FLUEZZE TABLETS

Summary of Product Characteristics

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1 NAME OF THE MEDICINAL PRODUCT

FLUEZZE TABLETS

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each uncoated Tablets contains

Paracetamol BP 500 mg

Chlorphaniramine Maleate BP 2 mg

Phenylephirine Hydrochloride USP 5 mg

Caffeine (Anhydrous) BP 30mg

Excipients q.s.
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORMS

Tablets

Light yellow & light pink colour bi layer tablet.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indication.

Symptomatic relief of symptoms of influenza, feverishness, chills and colds including feverish colds.

The symptomatic relief of nasal congestion and difficult breathing arising from this, sinusitis and its associated pain, acute nasal catarrh.

4.2 Posology and method of administration.

Adults, children aged 16 years and over and Elderly

2 caplets every 4 to 6 hours as required . Do not take more than 8 caplets in 24 hours.

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

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

Do not exceed the stated dose.

Use the lowest amount needed to achieve benefit for the shortest duration of treatment.

Not recommended for children under the age of 16 years.

4.3 Contraindications

Concomitant use of other sympathomimetic decongestants

Phaeochromocytoma

Closed angle glaucoma

Known hypersensitivity to paracetamol or any of the other constituents.

Hepatic or severe renal impairment, hypertension, hyperthyroidism, diabetes, and heart disease. Patients taking tricyclic antidepressants, or beta-blocking drugs and those who are taking or who have taken within the last two weeks monoamine oxidase inhibitors

4.4 Special warnings and precaution for use.

Contains paracetamol. Patients should be advised not to take other paracetamol-containing products concurrently. The concomitant use with other products containing paracetamol may lead to an overdose. Paracetamol overdose may cause liver failure which may require liver transplant or lead to death. Concomitant use of other decongestants or cold and flu medicines should be avoided.

The hazard of overdose is greater in those with non-cirrhotic alcoholic liver disease. Underlying liver disease increases the risk of paracetamol-related liver damage.

• Medical advice should be sought before using this product in patients with these conditions:

• Medical advice should be sought before taking this medicine in patients with: glutathione depletion due to metabolic deficiencies.An enlargement of the prostate gland

• Occlusive vascular disease (e.g. Raynaud's phenomenon)

• Cardiovascular disease

This product should not be used by patients taking other sympathomimetics (such as decongestants, appetite suppressants and amphetamine-like psychostimulants) (see interactions).

Excessive intake of caffeine (e.g. coffee, tea and some canned drinks) should be avoided while taking this product.

Do not exceed the stated dose.

If symptoms persist consult your doctor.

Keep out of the sight and reach of children.

Consult your doctor if you are taking warfarin.

Contains sunset yellow/ amaranth (E110) which may cause an allergic reaction.

Special Label Warnings

Contains paracetamol. Do not take with other flu, cold or decongestant products. Do not take anything else containing paracetamol while taking this medicine. Do not take more medicine than the label tells you to. If you do not get better, talk to your doctor.

Seek immediate medical advice if you take too much of this medicine even if you feel well.

Special Leaflet Warnings

Talk to a doctor at once if you take too much of this medicine even if you feel well, because of the risk of delayed, serious liver damage.

4.5 Interaction with other medicinal product and other forms of interaction.

Enzyme-inducing drugs may increase hepatic damage, as does excessive intake of alcohol. The speed of absorption of paracetamol may be increased by metoclopromide or domperidone and absorption reduced by colestyramine. These interactions are considered to be of unlikely clinical significance in acute use at the dosage regimen proposed.

Medical advice should be sought before taking paracetamol-caffeine phenylephrine in combination with the following drugs:

Monoamine oxidase inhibitors (including moclobemide)	Hypertensive interactions occur between sympathomimetic amines such as phenylephrine and monoamine Oxidase inhibitors (see contraindications).
Sympathomimetic amines	Concomitant use of phenylephrine with other sympathomimetics amines can increase the risk of cardiovascular side effects (see warnings and precautions).
Beta-blockers and other antihypertensives (including debrisoquine, guanethidine, reserpine, methyldopa)	Phenylephrine may reduce the efficacy of beta-blocking drugs and antihypertensive drugs. The risk of hypertension and other cardiovascular side effects may be increased (see contraindications).
Tricyclic antidepressants (e.g. amitriptyline)	May increase the risk of cardiovascular side effects with phenylephrine (see contraindications).
Digoxin and cardiac glycosides	Concimitant use of phenylephrine with digoxin or cardiac glycosides may increase the ris of irregular heartbeat or heart attack.
Ergot alkaloids (e.g. ergotamine and methylsergide)	Concomitant use of phenylephrine hydrochloride may cause an increased risk of ergotism (see Warnings and Precautions).
Warfarin and other coumarins	The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular daily use of paracetamol with an increased risk of bleeding; occasional doses have no significant effect.
Lithium	Caffeine can increase the elimination of lithium from the body. If taken concomitantly, it is recommended to reduce or moderate the intake of caffeine.

4.6 Pregnancy and Lactation.

Pregnancy

This product is not recommended for use in pregnancy due to the phenylephrine and caffeine content. There is a potential increased risk of lower birth weight and spontaneous abortion associated with caffeine consumption during pregnancy. Pregnant women should seek medical advice before taking paracetamol.

Breast-feeding

This product should not be used while breast-feeding without medical advice. Avoid the use of the product during lactation, unless the benefits to the mother outweigh the risks to the infant. If used, the lowest effective dose and shortest duration of treatment should be considered.

Paracetamol is excreted in breast milk but not in a clinically significant amount at recommended dosages.

Caffeine in breast milk may have a stimulating effect on breast-fed infants but significant toxicity has not been observed.

Phenylephrine may be excreted in breast milk.

4.7 Effect on the ability to drive and use machine.

Patients should be advised not to drive or operate machinery if affected by dizziness.

4.8 Undesirable effect.

Adverse events 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.

Paracetamol

Body System	Undesirable effect
Blood and lymphatic system disorders	Thrombocytopenia Agranulocytosis These were not necessarily causally related to paracetamol.
Immune system disorders	Anaphylaxis Cutaneous hypersensitivity reactions including skin rashes, angiodema Very rare cases of serious skin reactions have been reported.
Respiratory, thoracic and mediastinal disorders	Bronchospasm*
Hepatobiliary	Hepatic dysfunction

disorders	

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

Caffeine

Adverse reactions identified through post-marketing use with caffeine are listed below. The frequency of these reactions is unknown.

Body System	Undesirable effect
Central Nervous system	excitability dizziness and headache
Psychiatric disorders	Nervousness, insomnia, restlessness, anxiety and irritability
Cardiac disorders	Palpitations
Gastrointestinal disorders	Gastrointestinal disturbances

When the recommended paracetamol-caffeine dosing regimen is combined with dietary caffeine intake, the resulting higher dose of caffeine may increase the potential for caffeine-related adverse effects.

Phenylephrine

The following adverse events have been observed in clinical trials with phenylephrine and may therefore represent the most commonly occurring adverse events.

Body System	Undesirable effect
Psychiatric disorders	Nervousness
Nervous system disorders	Headache, dizziness, insomnia
Cardiac disorders	Increased blood pressure
Gastrointestinal disorders	Nausea, Vomiting

Adverse reactions identified during post-marketing use are listed below. The frequency of these reactions is unknown

Body System	Undesirable effect
Immune system disorders	Hypersensitivity, allergic dermatitis, urticaria
Eye disorders	Mydriasis, acute angle closure glaucoma, most likely to occur in those with closed angle glaucoma
Cardiac disorders	Tachycardia, palpitations
Skin and subcutaneous disorders	Rash
Renal and urinary disorders	Dysuria, urinary retention. This is most likely to occur in those with bladder outlet obstruction, such as prostatic hypertrophy.

4.9 Overdose.

Paracetamol

Paracetamol overdose may cause liver failure which may require liver transplant or lead to death. 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 and signs

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 and have peaked after 4-6 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.

Treatment

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. Acute pancreatitis has been observed, usually with hepatic dysfunction and liver toxicity.

Caffeine

Symptoms and signs

Overdose of caffeine may result in epigastric pain, vomiting, diurese, tachycardia or cardiac arrhythmia, CNS stimulation (insomnia, restlessness, excitement, agitation, jitteriness, tremors and convulsions).

It must be noted that for clinically significant symptoms of caffeine overdose to occur with this product, the amount ingested would be associated with serious paracetamol-related liver toxicity.

Treatment

No specific antidote is available, but supportive measures such as beta adrenoceptor antagonists to reverse the cardiotoxic effects may be used.

Phenylephrine
Symptoms and signs
Phenylephrine overdosage is likely to result in effects similar to those listed under adverse reactions. Additional symptoms may include, irritability, restlessness, hypertension, and possibly reflex bradycardia. In severe cases confusion, hallucinations, seizures and arrhythmias may occur. However the amount required to produce serious phenylephrine toxicity would be greater than that required to cause paracetamol-related liver toxicity.
Treatment
Treatment should be as clinically appropriate. Severe hypertension may need to be treated with alpha blocking drugs such as phentolamine.
If overdose is confirmed or suspected, seek immediate advice from your Poison Centre and refer patient to nearest Emergency Medical Centre for management and expert treatment. This should happen even in patients without symptoms or signs of overdose due to the risk of delayed liver damage.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties.

Paracetamol is a well established analgesic and antipyretic.

Phenylephrine hydrochloride is a sympathomimetic agent with mainly direct effects on adrenergic receptors (predominantly alpha-adrenergic activity) producing nasal decongestion. Caffeine is the most active xanthine derivative in respect of stimulation of the central nervous system, producing a condition of wakefulness and increased mental activity.

5.2 Pharmacokinetic properties.

Paracetamol is metabolised by the hepatic microsomal enzymes. It is rapidly and completely absorbed from the gastro-intestinal tract. Plasma concentration reaches a peak in half to one hour, the plasma half-life is one to three hours and it is uniformly distributed throughout the body.

Phenylephrine hydrochloride is irregularly absorbed from the gastro-intestinal tract. When injected intramuscularly it takes 10- *1* 5 minutes to act and subcutaneous and intramuscular injections are effective for about one hour. Intravenous injections are effective for about 20 minutes.

Caffeine is readily absorbed from the gastro-intestinal tract.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose Monohydrate	BP
Microcrystalline Cellulose	BP
Sodium Lauryl Sulphate	BP
Sodium Starch Glycolate	BP
Povidone	BP
Colour Quinolone yellow	BP
Purified Water	BP
Ponceau 4 R	BP
Magnesium Stearate	BP
Purified Talc	BP
Croscarmellose Sodium	BP

6.2 Incompatibilities
unknown

6.3 Shelf-life
36 months

6.4 Special precautions for storage
Do not store above 30°C. Store in a dry place.

6.5 Nature and composition of immediate packaging

10 tablets to packed in a blister made up of rigid non toxic PVC and printed aluminum foil. Such 10 blister are packed in a carton along with a leaflet.

6.6 Special precautions for the disposal of unused veterinary medicinal products or waste materials
None.

7 MARKETING AUTHORISATION/MANUFACTURER

DUPEN LABORATORIES PVT. LTD.
C 1 – 49/36, DEGAMROAD,
INDUSTRIAL TOWNSHIP
VAPI – 396195
GUJARAT INDIA.