SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Galpharm 4-In-One Flu Relief powder for oral solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active Ingredient	**mg/Sachet**
Paracetamol	500
Guaifenesin	200
Phenylephrine hydrochloride	10
Cetylpyridinium chloride	3

This product also contains the excipients aspartame and sodium (as sodium citrate) - see section 4.4.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Powder for oral solution.

Sachets containing the drug product, an off-white powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the short term symptomatic relief of the symptoms of colds and influenza, including aches and pains, headache, nasal congestion, tickly sore throat and chesty coughs.

4.2 Posology and method of administration

For oral use after dissolving the contents of the sachet in a standard mug of hot, but not boiling water (250 ml). Allow to cool to a drinkable temperature.

Adults, the elderly and children aged 12 years and over:

One sachet every four hours as required. Do not take more than 4 sachets (4 doses) in any 24 hour period.

Do not give to children under 12 years old.

4.3 Contraindications

Hypersensitivity to any of the ingredients.

Severe heart disease and cardiovascular disorders. Hypertension. Hyperthyroidism.

Contraindicated in patients currently receiving or within two weeks of stopping therapy with monoamine oxidase inhibitors because of a risk of hypertensive crisis.

Use in patients with glaucoma or urinary retention.

Use in patients who are currently receiving other sympathomimetic drugs (see section 4.5).

4.4 Special warnings and precautions for use

This product is not suitable for long term use.

Care is advised in the administration of paracetamol to patients with severe renal or hepatic impairment. The hazards of overdose are greater in those with non-cirrhotic alcoholic liver disease.

Cases of high anion gap metabolic acidosis (HAGMA) due to pyroglutamic acidosis have been reported in patients with severe illness such as severe renal impairment and sepsis, or in patients with malnutrition or other sources of glutathione deficiency (e.g. chronic alcoholism) who were treated with paracetamol at therapeutic dose for a prolonged period or a combination of paracetamol and flucloxacillin. If HAGMA due to pyroglutamic acidosis is suspected, prompt discontinuation of paracetamol and close monitoring is recommended. The measurement of urinary 5-oxoproline may be useful to identify pyroglutamic acidosis as underlying cause of HAGMA in patients with multiple risk factors.

Use with caution in patients with Raynaud's Phenomenon and diabetes mellitus.

Patients with prostatic hypertrophy may have increased difficulty with micturition.

Sympathomimetic-containing products should be used with great care in patients suffering from angina.

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

Contains a source of phenylalanine equivalent to 20 mg per sachet. May be harmful to people with phenylketonuria.

This medicinal product contains 117 mg of sodium per dose. To be taken into consideration by patients on a controlled sodium diet.

Special label warnings
If you are taking medication or are under medical care, consult your doctor before using this medicine. Do not take with other cold, flu or decongestant products.
Do not exceed the stated dose.
If symptoms persist or worsen, consult your doctor.
Keep all medicines out of the reach and sight of children.
Contains paracetamol. Do not take with any other paracetamol-containing products. Immediate medical advice should be sought in the event of an overdose, even if you feel well.

Special leaflet warnings
Contains paracetamol. Do not take with any other paracetamol-containing products.
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. If you are taking medication or are under medical care, consult your doctor before using this medicine. Do not take with other cold, flu or decongestant products.

4.5 Interaction with other medicinal products and other forms of interaction

PARACETAMOL

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, although occasional doses have no significant effect.

Drugs which induce hepatic microsomal enzymes, such as alcohol, barbiturates, monoamine oxidase inhibitors and tricyclic antidepressants, may increase the hepatotoxicity of paracetamol particularly after overdosage.

Caution should be taken when paracetamol is used concomitantly with flucloxacillin as concurrent intake has been associated with high anion gap metabolic acidosis due to pyroglutamic acidosis, especially in patients with risks factors (see section 4.4).

GUAIFENESIN

Guaifenesin may interfere with diagnostic measurements of urinary 5hydroxyindoleacetic acid or vanillylmandelic acid.

PHENYLEPHRINE HYDROCHLORIDE

Phenylephrine may adversely interact with other sympathomimetics, vasodilators and beta blockers.

Sympathomimetic-containing products should be used with great care in patients receiving phenothiazines or tricylic 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.

4.6 Fertility, Pregnancy and lactation

PARACETAMOL

Epidemiological studies in human pregnancy have shown no ill effects due to paracetamol used in the recommended dosage, but patients should follow the advice of their doctor regarding its use.

Paracetamol is excreted in breast milk but not in a clinically significant amount. Available published data do not contraindicate breast feeding.

GUAIFENESIN

The safety of guaifenesin in pregnancy and lactation has not been fully established but this constituent is not thought to be hazardous. However the product should only be used in pregnancy when considered essential by the doctor.

PHENYLEPHRINE HYDROCHLORIDE

Due to the vasoconstrictive properties of phenylephrine, the product should be used with caution in patients with a history of pre-eclampsia. Phenylephrine may reduce placental perfusion and the product should be used in pregnancy only if the benefits outweigh this risk. There is no information on use in lactation.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

The active ingredients are usually well tolerated in normal use.

PARACETAMOL

Adverse effects of paracetamol are rare but hypersensitivity including skin rashes may occur. There have been reports of blood dyscasias including thrombocytopenia and agranulocytosis, but these were not necessarily causally related to paracetamol.

Metabolism and nutrition disorders
High anion gap metabolic acidosis with frequency "Not known" (cannot be estimated from the available data)
Description of selected adverse reactions
High anion gap metabolic acidosis
Cases of high anion gap metabolic acidosis due to pyroglutamic acidosis have been observed in patients with risk factors using paracetamol (see section 4.4). Pyroglutamic acidosis may occur as a consequence of low glutathione levels in these patients.

Very rare cases of serious skin reactions have been reported.

GUAIFENESIN

Gastrointestinal discomfort has occasionally been reported with guaifenesin.

PHENYLEPHRINE HYDROCHLORIDE

Phenylephrine hydrochloride may elevate blood pressure with headache, dizziness, vomiting, diarrhoea and insomnia, and rarely palpitations, tachycardia or reflex bradycardia, tingling and coolness of the skin. There have been rare reports of allergic reactions.

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 the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard

4.9 Overdose

PARACETAMOL

Liver damage is possible in adults who have taken 10 g or more of paracetamol. Ingestion of 5 g 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 deplete 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 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 accordance with established treatment guidelines, see British National Formulary (BNF) overdose section.

Treatment with activated charcoal should be considered if the overdose has been taken within one hour. Plasma paracetamol concentration should be measured at four 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 eight 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 24 hours from ingestion should be discussed with the National Poisons Information Service (NPIS) or a liver unit.

GUAIFENESIN

Very large doses of guaifenesin can cause nausea and vomiting. Vomiting should be

treated by fluid replacement and monitoring of electrolytes.

PHENYLEPHRINE HYDROCHLORIDE

Severe overdosage may produce hypertension and associated reflex bradycardia. Treatment measures include early gastric lavage and symptomatic and supportive measures. The hypertensive effects may be treated with an alpha-receptor blocking agent (such as phentolamine mesylate 6 – 10 mg) given intravenously, and the bradycardia treated with atropine, preferably only after the pressure has been controlled.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: psycholeptics.	Paracetamol, combination excluding
ATC code:	N02BE51

PARACETAMOL

Analgesic:

The mechanism of analgesic action has not been fully determined. Paracetamol may act predominantly by inhibiting a 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.

Antipyretic:

Paracetamol probably produces antipyresis by acting 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.

GUAIFENESIN

Guaifenesin is a well known expectorant. Such expectorants are known to increase the volume of secretions in the respiratory tract and therefore to facilitate their removal by

cilary action and coughing.

PHENYLEPHRINE HYDROCHLORIDE

Sympathomimetic amines, such as phenylephrine, act on alpha-adrenergic receptors of the respiratory tract to produce vasoconstriction, which temporarily reduces the swelling associated with inflammation of the mucous membranes lining the nasal and sinus passages. This allows the free drainage of the sinusoidal fluid from the sinuses.

In addition to reducing mucosal lining swelling, decongestants also suppress the production of mucus, therefore preventing a build up of fluid within the cavities which could otherwise lead to pressure and pain.

CETYLPYRIDINIUM CHLORIDE

Cetylpyridinium Chloride is a cationic disinfectant with properties and uses similar to other cationic surfactants. These surfactants have bactericidal activity against Gram-positive and, at higher concentration against some Gram-negative organisms. Cetylpyridinium Chloride may be used in a variety of preparations for the local treatment of minor infections.

5.2 Pharmacokinetic properties

PARACETAMOL

Absorption and Fate

Paracetamol is rapidly absorbed from the gastro-intestinal tract with peak plasma concentrations occurring between 10 and 120 minutes after oral administration. It is metabolised in the liver and excreted in the urine mainly as the glucuronide and sulphate conjugates. Less than 5% is excreted as unchanged paracetamol. The elimination half-life varies from about 1 to 4 hours.

Plasma-protein binding is negligible at usual therapeutic concentrations but increases with increasing concentrations.

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

GUAIFENESIN

Guaifenesin is rapidly absorbed after oral administration. It is rapidly metabolised by oxidation to β-(2-methoxy-phenoxy)lactic acid, which is excreted in the urine.

PHENYLEPHRINE HYDROCHLORIDE

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

CETYLPYRIDINIUM CHLORIDE

Cetylpyridinium chloride has only a local effect.

5.3 Preclinical safety data

There are no preclinical data of relevance to the prescriber additional to that already covered in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maltodextrin

Citric acid (Anhydrous)

Tartaric acid

Sodium citrate

Acesulfame potassium E950

Aspartame E951

Powdered menthol flavour

Lemon flavour

Curcumin E100

6.2 Incompatibilities

None known.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

Pack sizes of five and ten sachets are available.

The sachet laminate comprises:

‘Surlyn’ (product contact layer)/aluminium foil /low density polyethylene /paper (outer layer).

6.6 Special precautions for disposal

None.

7 MARKETING AUTHORISATION HOLDER

Wrafton Laboratories Limited (T/A Perrigo)

Braunton

Devon

EX33 2DL

8 MARKETING AUTHORISATION NUMBER(S)

PL 12063/0107.

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