidase inhibitors, tricyclic antidepressants, beta-adrenergic agents, methyldopa, reserpine and veratrum alkaloids.

4.6 Pregnancy and lactation

Pregnancy

Fevagrip is not recommended for use during pregnancy due to the possible increased risk of lower birth weight and spontaneous abortion associated with caffeine consumption. Use of Chlorpheniramine Maleate during the third trimester may result in reactions in the newborn or premature neonates. Fevagrip should be avoided in pregnancy unless essential.

Lactation

Paracetamol, Caffeine, Phenylephrine HCl & Chlorpheniramine Maleate are excreted in breast milk. May have a stimulating effect on breast fed infants. Fevagrip should not be used during breast feeding.

4.7 Effects on ability to drive and use machines

Drowsiness, dizziness, blurred vision and psychomotor impairment, have been reported which can seriously hamper the patient's ability to drive and use machinery.

4.8 Undesirable effects

Nervousness, restlessness, insomnia, dizziness, lassitude, muscular weakness, headache, nausea and drowsiness may occur with usual doses of Chlorpheniramine Maleate.

Phenylephrine can cause raised blood pressure, tachycardia and occasionally bradycardia, insomnia, restlessness, tremor and anxiety have occasionally occurred, as have urinary retention and hallucinations.

Paracetamol is relatively nontoxic in therapeutic doses; however, rash, pruritus, urticaria, laryngeal edema and rarely, anaphylactoid reactions, agranulocytosis, leukopenia and pancytopenia may occur with large doses.

Caffeine may cause insomnia, headache, nausea and gastric ulceration.

4.9 Overdose

Symptoms

Symptoms of Fevagrip overdose includes liver damage, a dry mouth, large pupils, flushing, nausea, vomiting, abdominal pain, diarrhea, seizures, sweating, haemodynamic changes and cardiovascular collapse with respiratory depression. If above symptoms observed, seek emergency medical attention.

Treatment

Intravenous N-acetylcysteine (NAC) is effective when initiated within 8 hours of the paracetamol overdose. Patients should be treated symptomatically as required. Activated charcoal should be

considered. Alternatively, in adults gastric lavage should be considered within one hour of ingestion of potentially toxic amounts. Severe hypertension may need to be treated with alpha blocking drugs such as phentolamine.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other cold combination preparations

ATC Code: R05X

Paracetamol:

Paracetamol has antipyretic and mild analgesic actions together with some anti-inflammatory activity. These effects are thought to be related to inhibition of prostaglandin synthesis. Paracetamol produces analgesia by elevation of the pain threshold and antipyretic effect through action on the hypothalamic heat-regulating centre.

Caffeine Anhydrous:

Caffeine, or 1,3,7-trimethylxanthine, is related structurally to uric acid. It is metabolized by demethylation and oxidation. The major human pathway results in paraxanthine (1,7-dimethylxanthine), leading to the principal urinary metabolites, l-methylxanthine, 1-methyluric acid, and an acetylated uracil derivative. Minor degradation pathways involve the formation and metabolism of theophylline and theobromine. No evidence exists to suggest that methylxanthines are converted to uric acid or that their ingestion can exacerbate gout.

In most cases, metabolism obeys first-order elimination kinetics within the therapeutic range. At higher concentrations, however, zero-order kinetics occurs with the saturation of metabolic enzymes. This prolongs the decline of caffeine concentrations.

Phenylephrine Hydrochloride:

Phenylephrine is sympathomimetic vasoconstrictor that has been used as a decongestant. It is a relatively selective alpha-adrenoceptor agonist. The majority of the sympathomimetic action is due to direct stimulation of the adrenoceptors and relatively little is due to an indirect effect via release of noradrenaline. Its pressor action is weaker than that of noradrenaline but of longer duration. At therapeutic doses, it does not cause significant stimulation of the central nervous system.

Chlorpheniramine Maleate:

Chlorpheniramine is an antihistamine. The effectiveness of first-generation antihistamines in blocking sneezing in colds may be due primarily to neuropharmacological manipulation of histaminic and muscarinic receptors in the medulla. Guaiphenesin is an expectorant that increases

respiratory tract fluid secretions and helps loosen phlegm and bronchial secretions. By reducing the viscosity of secretions, guaiphenesin increases the efficiency of the mucociliary mechanism in removing accumulated secretions from the upper and lower airway. Guaifenesin inhibits cough reflex sensitivity in subjects with URI, whose cough receptors are transiently hypersensitive. Possible mechanisms include a central antitussive effect or a peripheral effect by increased sputum volume serving as a barrier shielding cough receptors within the respiratory epithelium from the tussive stimulus.

5.2 Pharmacokinetic properties

Paracetamol:

Paracetamol is readily absorbed from the gastro-intestinal tract with peak plasma concentrations occurring about 30 minutes 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 about 1 to 4 hours. Plasma-protein binding is negligible at usual therapeutic concentrations but increases with increasing concentrations.

A minor hydroxylated metabolite which is usually produced in very small amounts by mixed-function oxidases in the liver and which is usually detoxified by conjugation with liver glutathione may accumulate following paracetamol overdosage and cause liver damage.

Caffeine Anhydrous:

Caffeine is absorbed readily after oral administration and is widely distributed throughout the body. Caffeine is metabolised almost completely via oxidation, demethylation, and acetylation, and is excreted in the urine as 1-methyluric acid, 1-methylxanthine, 7-methylxanthine, 1,7-dimethylxanthine (paraxanthine), 5-acetylamino-6-formylamino-3-methyluracil (AFMU), and other metabolites with only about 1% unchanged.

Phenylephrine Hydrochloride:

Phenylephrine hydrochloride is readily and rapidly absorbed from the gastro-intestinal tract. Presystemic metabolism is high at about 60%, resulting in systemic bioavailability of about 40%. Peak plasma levels occur between 1 and 2 hours and the plasma half-life ranges from 2 – 3 hours. When taken by mouth as a nasal decongestant phenylephrine is usually given at intervals of 4 – 6 hours.

Chlorpheniramine Maleate:

Chlorphenamine is well absorbed from the gastro-intestinal tract, following oral administration. The effects develop within 30 minutes, are maximal within 1 to 2 hours and last 4 to 6 hours. The plasma half-life has been estimated to be 12 to 15 hours. Chlorphenamine is metabolised to the

monodesmethyl and didesmethyl derivatives. About 22% of an oral dose is excreted unchanged in the urine.

5.3 Preclinical safety data

Preclinical data from acute and repeated dose toxicity studies, as well as from genotoxicity, mutagenicity, and carcinogenicity studies with Paracetamol, Caffeine, Phenylephrine Hydrochloride and Chlorpheniramine Maleate Tablets revealed no specific hazard for humans at the intended therapeutic doses.

6. Pharmaceutical particulars

6.1 List of excipients

Maize starch, Microcrystalline Cellulose, P.V.P.K.- 30, Methyl Paraben, Propyl Paraben, Colour Sunset Yellow Supra, Magnesium Stearate, Sodium Starch Glycolate, Purified Talc & Purified Water.

6.2 Incompatibilities

None known.

6.3 Shelf life

4 years from the date of manufacture.

6.4 Special precautions for storage

Store in a cool & dark place below 30° C.

Protect from light & moisture.

Keep all medicine away from children.

6.5 Nature and contents of container

Alu /PVC Blister of 4 Tablets and Such 25 blisters are packed in card board box along with pack insert.

6.6 Special precautions for disposal and other handling

No special requirements.

Any unused product or waste material should be disposed of in accordance with local requirements

7. Applicant/Manufacturer

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