Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

CURAFLU (Paracetamol, Pheniramine Maleate, Phenylephrine Hydrochloride and Ascorbic acid Granules)

2. Qualitative and quantitative composition

Each 5g sachet contains: 325 mg of Paracetamol BP, 20 mg Pheniramine Maleate BP, 10 mg of Phenylephrine HCl BP and 50 mg Ascorbic acid BP.

Excipients with known effect:
Each sachet contains 3211.18mg of Sucrose and 81mg of Sodium Citrate.

For the full list of excipients, see section 6.1

3. Pharmaceutical form

Dry Powder / Granules

Off white coloured powder.

4. Clinical particulars

4.1 Therapeutic indications

For the short-term treatment of cold and influenza symptoms, such as:
•Nasal congestion and sinuses.
•Runny nose.
•Sneezing.
•Body aches and pain, such as sore throat, headache, muscle pain and pain in the paranasal sinuses.
•Increased body temperature and associated chills.

4.2 Posology and method of administration

Posology
Adults (including the elderly) and children aged 12 years and over:
One sachet to be taken every four to six hours as required.
Maximum daily dose: 4 sachets in any 24-hour period.
Minimum dosing interval: 4 hours
Not recommended for children under the age of 12 years.
Maximum duration of use without medical advice: 7 days.
If symptoms persist, consult a doctor.
Do not exceed the stated dose.
The lowest dose necessary to achieve efficacy should be used for the shortest duration of treatment.

Method of administration
For oral use.

The content of the sachet intended for the preparation of solution - dissolve the powder in a sufficient quantity of either cold or warm water.

4.3 Contraindications

• Hypersensitivity to paracetamol, pheniramine, phenylephrine, ascorbic acid or to any of the excipients.
• who are taking, or have taken, monoamine oxidase inhibitors (MAOIs) in the last two weeks, which are typically used to treat depression.
•Concomitant use of other sympathomimetic decongestants.
• Phaeochromocytoma.
• Closed angle glaucoma.
• Severe hepatocellular insufficiency.
• Avoid in patients with prostatic enlargement.

4.4 Special warnings and precautions for use

•Contains paracetamol. Do not use with any other paracetamol-containing products, decongestants (medicines for the relief congestion or blocked nose) or cold and flu medicines.
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.

•Cases of hepatic dysfunction/failure have been reported in patients with depleted glutathione levels, such as those who are severely malnourished, anorexic, have a low body mass index, are chronic heavy users of alcohol or have sepsis. Concomitant use of other decongestants and antihistamines should be avoided.

•Medical advice should be sought before taking this product in patients with:

- Hepatic or renal impairment. Underlying liver disease increases the risk of paracetamol related liver damage.
- Glutathione depleted states, such as severe infections (e.g., sepsis), severe wasting, underweight, and chronic alcoholism, as the use of paracetamol may increase the risk of metabolic acidosis. Immediately consult the doctor if you have the following symptoms of metabolic acidosis: deep, rapid, difficult breathing; feeling sick (nausea), vomiting; loss of appetite.
- Hypertension (high blood pressure), cardiovascular diseases, diabetes, hyperthyroidism (overactivity of the thyroid gland), angle closure glaucoma (elevated intraocular pressure), pheochromocytoma (a rare tumor of the adrenal gland), prostatic hypertrophy (problems of the prostate gland or difficulty urinating), occlusive vascular diseases (e.g., Raynaud's Phenomenon, which can manifest as numbness, tingling and discoloration (white, blue,

then red) of the fingers and toes when exposed to cold).

•Use with caution in patients taking the following medications: beta blockers and other antihypertensives, tricyclic antidepressants (for example, amitriptyline), other sympathomimetics (such as decongestants, appetite suppressants and amphetamine-like medications), digoxin and cardiac glycosides, ergot alkaloids (for example, ergotamine and methysergide).

•Use with caution in the elderly, who are more likely to experience adverse effects. Avoid use in elderly patients with confusion.
•Patients suffering from diabetes should consider that the product contains sucrose.
•Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltose insufficiency should not take this medicine.
•This medicinal product contains of sodium, which should be taken into consideration by patients on a controlled sodium diet.
•Do not use the drug from damaged sachets.
•Keep out of sight and reach of children.
• Do not exceed the recommended dose.
•Always read and follow the label. Beta blockers, and antihypertensives(including debrisoquine, guanethidine, reserpine, methyldopa)

4.5 Interaction with other medicinal products and other forms of interaction

Before taking the drug, consult a doctor, if you are taking;

Monoamine-oxidase inhibitors (MAOIs):	Hypertensive interactions occur between sympathomimetic amines such as phenylephrine and MAOIs
Sympathomimetic amines (e.g., decongestants, appetite suppressants and amphetamine–like medications)	Concomitant use of phenylephrine with other sympathomimetic amines can increase the risk of cardiovascular side effects
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
Tricyclic antidepressants (e.g. amitriptyline)	May increase the risk of cardiovascular side effects with phenylephrine
Digoxin and cardiac glycosides	Concomitant use of phenylephrine may increase the risk of irregular heartbeat or cardiac arrest
Ergot alkaloids (e.g., ergotamine and methysergide)	Concomitant use of phenylephrine may cause increased risk of ergotism

Warfarin and other coumarins	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.
Alcohol	Alcohol enhances the sedative effect of pheniramine.
Sedatives and Hypnotics (e.g. barbiturates, benzodiazepines, anxiolytics, and antidepressants)	Pheniramine increases the central depressive action of other sedatives.
Anticholinergics (e.g., other antihistamines, anti-Parkinson's medications and phenothiazine neuroleptics)	Pheniramine has anticholinergic activity and canenhance the anticholinergic effect of other drugs with anticholinergic activity.

You should inform your doctor or pharmacist about any other medications you are taking.

4.6 Pregnancy and Lactation

Pregnancy

There are insufficient data regarding the use of the product in pregnant women. Animal studies are insufficient with respect to reproductive toxicity. Avoid the use of the product during pregnancy, unless the benefits to the pregnant woman outweigh the risks to the foetus.

If used, the lowest effective dose and shortest duration of treatment should be considered. As with the use of any medicine during pregnancy, pregnant women should seek medical advice before taking paracetamol.
There are no animal studies or human clinical data on the use of pheniramine in pregnant women.

There are limited data on the use of phenylephrine in pregnant women.
A tolerable upper intake level (UL) recommended for ascorbic acid is 1800 mg/day (during pregnancy <18 years) and 2000 mg/day (during pregnancy >18 years). The UL is the maximum level of a daily nutrient intake that is likely to pose no risk of adverse health effects.

Lactation

Avoid the use of the product during lactation, unless the benefits to the mother outweigh the risk 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.
There are no animal studies or human clinical data on the use of pheniramine during lactation.
Phenylephrine may be excreted into breast milk.

A tolerable upper intake level (UL) recommended for ascorbic acid is 1800 mg/day (lactation <18 years) and 2000 mg/day (lactation >18 years). The UL is the maximum level of a daily nutrient intake that is likely to pose no risk of adverse health effects. The product should be avoided during lactation due to phenylephrine, which may be excreted in breast milk.

4.7 Effects on ability to drive and use machines

Pheniramine may cause drowsiness, dizziness, blurred vision, impaired cognitive function and motor coordination in some patients which may significantly affect ability to drive or use machinery. This could be further intensified by alcohol or other sedatives.

4.8 Undesirable effects

If an unusual reaction occurs, consult a doctor.

System Organ Class	**Adverse Reaction**	**Frequency**
Paracetamol		
Blood and lymphatic system disorders	Thrombocytopenia	Very rare
Immune system disorders	Anaphylaxis Cutaneous hypersensitivity reactions including, among others, Toxic Epidermal Necrolysis, Stevens Johnson syndrome, angioedema and skin rashes.	Very rare
Respiratory, thoracic and mediastinal disorders	Bronchospasm in patients sensitive to aspirin and other NSAIDs.	Very rare
Hepatobiliary disorders	Hepatic dysfunction	Very rare
Pheniramine		
System Organ Class	**Adverse Reaction**	**Frequency**
Blood and lymphatic system disorders	Leukopenia, thrombocytopenia, haemolytic anaemia	Unknown
Immune system disorders	Anaphylactic shock, angioedema, hypersensitivity, urticaria	Rare
Nervous system disorders	Anticholinergic symptoms, impaired motor coordination, tremors, loss of memory or concentration*, balance disorders*, dizziness*, sedation**, drowsiness**. Hallucination, confusion, excitation effects (agitation, nervousness, and insomnia)	Unknown
Eye disorders	Mydriasis, accommodation disorders	Unknown
Cardiac disorders	Palpitations	Unknown
Vascular disorders	Orthostatic hypotension	Unknown

Gastrointestinal disorders	Constipation	Unknown
Skin and subcutaneous disorders	Eczema, purpura, erythema, pruritus	Rare
Renal and urinary disorders	Urinary retention	Unknown
General disorders and administration site conditions	Dryness of mucous membrane	Unknown

Phenylephrine		
System Organ Class	**Adverse Reaction**	**Frequency**
Nervous system disorders	Dizziness, headache, insomnia	Common
Cardiac disorders	Increased blood pressure Tachycardia, palpitations	Commo n Rare
Gastrointestinal disorders	Vomiting, nausea	Common
Immune system disorders	Hypersensitivity, allergic dermatitis, urticaria	Rare
Eye disorders	Acute angle closure glaucoma (most likely to occur in those with closed angle glaucoma *(see the section 4.4 Special Warnings and Precautions for Use)*), mydriasis	Rare
Skin and subcutaneous disorders	Rash	Rare

* more frequently in elderly patients

**more marked at the start of treatment

Patient should stop taking the drug and consult a doctor in the cases of:

•Allergic reaction such as a rash or hives (itchy bumpy rash), sometimes with
•Difficulty breathing, redness and/or swelling of the mouth, face, lips, tongue, throat or eyes;

•Skin rashes, peeling of the skin or ulcers in the mouth;

•Breathing problems when using aspirin or other nonsteroidal anti-inflammatory drugs, as well as in the case of a similar reaction with this drug;

•Bruises or bleeding of unknown etiology;

•Darkening of the urine along with pale skin, dizziness and fatigue
•Hallucinations (visual or auditory);

•An excessively fast pulse or a feeling of an excessively fast irregular pulse;

•Blurred vision that may be associated with abnormally high blood pressure in the eye. The occurrence of this reaction is very rare and more likely in patients with glaucoma;

•Problem with urination. The occurrence of this reaction is more likely in men with prostatic hyperplasia.

These reactions occur rare or very rare.

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

If you have taken the drug more than recommended, consult a doctor immediately because of the risk of liver failure, even if you have no symptoms. Overdose can lead to loss of consciousness or coma. Seizures (fits) can occur in children.

Paracetamol

Symptoms and Signs

Experience following overdose with paracetamol indicates that the clinical signs of liver injury occur usually after 24 to 48 hours and have peaked after 4 to 6 days.

Overdose may cause liver failure which may require liver transplant or lead to death.

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

Treatment

Immediate medical management is required in the event of overdose, even if symptoms of overdose are not present.

If overdose is confirmed or suspected, seek immediate medical advice from your doctor or refer patient to nearest Emergency Medical Centre for management and treatment. This should happen even in patients without symptoms or signs of overdose due to the risk of delayed liver damage.

Administration of N-acetylcysteine or methionine may be required.

Pheniramine

Symptoms and signs

Pheniramine overdose may lead to convulsions (especially in children), disturbances of consciousness and coma.

Treatment

Treatment should be supportive and directed towards specific symptoms.

Phenylephrine

Symptoms and Signs

Over-dosage is likely to result in effects similar to those listed in the section 4.8 Undesirable effects.

Additional symptoms may include irritability, restlessness, hypertension and possibly reflux brachycardia. In severe cases, confusion, hallucinations, seizures and arrhythmias may occur.

Treatment

Treatment should be as clinically appropriate. Severe hypertension may need to be treated with an alpha blocking drug such as phentolamine.

Ascorbic Acid
High doses of ascorbic acid (>3000mg) may cause transient osmotic diarrhoea gastrointestinal effects such as nausea and abdominal discomfort. Effects of overdose of ascorbic acid would be subsumed by serious liver toxicity caused by paracetamol overdose.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group:
Other analgesics and antipyretics, paracetamol, combinations excluding psycholeptics. Nasal decongestant for systemic use, sympathomimetics, phenylephrine, combinations. ATC Code: N02BE51

Mechanism of action
Paracetamol
An analgesic and antipyretic. Its mechanism of action is believed to include inhibition of prostaglandin synthesis, primarily within the central nervous system.

Pheniramine maleate
An antihistamine acting on the H1-receptors.

Phenylephrine hydrochloride
Is a sympathomimetic agent with mainly direct effects on adrenergic receptors (predominantly alpha-adrenergic activity) producing nasal decongestion.

Ascorbic acid
An electron donor (reducing agent or antioxidant).

Pharmacodynamic effects
Paracetamol
The lack of peripheral prostaglandin inhibition confers important pharmacological properties such as the maintenance of the protective prostaglandins within the gastrointestinal tract. Paracetamol is, therefore, particularly suitable for patients with a history of disease or on concomitant medication, where peripheral prostaglandin inhibition would be undesirable (such as, for example, those with a history of gastrointestinal bleeding or the elderly).

Pheniramine maleate
It provides relief of the common allergic symptoms associated with respiratory tract disorders. It causes a moderate degree of sedation and has also antimuscarinic activity.

Phenylephrine hydrochloride

Phenylephrine hydrochloride has nasal decongestant activity and reduces oedema and swelling of the nasal mucosa.

Ascorbic acid
Vitamin C is usually included in the combination of anti-cold components, compensating for the loss of vitamin C that occurs during the initial stages of viral diseases, including the common cold.

5.2 Pharmacokinetic properties

Paracetamol
It is rapidly and almost completely absorbed from the gastrointestinal tract and is distributed in most tissues of the body. Maximum paracetamol plasma concentrations occurring about 10 to 60 minutes after oral doses. Binding to plasma proteins is minimal at therapeutic concentrations. It is metabolised in the liver and excreted in the urine mainly as glucuronide and sulphate conjugates. Less than 5% is excreted as unmodified paracetamol.

Pheniramine maleate
Reaches its peak plasma concentration in 1-2.5 hours; the half-life is 16-19 hours. 70-83% of the oral dose is excreted in the urine unchanged or in the form of metabolites.

Phenylephrine hydrochloride
Is irregularly absorbed from the gastrointestinal tract. It undergoes first-pass metabolism by monoamine oxidases in the gut and liver; orally administered phenylephrine thus has reduced bioavailability. It is excreted in the urine almost entirely as the sulphate conjugate.

Ascorbic Acid
Is rapidly absorbed from the gastrointestinal tract and is widely distributed throughout the body. It is 25% bound to plasma proteins. Ascorbic acid in excess of the body's needs is eliminated in the urine as metabolites.

5.3 Preclinical safety data

Non-clinical safety data on paracetamol, pheniramine maleate, phenylephrine hydrochloride and ascorbic acid, have not revealed findings which are of relevance to the recommended dosage and use of the product.

<u>Mutagenesis and Carcinogenesis:</u>
Data on the carcinogenic potential of pheniramine maleate are not available.
However, pheniramine maleate was not mutagenic when tested in vitro in the reverse mutation assay with Salmonella typhimurium and Escherichia coli as well as in the chromosomal aberration and sister

chromatid exchange assays with Chinese hamster ovary cells. All assays were conducted in both the presence and absence of metabolic activation.

Reproductive Toxicology:
Limited non-clinical data are available on the potential adverse reproductive and developmental effects of phenylephrine. Foetal growth restriction and premature delivery were reported in the offspring of pregnant rabbits following subcutaneous administration of phenylephrine at a dose that was 5-fold less than the clinical dose from the 22nd day of gestation until delivery

6. Pharmaceutical Particulars

6.1 List of Excipients

Sucrose BP
Maltodextrin BP
Colloidal anhydrous silica BP
Citric acid anhydrous BP
Sodium citrate BP
Sucralose BP
Neotame Titanium dioxide BP
Natural lemon flavour

6.2 Incompatibilities

None

6.3 Shelf-Life

24 months

6.4 Special Precautions for storage

Store below 30°C. Protect from direct sunlight, heat and moisture**.**

6.5 Nature and Content of container

1 x 5 g Sachet (Alu-Alu)

6.6 Special precautions for disposal and other handling

No special precautions required but general disposing & handling guidelines must be followed.
Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

7. Marketing Authorization Holder

VITACURA PHARMACEUTICALS
Plot No:235, 2nd Floor, 3rd cross street, Lakshmi Nagar extension,
Porur, Chennai-600 116, INDIA
INDIA

8. Marketing Authorization Number
CTD8635/17839

9. Date of first authorization/renewal of the authorization
2023

10. Date of revision of the text
19/05/2025