PROFESSIONAL INFORMATION FOR FAMUCAPS

SCHEDULING STATUS

S2

1. NAME OF THE MEDICINE

FAMUCAPS, hard capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each hard capsule contains:

Chlorphenamine maleate	2 mg
Phenylephrine hydrochloride	5 mg
Paracetamol	300 mg

Excipients with known effect:

Contains sugar (52 mg lactose monohydrate per hard capsule).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Hard capsules.

Size 0 gelatine capsules with a brown cap and opaque white body, containing a uniform white powder.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For the symptomatic relief of sinusitis, rhinitis and allergic conditions of the upper respiratory tract, hay fever and influenza.

4.2 Posology and method of administration

DO NOT EXCEED THE RECOMMENDED DOSE.

Adults: 2 capsules 3 times a day.

Children 6 – 12 years: 1 capsule 3 times a day.

Not recommended for children under the age of 6 years.

Do not use continuously for more than 10 days without consulting your doctor.

Method of administration

Oral administration only.

4.3 Contraindications

- Hypersensitivity to chlorphenamine maleate, phenylephrine hydrochloride, or any of the excipients listed in section 6.1.
- Severe renal impairment.
- Pregnancy and lactation (see section 4.6).
- Heart disease, epilepsy, hypertension, hyperthyroidism or diabetes.
- Phaeochromocytoma.
- Closed angle glaucoma.
- Concomitant use of other sympathomimetic decongestants (see sections 4.4).
- Patients taking tricyclic antidepressants or beta blocking medicines (see section 4.5).
- Patients on monoamine oxidase inhibitors or within 10 days of stopping such treatment (see section 4.5).
- Not recommended for use in children younger than 6 years.
- Patients suffering from hepatitis or alcoholism, or recovering from any form of liver disease, should not take medicines containing paracetamol, such as FAMUCAPS.

4.4 Special warnings and precautions for use

FAMUCAPS contains paracetamol which may be fatal in overdose. In the event of overdosage or suspected overdose and notwithstanding the fact that the person may be asymptomatic, the nearest doctor, hospital or poison centre must be contacted immediately.

Dosages in excess of the recommended dose can cause severe liver damage.

Do not use with any other paracetamol-containing medicines. The concomitant use with other medicines containing paracetamol may lead to an overdose. Paracetamol overdose may cause liver failure, which may require liver transplant or lead to death.

Concurrent use with medicines which can cause sedation, such as anxiolytics and hypnotics, may cause an increase in sedative effects.

The effects of alcohol may be increased and therefore concurrent use should be avoided.

Care should be taken in patients with:

- Pyloroduodenal obstruction, prostatic hypertrophy, emphysema, bronchitis, bronchiectasis, asthma, porphyria, paradoxical hyperexcitability, nervousness and insomnia.
- Glutathione depletion due to metabolic deficiencies.
- Occlusive vascular disease (e.g. Raynaud's phenomenon).

Children and elderly patients are more likely to experience neurological anticholinergic effects and paradoxical excitation (e.g. increased energy, restlessness and nervousness). The use of FAMUCAPS should be avoided in elderly patients with confusion.

FAMUCAPS may lead to drowsiness, dizziness, blurred vision, psychomotor impairment and impaired concentration, which may be aggravated by the simultaneous intake of alcohol or other central nervous system depressant medicines.

Severe cutaneous adverse reactions (SCARs)

Severe cutaneous adverse reactions (SCARs) such as toxic epidermal necrolysis (TEN), Steven-Johnson syndrome (SJS), acute generalised exanthematous pustulosis (AGEP), drug rash with

eosinophilia and systemic symptoms (DRESS) or drug-induced hypersensitivity syndrome (DIHS) and fixed drug eruptions (FDE) have been reported in patients treated with paracetamol containing medicines.
If a patient develops SCARs, treatment with FAMUCAPS must immediately be discontinued and appropriate treatment instituted.

FAMUCAPS contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take FAMUCAPS.

FAMUCAPS contains Sunset Yellow (E 110) and Ponceau 4R (E 124) which may cause allergic reactions.

4.5 Interaction with other medicines and other forms of interaction

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

Medicines tending to cause extrapyramidal reactions and those with anticholinergic effects may be potentiated. These include atropine, tricyclic antidepressants, maprotiline, reserpine, guanethidine and monoamine oxidase inhibitors.

Sedatives

All sedatives (e.g. hypnotics or anxiolytics), including alcohol, will potentiate depressant effects on the central nervous system if taken with antihistamines, as contained in FAMUCAPS (see section 4.4).

Monoamine oxidase inhibitors (including moclobemide)

Hypertensive interactions occur between sympathomimetic amines, such as phenylephrine and monoamine oxidase inhibitors (see section 4.3).

Phenytoin

Chlorphenamine inhibits phenytoin metabolism and can lead to phenytoin toxicity.

Sympathomimetic amines

Concomitant use of phenylephrine with other sympathomimetic amines can increase the risk of cardiovascular side effects (see section 4.4).

Beta blockers and other antihypertensives (including debrisoquine, guanethidine, reserpine and methyldopa)

Phenylephrine may reduce the efficacy of beta blockers and other antihypertensive medicines. The risk of hypertension and other cardiovascular side effects may be increased (see section 4.3).

Tricyclic antidepressants (e.g. amitriptyline)

May increase the risk of cardiovascular side effects with phenylephrine (see section 4.3).

Digoxin and cardiac glycosides

Concomitant use of phenylephrine with digoxin or cardiac glycosides may increase the risk of an irregular heartbeat or heart attack.

Ergot alkaloids (e.g. ergotamine and methysergide)

Concomitant use of phenylephrine may cause an 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 an increased risk of bleeding. Occasional doses have no significant effect.

Other

Antihistamines may suppress positive skin test results and should be stopped several days before the test.

4.6 Fertility, pregnancy and lactation

Pregnant and lactating women should not use FAMUCAPS (see section 4.3).

No fertility data available.

4.7 Effects on ability to drive and use machines

FAMUCAPS may lead to drowsiness, dizziness, blurred vision, psychomotor impairment and impaired concentration, which may be aggravated by the simultaneous intake of alcohol or other central nervous system depressant medicines. Patients should be warned not to drive a motor vehicle, handle heavy machinery or to climb dangerous heights, because impairment of concentration may lead to accidents.

4.8 Undesirable effects

The following side effects were reported:

Phenylephrine hydrochloride

System Organ Class	**Frequent**	**Frequency unknown**
Blood and lymphatic system disorders		Cerebral haemorrhage.
Metabolism and nutrition disorders		Appetite may be reduced, altered metabolism (including blood sugar levels).
Psychiatric disorders	Nervousness.	Fear, anxiety, restlessness,

		confusion, irritability, psychotic states.
Nervous system disorders	Headache, dizziness, insomnia.	Tremor.
Cardiac disorders	Hypertension.	Palpitations, tachycardia, reflex bradycardia, anginal pain in angina pectoris, cardiac arrest.
Respiratory, thoracic and mediastinal disorders		Dyspnoea, pulmonary oedema.
Gastrointestinal disorders	Nausea, vomiting, diarrhoea.	
Skin and subcutaneous tissue disorders		Flushing.
Renal and urinary disorders		Difficulty in micturition, urinary retention.
General disorders and administration site conditions		Weakness.

Chlorphenamine maleate

System Organ Class	**Frequency unknown**

Blood and lymphatic system disorders	Haemolytic anaemia, blood dyscrasias including agranulocytosis, leucopenia, thrombocytopenia.
Immune system disorders	Allergy, anaphylaxis.
Psychiatric disorders	Confusion, hallucinations, nervousness.
Nervous system disorders	Sedation, drowsiness, insomnia, incoordination, dizziness, tremors, convulsions, headache, cerebral stimulation (particularly in children).
Eye disorders	Blurred vision.
Ear and labyrinth disorders	Tinnitus.
Cardiac disorders	Tachycardia.
Vascular disorders	Hypotension.
Respiratory, thoracic and mediastinal disorders	Thickening of mucus.
Gastrointestinal disorders	Nausea, vomiting, dry mouth, epigastric pain, diarrhoea, reduction in tone and motility of the gastrointestinal tract, resulting in constipation and increased gastric reflux.
Skin and subcutaneous tissue disorders	Allergic dermatitis, skin rash, photosensitivity, flushing.
Musculoskeletal and connective tissue	Extrapyramidal effects with muscle spasm and dystonia, ataxia.

disorders	
Renal and urinary disorders	Urinary retention or frequency, dysuria.
General disorders and administration site conditions	Fatigue, medicine-induced fever, dryness of the nose.

Paracetamol

System Organ Class	**Frequency unknown**
Blood and lymphatic system disorders	Agranulocytosis, thrombocytopenia, leucopoenia, pancytopenia, neutropenia, anaemia.
Immune system disorders	Allergic reactions.
Hepato-biliary disorders	Pancreatitis, hepatitis.
Skin and subcutaneous tissue disorders	Dermatitis, skin rashes, which is usually erythematous or urticarial, but sometimes more serious and accompanied by fever and mucosal lesions.
Renal and urinary disorders	Renal colic, renal failure, sterile pyuria.

Post-marketing experience

Phenylephrine hydrochloride

System Organ Class	**Frequency unknown**
Immune system disorders	Hypersensitivity, allergic dermatitis, urticaria.
Eye disorders	Mydriasis, acute angle closure

	glaucoma, most likely to occur in those with closed angle glaucoma.
Skin and subcutaneous tissue disorders	Rash.
Renal and urinary disorders	Dysuria.

Chlorphenamine maleate

System Organ Class	**Frequency unknown**
Immune system disorders	Angioedema.
Metabolism and nutritional disorders	Anorexia.
Psychiatric disorders	Excitation, irritability, nightmares, depression.
Nervous system disorders	Somnolence, disturbance in attention.
Cardiac disorders	Palpitations, dysrhythmias.
Hepato-biliary disorders	Hepatitis, including jaundice.
Skin and subcutaneous tissue disorders	Exfoliative dermatitis, urticaria.
Musculoskeletal and connective tissue disorders	Muscle twitching, muscle weakness.
General disorders and administration site conditions	Chest tightness.

Paracetamol

System Organ Class	Frequency unknown
Immune system disorders	Anaphylaxis, cutaneous hypersensitivity reactions, angioedema, severe cutaneous adverse reactions (SCARs) such as toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome (SJS), acute generalised exanthematous pustulosis (AGEP), drug rash with eosinophilia and systemic symptoms (DRESS) or drug-induced hypersensitivity syndrome (DIHS) and fixed drug eruptions (FDE) (see section 4.4).
Respiratory, thoracic and mediastinal disorders	Bronchospasm.
Hepato-biliary disorders	Hepatic dysfunction.

Description of selected adverse reactions

Children and elderly patients are more likely to experience the neurological anticholinergic effects and paradoxical excitation (e.g. increased energy, restlessness and nervousness) associated with chlorphenamine maleate.

There have been cases of bronchospasm with paracetamol, but these are more likely in asthmatics sensitive to aspirin or other nonsteroidal anti-inflammatory drugs (NSAIDs).

Paracetamol dosages in excess to those recommended may cause liver damage.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of FAMUCAPS is important. It allows continued monitoring of the benefit/risk balance of FAMUCAPS. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the **6.04 Adverse Drug Reactions Reporting Form**, found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

An overdose may potentially be fatal, particularly in children and elderly patients.

Phenylephrine hydrochloride

Symptoms

Phenylephrine overdosage is likely to result in effects similar to those listed under adverse reactions (see section 4.8). Additional symptoms may include irritability, restlessness, hypertension, and possibly reflex bradycardia. In severe cases confusion, hallucinations, seizures and dysrhythmias may occur. The amount required to produce serious phenylephrine toxicity would be greater than that required to cause paracetamol-related liver toxicity.

Treatment

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

Chlorphenamine maleate

Symptoms

The estimated lethal dose of chlorphenamine is 25 to 50 mg/kg body mass. Overdose may result in drowsiness, sedation or paradoxical excitement of the central nervous system, toxic psychosis, hallucinations, ataxia, incoordination, athetosis, convulsions in susceptible persons and hypotension. Fixed, dilated pupils with a flushed face, sinus tachycardia, dyspnoea, apnoea and urinary retention, dry mouth, fever and dystonic reactions. Terminal: deepening coma, and cardiorespiratory collapse

including dysrhythmias. Children and elderly patients are more likely to exhibit anticholinergic and central nervous system stimulant effects. Elderly patients are prone to hypotension.

Treatment

Symptomatic and supportive measures should be provided with special attention to cardiac, respiratory, renal and hepatic functions as well as 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 dysrhythmias vigorously. Central nervous system convulsions may be treated with intravenous diazepam. Haemoperfusion may be used in severe cases.

Paracetamol

Symptoms

Prompt treatment is essential. In the event of an overdosage, consult a doctor immediately, or take the person directly to a hospital. A delay in starting treatment may mean that antidote is given too late to be effective. Evidence of liver damage is often delayed until after the time for effective treatment has lapsed.

Susceptibility to paracetamol toxicity is increased in patients who have taken repeated high doses (greater than 5 – 10 g/day) of paracetamol for several days, in chronic alcoholism, chronic liver disease, acquired immunodeficiency syndrome (AIDS), malnutrition, and with the use of medicines that induce liver microsomal oxidation such as barbiturates, isoniazid, rifampicin, phenytoin and carbamazepine.

Symptoms of paracetamol overdose in the first 24 hours include pallor, nausea, vomiting, anorexia and possibly abdominal pain. Nausea, vomiting, anorexia and abdominal pain may persist for a week or more. Mild symptoms during the first 2 days of acute poisoning, do not reflect the potential seriousness of the overdose.

Liver damage may become apparent 12 – 48 hours, or later, after ingestion, initially by elevation of serum transaminase and lactic dehydrogenase activity, increased serum bilirubin concentration and prolongation of prothrombin time. The liver damage may progress to encephalopathy, coma and death. Cerebral oedema and non-specific myocardial depression have also occurred.

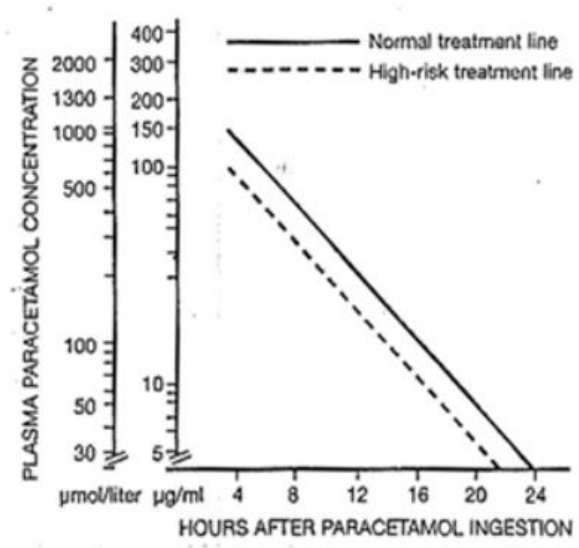
Acute renal failure with acute tubular necrosis may develop even in the absence of severe liver damage. Abnormalities of glucose metabolism and metabolic acidosis may occur. Cardiac dysrhythmias have been reported.

Treatment

N-acetylcysteine should be administered to all cases of suspected overdose as soon as possible, preferably within 8 hours of overdosage, although treatment up to 36 hours after ingestion may still be of benefit, especially if more than 150 mg/kg of paracetamol was taken. An initial dose of 150 mg/kg *N*-acetylcysteine in 200 mL dextrose injection given **intravenously** over 15 minutes, followed by an infusion of 50 mg/kg in 500 mL dextrose injection over the next 4 hours and then 100 mg/kg in a 1 000 mL dextrose injection over the next 16 hours. **The volume of intravenous fluids should be modified for children.**

Although the oral formulation is not the treatment of choice, 140 mg/kg dissolved in water may be administered initially, followed by 70 mg/kg every 4 hours for 17 doses.

A plasma paracetamol level should be determined 4 hours after ingestion in all cases of suspected overdose. Levels done before 4 hours, unless high, may be misleading. Patients at risk of liver damage and hence requiring continued treatment with *N*-acetylcysteine, can be identified according to their 4-hour plasma paracetamol level. The plasma paracetamol level can be plotted against time since ingestion in the nomogram below. The nomogram should be used only in relation to a single acute ingestion.



Source: Goodman & Gilman's The Pharmacological Basis of Therapeutics, 11th Ed.

Those whose plasma paracetamol levels are above the "normal treatment line", should continue *N*-acetylcysteine treatment with 100 mg/kg intravenous over sixteen hours repeatedly until recovery. Patients with increased susceptibility to liver damage, as identified above, should continue treatment if concentrations are above the "high risk treatment line". Prothrombin index correlates best with survival.

All patients with significant overdose should be monitored for at least 96 hours. Symptoms of liver damage, which may be fatal, may only appear after a few days.

5. PHARMACOLOGICAL PROPERTIES

A 5.8 Preparations for the common cold, including nasal decongestants.

5.1 Pharmacodynamic properties

Phenylephrine hydrochloride is a sympathomimetic decongestant.

Chlorphenamine maleate is a potent antihistamine (H_1-antagonist). Antihistamines diminish or abolish the actions of histamine in the body by competitive reversible blockade of histamine H_1-receptor sites on tissues. Chlorphenamine also has anticholinergic activity. Antihistamines act to prevent the release of histamine, prostaglandins and leukotrienes and have been shown to prevent

the migration of inflammatory mediators. The actions of chlorphenamine 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 is an analgesic and antipyretic.

5.2 Pharmacokinetic properties

Phenylephrine hydrochloride

Absorption

Phenylephrine hydrochloride is irregularly absorbed from the gastrointestinal tract.

Biotransformation

Phenylephrine hydrochloride undergoes first-pass metabolism by monoamine oxidase in the gut and liver. Orally administered phenylephrine thus has reduced bioavailability.

Elimination

Phenylephrine hydrochloride is excreted in the urine almost entirely as the sulphate conjugate.

Chlorphenamine maleate

Absorption

Chlorphenamine is well absorbed from the gastrointestinal tract, following oral administration. The effects develop within 30 minutes, are maximal within 1 to 2 hours and last 4 to 6 hours. The plasma half-life has been estimated to be 12 to 15 hours.

Biotransformation

Chlorphenamine is metabolised to the monodesmethyl and didesmethyl derivatives.

Elimination

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

Paracetamol

Absorption

Paracetamol is readily absorbed from the gastrointestinal tract.

Biotransformation and elimination

Paracetamol is metabolised in the liver and excreted in the urine, mainly as glucuronide and sulphate conjugates.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule content:

Lactose monohydrate

Magnesium stearate

Maize starch.

Capsule shell:

Brilliant Blue (E133)

Gelatine

Ponceau 4R (E124)

Sunset Yellow (E110)

Titanium dioxide (E171).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Keep at or below 25 °C. Protect from moisture.

6.5 Nature and contents of container

20 capsule pack size: White polyethylene securitainer with a white polyethylene push-on lid.

1 000 capsule pack size: 2,5 litre white polypropylene bucket lined with a plastic bag (polyethylene) with a white polypropylene push-on lid including a desiccant.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Brunel Laboratoria (Pty) Ltd

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8. REGISTRATION NUMBER

G1235 (Act 101/1965)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

14 December 1979 (Act 101/1965)

10. DATE OF REVISION OF THE TEXT

27 October 2023