SUMMARY OF PRODUCT CHARACTERISTICS

CORILIEF® 5 FLU Tablets

1. Name of the medicinal product

CORILIEF® 5 FLU tablets

2. Qualitative and quantitative composition

Each tablet contains:

Diphenhydramine hydrochloride 12.5 mg

Paracetamol 500 mg

Pseudoephedrine hydrochloride 22.5 mg

For full list of excipients, see section 6.1

3. Pharmaceutical form

Yellow oval-shaped tablets embossed with 4RFLU on one side and plain on the reverse side

4. Clinical particulars

4.1.Therapeutic indications

For the relief of symptoms associated with colds and flu; including relief of nasal congestion and congestion of mucous membranes of the upper respiratory tract, sneezing, runny nose, coughing, fever, headache, muscular aches and pains.

4.2.Posology and method of administration

For oral use

Adults, the elderly and children and over 16 years:

Adults and children aged 16 years and over	Take two tablets, up to 4 times a day
Children 10 – 15 years	Take one tablet, up to 4 times a day

This medicine is not recommended for children under **10 years** old.

4.3.Contraindications

Known hypersensitivity to diphenhydramine, paracetamol, pseudoephedrine or to any of the excipients.

Concomitant use of other sympathomimetic agents including those given by other routes, beta-blockers (see section 4.5) and monoamine oxidase inhibitors (MAOIs), or within 14 days of stopping MAOI treatment (see section 4.5)

Cardiovascular disease including

hypertension Diabetes mellitus

Phaeochromocytoma

Hyperthyroidism Closed

angle glaucoma Severe

renal impairment

Not to be used in children under the age of 10 years.

4.4.Special warnings and precautions for use

As both diphenhydramine and pseudoephedrine have been associated with central nervous system adverse events (see section 4.8), there is a possibility that the risk of experiencing such adverse events may be incre by use of the combination.

If any of the following occur, Corilief® 5 Flu Tablets should be stopped

- Hallucinations
- Restlessness
- Sleep disturbances

Use with caution in prostatic hypertrophy, urinary retention, susceptibility to angle-closure glaucoma, mode renal impairment, hepatic disease or occlusive vascular disease.

The hazard of overdose is greater in those with non-cirrhotic alcoholic liver disease.

The product may cause drowsiness. This product should not be used to sedate a

child. The product labelling will contain the following advice:-

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

Do not take with any paracetamol-containing products.

If symptoms persist, consult your doctor or pharmacist.

Keep out of the reach and sight of children

Do not use to sedate a child.

Ask a doctor before use if you suffer from a chronic or persistent cough, if you have asthma, are suffering f an acute asthma attack or where cough is accompanied by excessive secretions.

4.5.Interaction with other medicinal products and other forms of interaction

CNS depressants: may enhance the sedative effects of CNS depressants including barbiturates, hypnotics, opioid analgesics, anxiolytic sedatives, antipsychotics and alcohol.

Antimuscarinic drugs: may have an additive muscarinic action with other drugs, such as atropine and some antidepressants.

• MAOIs (see section 4.3) and/or RIMAs: Not to be used in patients taking MAOIs or within 14 days of stopping treatment as there is a risk of serotonin syndrome (diphenhydramine) or hypertensive crisis (pseudoephedrine).

• Moclobemide: risk of hypertensive crisis.

• Antihypertensives (including adrenergic neurone blockers & beta-blockers – see section 4.3): Corilief® 5 Flu Tablets may block the hypotensive effects.

• Cardiac glycosides: increased risk of dysrhythmias

• Ergot alkaloids (ergotamine & methysergide): increased risk of ergotism

• Appetite suppressants and amphetamine-like psychostimulants: risk of hypertension

• Oxytocin – risk of hypertension

• Enhances effects of anticholinergic drugs (such as TCAs)

The speed of absorption of paracetamol may be increased by metoclopramide or domperidone, and absorption reduced by cholestyramine.

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.

The use of drugs which induce hepatic microsomal enzymes, such as anticonvulsants and oral contraceptive steroids, may increase the extent of metabolism of paracetamol, resulting in reduced plasma concentrations of the drug and a faster elimination rate.

4.6.Pregnancy and lactation

The active ingredients in Corilief® 5 Flu have not been conclusively associated with adverse effects on the developing foetus; but as with all drugs, care should be exercised in use of the product, particularly during the first trimester.

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

All of the actives are excreted into breast milk, although few adverse effects have been reported as a result of ingestion, cautious use of Corilief® 5 Flu is advised during lactation.

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

4.7.Effects on ability to drive and use machines

Corilief® 5 Flu may cause drowsiness. If patients are affected they should not drive or use machinery.

4.8.Undesirable effects

System Organ Class	Adverse Event
Blood and the lymphatic system disorders	Blood disorders; blood dyscrasias such as thrombocytopenia and agranulocytosis have been reported following paracetamol use, but were not necessarily causally related to the drug
Immune system disorders	Hypersensitivity reactions, including skin rash and cross- sensitivity with other sympathomimetics
Psychiatric disorders	Confusion; depression; sleep disturbances; irritability; anxiety; restlessness; excitability; insomnia; hallucinations and paranoid delusions
Nervous system disorders	Drowsiness (usually diminishes within a few days); paradoxical stimulation; headache; psychomotor impairment; extrapyramidal effects; dizziness; tremor; convulsions
Eye disorders	Blurred vision
Cardiac disorders	Palpitations; tachycardia; arrhythmia; other cardiac dysrhythmias
Vascular disorders	Hypotension; hypertension
Respiratory, thoracic and mediastinal disorders	Thickened respiratory tract secretions

Gastrointestinal disorders	Gastrointestinal disturbances; dry mouth; nausea and/or vomiting
Hepato-biliary disorders	Liver dysfunction
Skin and subcutaneous tissue disorders	Rash
Renal and urinary disorders	Urinary retention

4.9.Overdose

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' 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, cachexi

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 gluco metabolism and metabolic acidosis may occur. In severe poisoning, hepatic failure may progress to encephalopathy, haemorrhage, hypoglycaemia, cerebral oedema, coma and death. Acute renal failure with acute tubular necrosis, strongly suggested by loin pain, haematuria and proteinuria, may develop even in th 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. Symptom 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.

Treatment with activated charcoal should be considered if the overdose has been taken within 1 hour. Plasm paracetamol concentration should be measured at 4 hours or later after ingestion (earlier concentrations 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-acetylcystein in line with the established dosage schedule. If vomiting is not a problem, oral methionine may be a suitabl alternative for remote areas, outside hospital. Management of patients who present with serious hepatic dysfunction beyond 24h from ingestion should be discussed with the local centres and/or experts that provi advice on poisons and overdoses or a liver unit.

Diphenhydramine:

Symptoms of overdose may include drowsiness, hyperpyrexia and anticholinergic effects. With higher dose and particularly in children, symptoms of CNS excitation include insomnia, nervousness, tremors and epileptiform convulsions. With massive overdose, coma or cardiovascular collapse may follow.

Treatment of overdosage should be symptomatic and supportive. Measures to promote gastric emptying (su as induced emesis or gastric lavage), and in cases of acute poisoning activated charcoal, may be useful.

Pseudoephedrine:

As with other sympathomimetic agents, symptoms of overdose include irritability, restlessness, tremor, convulsions, palpitations, hypertension and difficulty in micturition.

Necessary measures should be taken to maintain and support respiration and control convulsions. Gastric lavage should be performed if indicated. Catheterisation of the bladder may be necessary. If desired, the elimination of pseudoephedrine can be accelerated by acid diuresis or by dialysis.

5. Pharmacological properties

5.1.Pharmacodynamic properties

Diphenhydramine has a potent antihistaminic action although the actions most beneficial in influenza are its antitussive and to a lesser extent anticholinergic properties, which may alleviate mucus hypersecretion.

Paracetamol has central analgesic and antipyretic actions and pseudoephedrine is an indirectly acting sympathomimetic which has vasoconstrictor, bronchodilator and decongestant effects.

5.2.Pharmacokinetic properties

Diphenhydramine is well absorbed after oral administration with peak plasma levels at 2.5 hours and is subject to extensive first pass metabolism. The drug is 75% bound to plasma proteins, but binding decreases with chronic liver disease. Metabolism is by 2 successive N-demethylations followed by oxidation to a carboxylic acid. The terminal half life lies between 3.4 and 9.3 hours.

Paracetamol is rapidly and completely absorbed with peak plasma levels seen within 30 to 60 minutes. Less than 50% is protein bound and the drug is uniformly distributed throughout the body fluids. Paracetamol is eliminated by metabolism to inactive conjugates followed by urinary excretion. The half life is 2.75 - 3.25 hours.

Pseudoephedrine is rapidly absorbed, with peak serum levels after approximately 2.6 hours and onset of effect within about 30 minutes. It is well distributed throughout body fluids and tissues. Approximately 50% of the drug is excreted unchanged, the remainder undergoes metabolism to inactive metabolites. About 6% is converted to the active metabolite norpseudoephedrine.

5.3.Preclinical safety data

The active ingredients of Corilief® 5 Flu tablets are well known constituents of medicinal products and their safety profile is well documented. The results of preclinical studies do not add anything of relevance for therapeutic purposes.

6. Pharmaceutical particulars

6.1.List of excipients

Pregelatinised Starch
Crospovidone
Povidone K30
Croscarmellose
sodium
Microcrystalline Cellulose
Stearic acid
Magnesium Stearate

6.2.Incompatibilities

None known.

6.3. Shelf life

Two years.

6.4.Special precautions for storage

Do not store above 30 °C.

6.5.Nature and contents of container

20s in HDPE round bottles with aluminium waded HDPE screw caps.
24s in PVC-Aluminium blister packs

6.6.Special precautions for disposal and other handling

For detailed instructions for use refer to the Patient Information Leaflet in every pack.

7. Marketing Authorization Number

Varichem Pharmaceuticals (Pvt) Ltd
194 Gleneagles Road
Willowvale
Harare
Tel: +263 (04) 620181-7
Fax: +263 (04) 660424
Email: marketing@varipharm.co.zw

8. **Marketing Authorization Number**
   TAN 22 HM 0277

9. **Date of first authorization/renewal of authorization**
   19th July, 2022

10. **Date of revision of the text**

11. **Category of Distribution**
    Pharmacy Only