

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Uniflu with Vitamin C Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Uniflu tablet contains:

Caffeine	30.00	mg
Diphenhydramine hydrochloride.	15.00	mg
Paracetamol	500.00	mg
Phenylephrine hydrochloride	10.00	mg

Excipients: contains 0.06mg carmoisine (E122)

For a full list of excipients, see section 6.1.

Each Vitamin C tablet contains

Ascorbic Acid (as ascorbic acid /sodium ascorbate)	300.00	mg
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Excipients: contains 5.00mg lactose and 266.6mg sucrose.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Uniflu:

Film-coated tablet
Pink, oblong, film-coated tablet

Vitamin C:

Chewable tablet.
Yellow, biconvex, circular, plain, lemon flavoured chewable tablet.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Uniflu:

For the symptomatic relief from the discomforts associated with influenza and colds i.e. nasal and sinus congestion, headache, fever, aching limbs, coughing and runny nose.

Vitamin C:

For use as a vitamin C supplement during cold and influenza infections.

4.2 Posology and method of administration

Uniflu:

Adults: One Uniflu tablet to be swallowed whole with water, followed by one tablet every six hours until the symptoms disappear.

Not more than four tablets of Uniflu to be taken in 24 hours.

Elderly: As adult dose.

Children: Under 12 years – not recommended.

Over 12 years – One tablet every eight hours until symptoms disappear.

Not more than three tablets of Uniflu to be taken in 24 hours.

Vitamin C:

Adults: One Vitamin C tablet to be swallowed whole, sucked or chewed every six hours.

Elderly: As adult dose.

Children: Over 12 years – One tablet to be swallowed whole, sucked or chewed every eight hours.

Under 12 years – Not recommended.

4.3 Contraindications

Uniflu:

Hypersensitivity to paracetamol or any of the other constituents. The phenylephrine content of Uniflu tablets contraindicates their use in hyperthyroidism and hypertension, cardiovascular and coronary disease and should not be given to patients being treated with monoamine oxidase inhibitors or within fourteen days of stopping such treatment. Phenylephrine also contraindicates use in patients with glaucoma or urinary retention and use in patients who are currently receiving other sympathomimetic drugs. Uniflu tablets are contraindicated in chronic obstructive airways disease.

Vitamin C

Hypersensitivity to ascorbic acid or any of the other constituents.

4.4 Special warnings and precautions for use

Uniflu:

Regarding paracetamol, Uniflu should be administered with care to patients with severe renal or severe hepatic impairment. The hazard of overdose is greater in those with non-cirrhotic alcoholic liver disease. Caution is required in patients with epilepsy and prostatic hypertrophy.

Do not exceed the stated dose. Keep out of the reach of children. If symptoms persist or worsen consult your doctor. Patients receiving other regular medication especially medication for depression should be warned to consult their physician before using this product. Patients should be advised not to take other paracetamol-containing products concurrently.

The product should not be taken for persistent or chronic cough such as occurs with smoking, asthma or emphysema or if cough is accompanied by excessive mucous/phlegm unless directed by the doctor.

The physician or pharmacist should check that sympathomimetic containing preparations are not simultaneously administered by several routes i.e. orally and topically (nasal, aural and eye preparations).

Sympathomimetic-containing products should be used with great care in patients suffering from angina and in patients receiving phenothiazines or tricyclic antidepressants.

Sympathomimetic-containing products should be used with caution in patients receiving digitalis, beta-adrenergic blockers, guanethidine, reserpine, methyldopa or anti-hypertensive agents.

Concurrent use with halogenated anaesthetic agents such as chloroform, cyclopropane, halothane, enflurane or isoflurane may provoke or worsen ventricular arrhythmias.

Sympathomimetic-containing products may act as cerebral stimulants giving rise to insomnia, nervousness, hyperpyrexia, tremor and epileptiform convulsions.

Vitamin C:

As this medicine contains lactose and sucrose, patients with rare hereditary problems of fructose or galactose intolerance, glucose-galactose malabsorption, the Lapp lactase deficiency or sucrase-isomaltase insufficiency should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interactions

Refer to these interactions in Section 4.4.

Uniflu:

Alcohol and other central nervous system depressants can potentiate the sedative effect of Uniflu tablets. Patients are warned to avoid alcoholic drink whilst using the product. Phenylephrine may antagonise the effects of concurrent antihypertensive therapy. The speed absorption of paracetamol may be increased by metoclopramide or domperidone and absorption reduced by cholestyramine.

Paracetamol may cause a marginal increase in blood levels of chloramphenicol.

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.

The effects of anticholinergics e.g. some psychotropic drugs and atropine, may be potentiated giving rise to tachycardia, mouth dryness, gastrointestinal disturbances e.g. colic, urinary retention and headache.

Vitamin C:

There are no known clinically significant interactions with other medicaments.

4.6 Fertility, pregnancy and lactation

Pregnancy

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Uniflu:

The safe use of Uniflu tablets in pregnancy has not been established. They should not, therefore, be used in pregnancy except under close medical supervision.

A large amount of data on pregnant women indicate neither malformative, nor feto/neonatal toxicity from paracetamol. Epidemiological studies on neurodevelopment in children exposed to paracetamol in utero show inconclusive results. If

clinically needed, paracetamol can be used during pregnancy however it should be used at the lowest effective dose for the shortest possible time and at the lowest possible frequency.

Vitamin C:

Vitamin C may be administered to pregnant women under the supervision of a doctor.

Breast-feeding

Uniflu:

Paracetamol is excreted in breast milk but not in a clinically significant amount. Available published data do not contraindicate breast feeding. Uniflu tablets should be avoided in nursing mothers.

Vitamin C:

Vitamin C may be administered to lactating women under the supervision of a doctor.

Fertility

No data available.

4.7 Effects on ability to drive and use machines

Uniflu:

Drowsiness may be experienced during treatment with Uniflu tablets and patients are advised not to drive or operate machinery if affected.

Vitamin C:

Vitamin C has no or negligible influence on the ability to drive or use machines.

4.8 Undesirable effects

Uniflu:

Side effects are listed below by body system in order of decreasing severity.

Vascular Disorders

Hypertension

Gastrointestinal Disorders

Gastro-intestinal disturbances, dry mouth.

Nervous System Disorders

Headache, tremors

Blood and Lymphatic Disorders

Blood disorder, Thrombocytopenia, Agranulocytosis

Psychiatric Disorders

Insomnia and nervousness

Eye Disorders

Vision blurred.

Renal and Urinary Disorders

Urinary retention.

Hypersensitivity e.g., skin rash. Very rare cases of serious skin reactions have been reported.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRRA Pharmacovigilance, Earlsfort Terrace, IRL – Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

Uniflu:

Overdosage may lead to tachycardia, hypertension, nausea, vomiting, delayed onset hepatic failure due to paracetamol.

Immediate medical advice should be sought in the event of an overdose, even if you feel well, because of the risk of delayed, serious liver damage.

Treatment consists of supportive measures, gastric lavage, as well as correction of any fluid or electrolyte imbalance. Intravenous N-acetylcysteine and naloxone may be needed as antidotes in severe cases. In cases of severe hypertension, intravenous phentolamine may be required.

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, coma and death. Acute renal failure with acute tubular necrosis may develop even in the absence of severe liver damage. Cardiac arrhythmias and pancreatitis have been reported. Liver damage is possible in adults who have taken excess of recommended doses of paracetamol. It is considered that excess quantities of a toxic metabolite (usually adequately detoxified by glutathione when normal doses of paracetamol are ingested), become irreversibly bound to liver tissue.

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 and any patient who has ingested a significant amount of paracetamol in the preceding 4 hours should undergo gastric lavage. Administration of oral methionine or intravenous N-acetylcysteine which may have a beneficial effect up to at least 48 hours after the overdose, may be required. General supportive measures must be available.

Vitamin C:

No cases of overdosage have been reported.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Uniflu:

ATC Classification: N02BE51

Caffeine

Caffeine, like other xanthines, stimulates the central nervous system, increases respiration, affects smooth muscle and exerts a diuretic effect. These effects are all thought to be mediated by the inhibition of phosphodiesterase resulting in a raised cyclic AMP concentration. Of the xanthines, caffeine is the most active in stimulating the central nervous system and is principally used for this purpose and has the least diuretic effect. Its action on the central nervous system is mainly on the higher centres producing a condition of wakefulness and increased mental activity. Caffeine may stimulate the respiratory centre and increase the rate and depth of respiration.

Diphenhydramine hydrochloride

Diphenhydramine hydrochloride is an ethanolamine derivative with the properties and use of antihistamine. It is less potent than promethazine hydrochloride but has a shorter duration of action. It has sedative, anti-emetic, anticholinergic and local anaesthetic properties.

Diphenhydramine hydrochloride is a histamine H₁-receptor antagonist. It has action on the contraction of smooth muscle and the dilation and increased permeability of the capillaries. It also has anticholinergic activity.

Paracetamol

Paracetamol has both antipyretic and analgesic activities but no useful anti-inflammatory properties. Its mechanism of analgesic effect is not yet defined. Prostaglandin synthetase from the central nervous system is sensitive to paracetamol, explaining its antipyretic effect. It does not, however, have an anti-inflammatory effect as the peripheral tissue prostaglandin synthetase is not affected.

Phenylephrine hydrochloride

Phenylephrine hydrochloride is a sympathomimetic agent with mainly direct effects on adrenergic receptors. It has predominantly alpha-adrenergic activity and is used to elicit sympathetic responses (vasoconstriction) where there is congestion and inflammation of the nasal mucosa.

Vitamin C:

Ascorbic Acid (vitamin C) cannot be synthesized by man, therefore a dietary source is necessary.

Ascorbic acid (vitamin C) acts as a cofactor in numerous biological processes including the hydroxylation of proline to hydroxyproline. In deficiency, the formation of collagen is therefore impaired.

Ascorbic acid (vitamin C) is important in the hydroxylation of dopamine to noradrenaline and in hydroxylations occurring in steroid synthesis in the adrenals.

Ascorbic acid (vitamin C) is a reducing agent in tyrosine metabolism and by acting as an electron donor in the conversion of folic acid to tetrahydrofolic acid is directly involved in the synthesis of purine to thymine.

Ascorbic acid (vitamin C) is also necessary for the incorporation of iron into ferritin.

Ascorbic acid (vitamin) increases the phagocytic function of leucocytes; it possesses anti-inflammatory activity and promotes wound healing.

Deficiency can cause scurvy. Features include swollen inflamed gums, petechial haemorrhages and subcutaneous bruising.

The deficiency of collagen leads to development of thin watery ground substances in which blood vessels are insecurely fixed and readily ruptured. The supportive components of bone and cartilage are also deficiency causing bones to fracture easily and teeth to become loose.

Anaemia commonly occurs probably due to the role of ascorbic acid (vitamin C) in iron metabolism.

5.2 Pharmacokinetic properties

Uniflu:

Caffeine

Caffeine is absorbed erratically from the gastro-intestinal tract and does not appear to accumulate in any particular tissue. It passes readily into the central nervous system and saliva.

Caffeine is almost completely metabolised and is excreted in the urine as 1-methyluric acid, 1-methylxanthine and other metabolites. Only about 1% remains unchanged.

Diphenhydramine hydrochloride

Diphenhydramine hydrochloride is absorbed from the gastro-intestinal tract, metabolised by the liver and excreted mainly as metabolites in the urine. Any unchanged diphenhydramine is eliminated more rapidly than its metabolites. It has been reported to be 98% bound to plasma proteins with a normal half-life of 4 to 7 hours.

Paracetamol

Paracetamol is a weak acid which is readily absorbed from the gastro-intestinal tract with peak plasma concentration occurring about 30 minutes to 2 hours after ingestion. Following absorption it is mainly biotransformed by conjugation to the sulphate and glucuronide. Plasma-protein binding is negligible at the usual therapeutic concentrations.

The elimination of paracetamol does not appear to follow saturation kinetics. The half-life of paracetamol ranges from 2-4 hours in healthy adults. In adults, the sulphate and glucuronide account for about 90% of the urinary recovery of paracetamol, each metabolite contributing to half this amount. Less than 5% is excreted as unchanged paracetamol.

In the overdose situation, the defence mechanisms of the liver which lead to non-toxic glucuronide and sulphate formation are overwhelmed. Normally minor metabolic pathways therefore participate actively in the overall biotransformation of the drug and these produce hepatotoxic metabolites.

Phenylephrine hydrochloride

The bioavailability of phenylephrine is reduced due to first pass metabolism by monoamine oxidase in the gut and liver.

Vitamin C:

Ascorbic acid (vitamin C) is a water soluble vitamin which is readily absorbed from the gastro-intestinal tract and is widely distributed in the body tissues.

Ascorbic acid (vitamin C) is reversibly oxidised to dehydroascorbic acid; some is metabolised to ascorbate-2-sulphate, which is inactive, and oxalic acid which are excreted in the urine.

Ascorbic acid (vitamin C) in excess of the body's needs is also rapidly eliminated unchanged in the urine.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

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

Uniflu tablets - Cores

Acacia
Protein S (Byco C) hydrolysed gelatin
Alginic Acid (E400)
Magnesium Stearate
Stearic Acid
Sodium Starch Glycollate (Type A)

Uniflu tablets – Film Coating

Opadry II Pink

Contains: polyvinyl alcohol, titanium dioxide (E171), indigo carmine aluminium lake (E132), carmoisine aluminium lake (E122), lecithin, macrogol, talc)

Vitamin C tablets

Saccharin Sodium

Stearic Acid

Magnesium Stearate

Compressible sugar

Lemon flavour E2954 (includes maltodextrin, acacia, lactose)

Quinoline yellow lake (E104)

Pectin

Hypromellose

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25°C. Store in the original package to protect from moisture.

6.5 Nature and contents of container

The product is presented in press through blisters containing six Uniflu tablets with six Vitamin C tablets. The blister pack is made from PVC/PVdC with a printed aluminium foil lidding.

The product is available in two pack sizes:

- i. 12 tablet box containing 1 blister strip.
- ii. 24 tablet box containing 2 blister strips.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Phoenix Labs
Suite 12, Bunkilla Plaza
Bracetown Business Park
Clonee
Co. Meath.
Ireland

8 MARKETING AUTHORISATION NUMBER

PA1113/005/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10 December 2019

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