Front

TN6129I

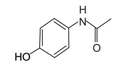
CHLORPHENAMINE MALEATE,
PARACETAMOL & VITAMIN C SYRUP

APFLU SYRUP

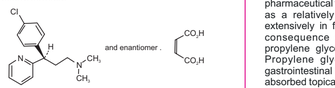
COMPOSITION:
Each 5ml contains:

Chlorphenamine Maleate BP	0.50mg
Paracetamol BP	120mg
Vitamin C BP	50mg
Flavoured syrup base	q.s.
Colour: Caramel	

DESCRIPTION:
Paracetamol
Paracetamol is also called as acetaminophen, is an analgesic antipyretic derivative of acetanilide. Its chemical name is N-(4-hydroxyphenyl) acetamide. Its molecular formula is $C_8H_9NO_2$. Its molecular weight is 151.165. Paracetamol has following structural formula:



Chlorphenamine Maleate
Chlorpheniramine maleate is a histamine H1 antagonist used in allergic reactions, hay fever, rhinitis, urticaria, and asthma. Its chemical name is (3RS)-3-(4-Chlorophenyl)-N,N-dimethyl-3- (pyridin-2-yl) propan-1-amine hydrogen (Z)- butenedioate. Its molecular formula is $C_{16}H_{19}ClN_2.\ C_4H_4O_4$. Its molecular weight is 390.9. Chlorphenamine Maleate has following structural formula:



Vitamin C:
Vitamin C is a vitamin. Vitamin C is used most often for preventing and treating the common cold. Its chemical name is (2R)-2-[(1S)-1,2-dihydroxyethyl]-3,4-dihydroxy-2H-furan-5-one. Its molecular formula is $C_6H_8O_6$. Its molecular weight is 176.1 g/mole. Vitamin C has following structural formula:

EXCIPIENT LIST:
Paracetamol BP, Ascorbic acid BP, Chlorphenamine Maleate BP, Sugar commercial IH, Glycerol BP, Propylene glycol BP, Methyl Hydroxybenzoate BP, propyl Hydroxybenzoate BP, Sodium metabisulfite BP, Sodium chloride BP, Saccharin sodium BP, Mango flavour ASV IH, Liquid caramel colour IH, Disodium EDTA BP, Sodium dihydrogen phosphate dihydrate BP, Disodium Hydrogen Phosphate Dihydrate BP, Hyflosupercel IH.

CLINICAL PARTICULARS
Therapeutic indications:
Apflu Syrup (Acetaminophen, chlorpheniramine, and Vit. C) is a combination medicine used to treat headache, fever, body aches, runny or stuffy nose, sneezing, itching, watery eyes, and sinus congestion caused by allergies, the common cold, or the flu.
Also indicated for the reduction of toothache.

Notorious effects of excipients:
The Apflu Syrup Chlorphenamine Maleate, Paracetamol & Vitamin C Syrup contains
1. Sugar commercial IH:
Sugar is hydrolyzed in the small intestine by the enzyme sucrase to yield dextrose and fructose, which are then absorbed. When administered intravenously, sucrose is excreted unchanged in the urine. Although sucrose is very widely used in foods and pharmaceutical formulations, sucrose consumption is a cause of concern and should be monitored in patient.

2. Glycerol BP:
Glycerin occurs naturally in animal and vegetable fats and oils that are consumed as part of a normal diet. Glycerin is readily absorbed from the intestine and is either metabolized to carbon dioxide and glycogen or used in the synthesis of body fats. Glycerin is used in a wide variety of pharmaceutical formulations including oral, ophthalmic, parenteral, and topical preparations.
Adverse effects are mainly due to the dehydrating properties of glycerin. Oral doses are demulcent and mildly laxative in action.

3. Propylene glycol BP:
Propylene glycol is used in a wide variety of pharmaceutical formulations and is generally regarded as a relatively nontoxic material. It is also used extensively in foods and cosmetics. Probably as a consequence of its metabolism and excretion, propylene glycol is less toxic than other glycols. Propylene glycol is rapidly absorbed from the gastrointestinal tract; there is also evidence that it is absorbed topically when applied to damaged skin. It is extensively metabolized in the liver, mainly to lactic and pyruvic acids, and is also excreted unchanged in the urine In animal studies, there has been no evidence that propylene glycol is teratogenic or mutagenic. Rats can tolerate a repeated oral daily dose of up to 30 mL/kg body-weight in the diet over 6 months, while the dog is unaffected by a repeated oral daily dose of 2 g/kg in the diet for 2 years.(14) LD50 (mouse, IP): 9.72 g/kg, LD50 (mouse, IV): 6.63 g/kg, LD50 (mouse, oral): 22.0 g/kg LD50 (mouse, SC): 17.34 g/kg, LD50 (rat, IM): 0.01 g/kg LD50 (rat, IP): 6.66 g/kg, LD50 (rat, IV): 6.42 g/kg, LD50 (rat, oral): 0.02 g/kg, LD50 (rat, SC): 22.5 g/kg

4. Methyl Hydroxybenzoate BP
Methylparaben and other parabens are widely used as antimicrobial preservatives in cosmetics and oral and topical pharmaceutical formulations. Although parabens have also been used as preservatives in injections and ophthalmic preparations, Parabens are nonmutagenic, nonteratogenic, and noncarcinogenic.Sensitization to the parabens is rare, and these compounds do not exhibit significant levels of photocontact sensitization or phototoxicity.

5. Propyl Hydroxybenzoate BP:
Propylparaben and other parabens are widely used as antimicrobial preservatives in cosmetics, food products, and oral and topical pharmaceutical formulations. Propylparaben and methylparaben have been used as preservatives in injections and ophthalmic preparations; The WHO has set an estimated acceptable total daily intake for methyl, ethyl, and propyl parabens at up to 10 mg/kg body-weight. LD50 (mouse, IP): 0.2 g/kg LD50 (mouse, oral): 6.33 g/kg LD50 (mouse, SC): 1.65 g/kg
6. Sodium metabisulfite BP:
Sodium metabisulfite is widely used as an antioxidant in oral, topical, and parenteral pharmaceutical formulations; it is also widely used in food products.
Although it is extensively used in a variety of preparations, In Europe, the acceptable daily intake of sodium metabisulfite and other sulfites used in foodstuffs has been set at up to 3.5 mg/kg body-weight, calculated as sulfur dioxide (SO_2). The WHO has similarly also set an acceptable daily intake of sodium metabisulfite, and other sulfites, at up to 7.0 mg/kg body-weight, calculated as sulfur dioxide (SO_2). LD50 (rat, IV): 0.12 g/kg.

7. Sodium chloride BP:
Sodium chloride is the most important salt in the body for maintaining the osmotic tension of blood and tissues. About 5–12 g of sodium chloride is consumed daily, in the normal adult diet, and a corresponding amount is excreted in the urine. As an excipient, sodium chloride may be regarded as an essentially nontoxic and nonirritant material.

8. Saccharin Sodium BP:
The WHO has set a temporary acceptable daily intake for saccharin, including its calcium, potassium, and sodium salts, at up to 2.5 mg/kg body-weight. In the UK, the Committee on Toxicity of Chemicals in Food, Consumer Products, and the Environment (COT) has set an acceptable daily intake for saccharin and its calcium, potassium, and sodium salts (expressed as saccharin sodium) at up to 5 mg/kg body-weight. Adverse reactions to saccharin, although relatively few in relation to its widespread use, include: urticaria with pruritus following ingestion of saccharin-sweetened beverages and photosensitization reactions. LD50 (mouse, oral): 17.5 g/kg (13) LD50 (rat, IP): 7.10 g/kg LD50 (rat, oral): 14.2 g/kg.

9. Mango flavour ASV IH
No data available

10. Liquid caramel colour IH
Caramel color has been used in foods and beverages for over 150 years and is globally regulated as a color additive. The four distinct classes of caramel color (Plain Caramel, Sulfite Caramel, Ammonia Caramel, and Sulfite Ammonia Caramel) are well characterized and each have specifications that take into account processing variables including reactants that can give rise to low molecular weight constituents (e.g., 4-MeI and THI) that may have toxicological significance for evaluating safety.
Extensive safety testing has been conducted with the different classes of caramel color and its constituents, including toxicokinetics, genotoxicity, subchronic toxicity, carcinogenicity, and reproductive/developmental toxicity studies. In addition, data is available on uses and use levels that have been used to estimate intakes of caramel colors and their constituents. No Observable Adverse Effect Levels (NOAEL) have been identified for all classes and Acceptable Daily Intakes have been established to ensure safety of use. Available studies support a conclusion that caramel colors are not genotoxic or carcinogenic, and exposure estimates indicate that intake of caramel colors and constituents do not pose undue safety risks. This update summarizes available relevant safety studies and authoritative reviews on caramel colors and its toxicologically important constituents, 4-MeI and THI.

11. Disodium EDTA
It is used widely in topical, oral, and parenteral pharmaceutical formulations; it is used extensively in cosmetic and food products. Disodium edetate and edetate calcium disodium are used in a greater number and variety of pharmaceutical formulations than is edetic acid. Both disodium edetate and edetate calcium disodium are poorly absorbed from the gastrointestinal tract and are associated with few adverse effects when used as excipients in pharmaceutical formulations. Although disodium edetate is generally considered safe, there have been reports of disodium edetate toxicity in patients receiving chelation therapy.

12. Sodium dihydrogen phosphate dihydrate BP
It is widely used as an excipient in parenteral, oral, and topical pharmaceutical formulations. Phosphate occurs extensively in the body and is involved in many physiological processes since it is the principal anion of intracellular fluid. Most foods contain adequate amounts of phosphate, making hypophosphatemia (1) virtually unknown except in certain disease states (2) or in patients receiving total parenteral nutrition. Treatment is usually by the oral administration of up to 100 mmol of phosphate daily. Approximately two-thirds of ingested phosphate is absorbed from the gastrointestinal tract, virtually all of it being excreted in the urine, and the remainder is excreted in the feces.

13. Disodium Hydrogen Phosphate Dihydrate BP:
It is widely used as an excipient in parenteral, oral, and topical pharmaceutical formulations. Phosphate occurs extensively in the body and is involved in many physiological processes since it is the principal anion of intracellular fluid. Most foods contain adequate amounts of phosphate, making hypophosphatemia (phosphate deficiency) virtually unknown except for certain disease states or in patients receiving total parenteral nutrition. Treatment is usually by the oral administration of up to 100 mmol of phosphate daily. Approximately two-thirds of ingested phosphate is absorbed from the gastrointestinal tract, virtually all of it being excreted in the urine, and the remainder is excreted in the feces.

14. Hyflosupercel IH.
Synonym is colloidal silicon dioxide is widely used in oral and topical pharmaceutical products and is generally regarded as an essentially nontoxic and nonirritant excipient. However, intraperitoneal and subcutaneous injection may produce local tissue reactions and/or granulomas. Colloidal silicon dioxide should therefore not be administered parenterally.
LD50 (rat, IV): 0.015 g/kg
LD50 (rat, oral): 3.16 g/kg

Posology and methods of administration:
Oral administration only
Do not exceed the stated dose or frequency of dosing

Children:
- 01 – 02 Years: 5 ml X 4 times daily
- 02 – 08 Years: 10 ml X 4 times daily
- 08 – 10 Years: 15 ml X 4 times daily
- 10 – 12 Years: 20 ml X 4 times daily

CONTRAINDICATION:
- Hypersensitivity to antihistamines or paracetamol or to any of the excipients
- Patients with severe hepatic dysfunction.
- The anticholinergic properties of chlorphenamine are intensified by monoamine oxidase inhibitors (MAOIs). Therefore, contra-indicated in patients who have been treated with MAOIs within the last fourteen days.
- Ascorbic acid should not be given to patients with hyperoxaluria.

SPECIAL WARNING AND PRECAUTIONS FOR USE:
Chlorphenamine
Chlorphenamine, in common with other drugs having anticholinergic effects, should be used with caution in epilepsy; raised intra-ocular pressure including glaucoma; prostatic hypertrophy; severe hypertension or cardiovascular disease; bronchitis, bronchiectasis and asthma; hepatic impairment; renal impairment. Children and the elderly are more likely to experience the neurological anticholinergic effects and paradoxical excitation (e.g. increased energy, restlessness, nervousness). Avoid use in elderly patients with confusion.
The anticholinergic properties of chlorphenamine may cause drowsiness, dizziness, blurred vision and psychomotor impairment in some patients, which may seriously affect ability to drive and use machinery.
The effects of alcohol may be increased and therefore concurrent use should be avoided.
Should not be used with other antihistamine containing products, including antihistamine containing cough and cold medicines.
Concurrent use with drugs, which cause sedation such as anxiolytics and hypnotics, may cause an increase in sedative effects; therefore, medical advice should be sought before taking chlorphenamine concurrently with these medicines.

Paracetamol
Care is advised in the administration of paracetamol to patients with severe renal or severe hepatic impairment. The hazards of overdose are greater in those with non-cirrhotic alcoholic liver disease.
Do not give with any other paracetamol-containing products.
Medical monitoring is required in patients with impaired renal or hepatic functions because various adverse events attributed to propylene glycol have been reported such as renal dysfunction (acute tubular necrosis), acute renal failure and liver dysfunction.

Ascorbic Acid
Increased intake of ascorbic acid over a prolonged period may result in an increased renal clearance of ascorbic acid, and deficiency may result if the intake is reduced or withdrawn rapidly.

Interference with serological testing
Ascorbic acid may interfere with tests and assays for urinary glucose, giving false-negative results with methods utilising glucose oxidase with indicator (e.g. Labstix, Tes-Tape) and false-positive results with neocuproine methods.
Estimation of uric acid by phosphotungstate or uricase with copper reduction and measurement of creatinine in non-deproteinised serum may also be affected.
High doses of ascorbic acid may give false-negative reading in faecal occult blood tests.

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION:
Concurrent use of chlorphenamine and hypnotics or anxiolytics may cause an increase in sedative effects; concurrent use of alcohol may have a similar effect therefore medical advice should be sought before taking chlorphenamine concurrently with these medicines.
Chlorphenamine inhibits phenytoin metabolism and can lead to phenytoin toxicity.
The anticholinergic effects of chlorphenamine are intensified by MAOIs
The hepatotoxicity of Paracetamol, particularly after overdosage, may be increased by drugs, which induce liver microsomal enzymes such as barbiturates, tricyclic antidepressants, and alcohol.
Chronic alcohol intake can increase the hepatotoxicity of paracetamol overdose and may have contributed to the acute pancreatitis reported in one patient who had taken an overdose of paracetamol. Acute alcohol intake may diminish an individual's ability to metabolize large doses of paracetamol, the plasma half-life of which can be prolonged.
The speed of absorption of paracetamol may be increased by metoclopramide or domperidone and absorption reduced by colestyramine.
The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular use of paracetamol with increased risk of bleeding; occasional doses have no significant effect.
Antivirals: Regular use of Paracetamol possibly reduces metabolism of Zidovudine (increased risk of neutropenia).
The use of drugs that induce hepatic microsomal enzymes such as anticonvulsants and oral contraceptives may increase the extent of metabolism of paracetamol resulting in reduced plasma concentrations of the drug and a faster elimination rate.
Ascorbic acid increases the renal excretion of amphetamine. The plasma concentration of ascorbate is decreased by smoking and oral contraceptives.
Ascorbic acid increases the absorption of iron.
Concomitant administration of aspirin and ascorbic acid may interfere with absorption of ascorbic acid.
Renal excretion of salicylate is not affected and does not lead to reduced anti-inflammatory effects of aspirin.
Concomitant administration of aluminium-containing antacids may increase urinary aluminium elimination.
Concurrent administration of antacids and ascorbic acid is not recommended, especially in patients with renal insufficiency.
Co-administration with amygdalin (a complementary medicine) can cause cyanide toxicity.
Concurrent administration of ascorbic acid with desferrioxamine enhances urinary iron excretion. Cases of cardiomyopathy and congestive heart failure have been reported in patients with idiopathic haemochromatosis and thalassaemias receiving desferrioxamine who were subsequently given ascorbic acid. Ascorbic acid should be used with caution in these patients and cardiac function monitored.
Ascorbic acid may interfere with biochemical determinations of creatinine, uric acid and glucose in samples of blood and urine.

USE IN SPECIFIC POPULATIONS:
Pregnancy
There are no adequate data from the use of chlorphenamine in pregnant women. The potential risk for humans is unknown; Use during the third trimester may result in reactions in the new born or premature neonates. Not to be used during pregnancy unless considered essential by a physician.

Lactation
Chlorphenamine maleate and other antihistamines may inhibit lactation and may be secreted in breast milk. Not to be used during lactation unless considered essential by a physician.
EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:
The anticholinergic properties of chlorphenamine in Apflu Syrup may cause drowsiness, dizziness, blurred vision and psychomotor impairment, which can seriously hamper the patients' ability to drive and use machinery.
Ascorbic acid has no known effect on an individual's ability to drive or operate machinery.

UNDESIRABLE EFFECTS:
Chlorphenamine
The following convention has been utilised for the classification of the frequency of adverse reactions: very common (>1/10), common (>1/100 to <1/10), uncommon (>1/1000 to <1/100), rare (>1/10,000 to <1/1000) and very rare (<1/10,000), not known (cannot be estimated from available data).
Adverse reactions identified during post-marketing use with chlorphenamine are listed below. As these reactions are reported voluntarily from a population of uncertain size, the frequency of some reactions is unknown but likely to be rare or very rare:

System Organ Class	Adverse Reaction	Frequency
Nervous system disorders*	Sedation, somnolence	Very common
	Disturbance in attention, abnormal coordination, dizziness headache	Common
Eye disorders	Blurred Vision	Common
Gastrointestinal disorders	Nausea, dry mouth	Common
	Vomiting, abdominal pain, diarrhoea, dyspepsia	Unknown
Immune system disorders:	Allergic reaction, angioedema, anaphylactic reactions	Unknown
Metabolism and nutritional disorders	Anorexia	Unknown
Blood and lymphatic system disorders	Haemolytic anaemia, blood dyscrasias	Unknown
Musculoskeletal and connective tissue disorders	Muscle twitching, muscle weakness	Unknown
Psychiatric disorders	Confusion*, excitation*, irritability*, nightmares*, depression	Unknown
Renal and urinary disorders	Urinary retention	Unknown
Skin and subcutaneous disorders	Exfoliative dermatitis, rash, urticaria, photosensitivity	Unknown
Respiratory, thoracic and mediastinal disorders	Thickening of bronchial secretions	Unknown
Vascular disorders	Hypotension	Unknown
Hepatobiliary disorders	Hepatitis, including jaundice	Unknown
Ear and labyrinth disorders	Tinnitus	Unknown
Cardiac disorders	Palpitations, tachycardia, arrhythmias	Unknown
General disorders and administration site conditions	Fatigue	Common
	Chest tightness	Unknown

*Children and the elderly are more susceptible to neurological anticholinergic effects and paradoxical excitation (eg increased energy, restlessness, nervousness)

Paracetamol
Adverse effects of paracetamol are rare but hypersensitivity including skin rash may occur. There have been reports of blood dyscrasias including thrombocytopenia and agranulocytosis, but these were not necessarily causality related to paracetamol.
Very rare cases of serious skin reactions have been reported.
Cases of acute pancreatitis have been reported. Paracetamol has been widely used and reports of adverse reactions are rare, and are generally associated with overdosage.
Allergic reactions occur occasionally.
Chronic hepatic necrosis has been reported in a patient who took daily therapeutic doses of paracetamol for about a year and liver damage has been reported after daily ingestion of excessive amounts for shorter periods. A review of a group of patients with chronic active hepatitis failed to reveal differences in the abnormalities of liver function in those who were long-term users of paracetamol nor was the control of the disease improved after paracetamol withdrawal.
Low-level transaminase elevations may occur in some patients taking therapeutic doses of paracetamol; these are not accompanied with liver failure and usually resolve with continued therapy or discontinuation of paracetamol.
Nephrotoxic effects are uncommon and have not been reported in association with therapeutic doses, except after prolonged administration.

Ascorbic acid
Nervous system disorders: headache.
Vascular disorders: flushing.
Gastrointestinal disorders: nausea, vomiting and stomach cramps. Large doses of ascorbic acid may cause diarrhoea.
Skin and subcutaneous tissue disorders: redness of skin.
Renal and urinary disorders: Patients known to be at risk of hyperoxaluria should not ingest ascorbic acid doses exceeding 1g daily as there may be increased urinary oxalate excretion. However, such risk has not been demonstrated in normal, non-hyper oxaluric individuals. Ascorbic acid has been implicated in precipitating haemolytic anaemia in certain individuals deficient of glucose-6-phosphate dehydrogenase.
Increased intake of ascorbic acid over a prolonged period may result in increased renal clearance of ascorbic acid, and deficiency may result if the intake is reduced or withdrawn rapidly. Doses of more than 600mg daily have a diuretic effect.

OVERDOSE:
Chlorphenamine
Symptoms and signs
The estimated lethal dose of chlorphenamine is 25 to 50mg/kg body weight. Symptoms and signs include sedation, paradoxical excitation of the CNS, toxic psychosis, convulsions, apnoea, anticholinergic effects, dystonic reactions and cardiovascular collapse including arrhythmias.

Treatment
Management should be as clinically indicated or as recommended by the national poisons centres where available. Symptomatic and supportive measures should be provided with special attention to cardiac, respiratory, renal and hepatic functions and fluid and electrolyte balance. If overdosage is by the oral route, treatment with activated charcoal should be considered provided there are no contraindications for use and the overdose has been taken recently (treatment is most effective if given within an hour of ingestion). Treat hypotension and arrhythmias vigorously. CNS convulsions may be treated with i.v. diazepam. Haemoperfusion may be used in severe cases.

Paracetamol
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, phenobarbital, 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.
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

Pharma Code : 100000 Standard

Direction for Travel

Date	: 24.05.2023
Artist	: Ganesh
Product	: Apflu Syrup
Actual Size	: 630 x 210 mm
Ref artwork	: TN6107I
Colour	: Black
Country	: Rwanda

BACK

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 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.

Ascorbic acid
Symptoms
At doses of over 3g per day unabsorbed ascorbic acid is mainly excreted unmetabolised in the faeces. Absorbed ascorbic acid additional to the body's needs is rapidly eliminated. Large doses of ascorbic acid may cause diarrhoea and the formation of renal oxalate calculi. Symptomatic treatment may be required.
Ascorbic acid may cause acidosis or haemolytic anaemia in certain individuals with a deficiency of glucose 6-phosphate dehydrogenase. Renal failure can occur with massive ascorbic acid overdosage.
Management
Gastric lavage may be given if ingestion is recent otherwise general supportive measure should be employed as required.

PHARMACOLOGICAL PROPERTIES:
Pharmacodynamics
Chlorphenamine
Mechanism of Action
Chlorphenamine is a potent antihistamine (H1-antagonist).
Antihistamines diminish or abolish the actions of histamine in the body by competitive reversible blockade of histamine H1-receptor sites on tissues. Chlorphenamine also has anticholinergic activity.
Antihistamines act to prevent the release of histamine, prostaglandins and leukotrines and have been shown to prevent the migration of inflammatory mediators. The actions of chlorphenmine include inhibition of histamine on smooth muscle, capillary permeability and hence reduction of oedema and wheal in hypersensitivity reactions such as allergy and anaphylaxis.

Paracetamol
Mechanism of Action
The mechanism of analgesic action has not been fully determined. Paracetamol may act predominantly by inhibiting prostaglandin synthesis in the central nervous system (CNS) and, to a lesser extent, through a peripheral action by blocking pain impulse generation. The peripheral action may also be due to inhibition of prostaglandin synthesis or to inhibition of the synthesis or actions of other substances that sensitise pain receptors to mechanical or chemical stimulation.
Paracetamol probably produces antipyresis by acting centrally on the hypothalamic heat-regulating centre to produce peripheral vasodilation resulting in increased blood flow through the skin, sweating and heat loss. The central action probably involves inhibition of prostaglandin synthesis in the hypothalamus.

Ascorbic acid
Mechanism of Action
Ascorbic acid is a source of vitamin C, which may be beneficial during infection when vitamin C levels are believed to fall.

PHARMACOKINETIC PROPERTIES:
Chlorphenamine:
Absorption
Chlorphenamine is well absorbed from the gastro-intestinal tract, following oral administration. The effects develop within 30 minutes, are maximal within I 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.

Metabolism
Chlorphenamine is metabolised to the monodesmethyl and didesmethyl derivatives

Excretion
About 22% of an oral dose is excreted unchanged in the urine.

Paracetamol:
Oral absorption is rapid and almost complete; it may be decreased if Paracetamol is taken following a high carbohydrate meal.
There is no significant protein binding with doses producing plasma concentrations of below 60mcg (µg)/ml, but may reach moderate levels with high or toxic doses.
Approximately 90 - 95% of a dose is metabolised in the liver, primarily by conjugation with glucuronic acid, sulphuric acid and cysteine. An intermediate metabolite, which may accumulate in overdosage after primary metabolic pathways become saturated, is hepatotoxic and possibly nephrotoxic.
Half-life is 1 to 4 hours; does not change with renal failure but may be prolonged in acute overdosage, in some forms of hepatic disease, in the elderly, and in the neonate; may be somewhat shortened in children.
Time to peak concentration, 0.5 - 2 hours; peak plasma concentrations, 5 - 20mcg (µg)/ml (with doses up to 650mg); time to peak effect, 1- 3 hours; duration of action, 3- 4 hours.

Elimination is by the renal route, as metabolites, primarily conjugates, 3% of a dose may be excreted unchanged.
Peak concentration of 10 - 15mcg(µg)/ml have been measured in breast milk, 1 - 2 hours following maternal ingestion of a single 650mg dose. Half-life in breast milk is 1.35 - 3.5 hours.

Ascorbic acid
Ascorbic acid is readily absorbed from the gastrointestinal tract and widely distributed in the body tissues. Ascorbic acid is reversibly oxidised to dehydro ascorbic acid; some is metabolised to ascorbate-2-sulphate, which is inactive, and oxalic acid, which are excreted in the urine. Ascorbic acid crosses the placenta and is distributed into breast milk.

PRECLINICAL SAFETY DATA:
Conventional studies using the currently accepted standards for the evaluation of toxicity to reproduction and development are not available.

PHARAMCEUTICAL PARTICULARS:
INCOMPATIBILITY:
Not applicable

SPECIAL PRECAUTIONS FOR STORAGE
Not-available.

STORAGE CONDITION
Keep in cool place at temperature below 30°C. Protect from light.

NATURE AND CONTENTS OF CONTAINER
Available in 100 ml Amber Glass bottle in a carton along with pack insert

VERSION No.: 01

LAST REVISION DATE: May, 2023

Manufacturing Authorization Holder and Manufacturing Site

Manufacturing Authorization Holder	Manufacturing site
Ajanta Pharma Limited Ajanta House, Charkop Kandivli (West) Mumbai - 400 067. India. Tel : +91-69132111/2112 Fax : +91-22-6913 2070 Email : md.info@ajantapharma.com	Ajanta Pharma Limited 31-O, M.I.D.C. Area, Chikalthana, Aurangabad 431 210. India Tel: +91-69132111/2112 Fax: +91-22-6913 2070 Email: md.info@ajantapharma.com

APFLU SYRUP

Chlorphenamine Maleate 0.50 mg, Paracetamol 120 mg and Vitamin C 50 mg Syrup
Patient Information Leaflet

Active substances
Chlorphenamine Maleate BP
Paracetamol BP
Vitamin C BP

Read all of this leaflet carefully before you start taking Apflu syrup.
- Keep this leaflet, you may need to read it again.
- If you have any further questions, ask your doctor, health care provider or nurse.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor, health care provider or nurse.

In this leaflet:

1. What Apflu Syrup is and what it is used for
Apflu Syrup provides antihistaminic and antipyretic effect along with additional benefits of vitamin C.
Antihistaminic effects- itchiness, redness, swelling, tenderness and irritation that can be caused by:
- Hayfever and other allergies e.g. pet, house dust mite and mould spore allergies
- Nettle rash and hives
- Skin allergies and dermatitis
- Prickly heat and heat rash
- Reactions to food, food additives or medicines
- Insect bites and stings
- The itchy rash of chickenpox.

Antipyretic effect- To relieve mild to moderate pain and to reduce fever in many conditions including headache, toothache, teething, feverishness, colds and influenza and following vaccination

Vitamin C supplementation. Despite the popular belief that vitamin C can cure the common cold, scientific evidence doesn't support that theory. Taking vitamin C supplements regularly (not just at the beginning of a cold) produces only a small reduction in the duration of a cold (about 1 day). The only other piece of evidence supporting vitamin C for preventing colds comes from studies examining people exercising in extreme environments (athletes, such as skiers and marathon runners, and soldiers in the Arctic). In these studies, vitamin C did seem to reduce the risk of getting a cold.
Studies suggest that vitamin C may also be helpful for:
- Boosting immunity
- Maintaining healthy gums
- Improving vision for those with uveitis (an inflammation of the middle part of the eye)
- Treating allergy-related conditions, such as asthma, eczema, and hay fever (called allergic rhinitis)
- Reducing effects of sun exposure, such as sunburn or redness (called erythema)
- Alleviating dry mouth, particularly from antidepressant medications (a common side effect from these drugs)
- Healing burns and wounds
- Decreasing blood sugar in people with diabetes
- Some viral conditions, including mononucleosis - Although scientific evidence is lacking, some doctors may suggest high-dose vitamin C to treat some viruses

2. Check before you take Apflu Syrup
This medicine can be given to children from the age of 1 year. However, some children should not be given this medicine or you should seek the advice of their pharmacist or doctor first.
Do not take Apflu Syrup:
- If your child is under 1 year
- If you have ever had an allergic reaction to paracetamol, Chlorphenamine Maleate, ascorbic acid or any of the other ingredients.
- If you have kidney or liver problems.
- If your child is having an asthma attack.
- If your child is allergic to any of the ingredients, or any other antihistamines (your child may have had a rash, difficulty breathing, swollen lips or face after taking them).
- If your child is taking monoamine oxidase inhibitors (for depression) or has taken them in the last 14 days.

Talk to your pharmacist or doctor:
For child:
- If your child has epilepsy, heart or circulatory disease, liver problems
- If your child has high blood pressure or glaucoma
- If your child has asthma, bronchitis or bronchiectasis
- If your child has an overactive thyroid
- If your child has difficulty passing urine
- If your child has an obstruction in their intestine
- If your child has a rare blood disease called porphyria

For adult:
- Talk to your doctor before you take this syrup if you have very high blood pressure, heart disease, epilepsy, glaucoma, enlarged prostate, liver disease, kidney disease, bronchitis, asthma, bronchiectasis or chronic lung disorders (difficulty in breathing and cough that won't go away).
- Avoid drinking alcohol with this medicine.
- Immediate medical advice should be sought in the event of an overdose, even if the child seems well, because of the risk of delayed serious liver damage.

Information for adults intending to take this medicine
Driving and using machines:
- If the syrup makes you feel drowsy, dizzy or if you experience blurred vision.
- The anticholinergic properties of chlorphenamine in Apflu Syrup may cause drowsiness, dizziness, blurred vision and psychomotor impairment, which can seriously hamper the patients' ability to drive and use machinery.
- Ascorbic acid has no known effect on an individual's ability to drive or operate machinery.

Pregnancy and breastfeeding: Do not take this medicine.

If your child takes other medicines
Before you give this medicine, make sure that you tell your pharmacist about ANY other medicines you might be giving your child at the same time, particularly the following:
- Other antihistamines
- Strong painkillers
- Sleeping tablets
- Tranquillisers, antidepressants or other medicines for mental problems
- Phenytoin (for epilepsy)
- Atropine
- Metoclopramide or domperidone (for nausea [feeling sick] or vomiting [being sick]).
- Ergotamine or methylsergide (for migraine).
- Cholestyramine (to lower blood cholesterol) or drugs to lower blood pressure; appetite. suppressants or stimulants; or heart disease (e.g. digoxin).
- If you take blood thinning drugs (anticoagulants e.g. warfarin).

Vitamin C increases the amount of iron absorbed from foods. People with hemochromatosis, an inherited condition where too much iron builds up in the body, should not take vitamin C supplements.
If you are unsure about interactions with any other medicines, talk to your pharmacist. This includes medicines prescribed by your doctor and medicine you have bought for your child, including herbal and homeopathic remedies.

3. How to take Apflu Syrup
Check the seal is not broken before first use. If it is, do not give the medicine.
Do not give to children under 1 year.
Oral administration only.
Do not exceed the stated dose or frequency of dosing.
Children:
- 01 – 02 Years: 5 ml X 4 times daily
- 02 – 08 Years: 10 ml X 4 times daily
- 08 – 10 Years: 15 ml X 4 times daily
- 10 – 12 Years: 20 ml X 4 times daily

Do not give more than the amount recommended above.
If symptoms do not go away within 5 days talk to your pharmacist or doctor.
After use replace the cap on the top of the bottle tightly.
If you give too much:
For child:
Contact your doctor or casualty department.
For adult:
Contact your doctor or casualty department.
Do not drive if you have taken too much.

4. Possible side effects
Most people will not have problems, but some may get some:
- Disturbance in concentrating.
- Un-coordination.
- Dizziness, headache.
- Blurred vision.
- Feeling or being sick, dry mouth
- Fatigue
- Drowsiness (which may make your child fall asleep)
- Difficulty in passing urine, sweating
- Skin rash, sensitivity to sunlight, other allergic reactions
- Indigestion, stomach pain, loss of appetite
- Tremors, muscle pain or weakness, impaired movement or co-ordination, pins and needles
- Change in heart rate, palpitations, low blood pressure, ringing in the ears, hair loss
- Blood problems such as anemia, weariness
- Sleep disturbance
- Liver problems (which may cause yellowing of the skin or eyes)
- Chest pain
- Cough, phlegm on the chest – these may be caused by thickened bronchial secretions (mucous) in your lungs
- Irritability, depression
- Hyperactivity in children
- Confusion in the elderly

Very young children and elderly adults may be more likely to get some of these side effects.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Apflu Syrup
Keep out of the reach and sight of children.
Keep in cool place at temperature below 30°C. Protect from light.
Store in the original container.
Do not use Apflu Syrup after the expiry date which is stated on the carton after EXP. The expiry date refers to the last day of that month.
Do not use Apflu Syrup if you notice any visible signs of deterioration.
Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help protect the environment.

6. Further Information
What Apflu Syrup contains
APFLU SYRUP (Chlorphenamine Maleate 0.50 mg, Paracetamol 120 mg and Vitamin C 50 mg Syrup)
The active ingredients are
Each 5ml contains:
Chlorphenamine Maleate BP……0.50mg
Paracetamol BP ……120mg
Vitamin C BP …….. 50mg
Flavoured syrup base ……. q.s.
Colour: Caramel

The other ingredients are:
Sugar commercial, Glycerol, Propylene Glycol, Methyl Hydroxybenzoate, Propyl Hydroxybenzoate, Sodium Metabisulfite, Sodium Chloride, Saccharin Sodium, Mango flavour ASV, Liquid caramel colour, Disodium EDTA, Sodium Dihydrogen Phosphate Dihydrate, Disodium Hydrogen Phosphate Dihydrate, Hyflosupercel.

What Apflu Syrup looks like and contents of the pack
Brown to light brown coloured syrup with characteristic odour and taste.
Available in 100 ml Amber Glass bottle in a carton along with pack insert

Manufacturing Authorization Holder and Manufacturing Site

Manufacturing Authorization Holder	Manufacturing site
Ajanta Pharma Limited Ajanta House, Charkop Kandivli (West) Mumbai - 400 067. India. Tel : +91-69132111/2112 Fax : +91-22-6913 2070 Email : md.info@ajantapharma.com	Ajanta Pharma Limited 31-O, M.I.D.C. Area, Chikalthana, Aurangabad 431 210. India Tel: +91-69132111/2112 Fax: +91-22-6913 2070 Email: md.info@ajantapharma.com

For any information about this medicinal product, please contact the Manufacturing Authorization Holder.

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