



**National Agency for Food & Drug
Administration & Control (NAFDAC)**

**Registration & Regulatory Affairs (R & R)
Directorate**

**SUMMARY OF PRODUCT CHARACTERISTICS
(SmPC) TEMPLATE**

1. Name of the medicinal product

Avrolin Cough and Cold Caplets.

2. Qualitative and quantitative composition

Each caplet contains paracetamol 250 mg, guaifenesin 100 mg and phenylephrine hydrochloride 5 mg

For a full list of excipients, see section 6.1.

3. Pharmaceutical form

Caplets.

White, uncoated caplets embossed with an 'AVRO' on one side and "ALN" on the reverse side.

4. Clinical particulars

4.1 Therapeutic indications

Avrolin Cough and Cold Caplets is used for the relief of symptoms associated with colds and flu including fever, headache, sore throat, catarrh, blocked nose, sinusitis, chills, chesty coughs, body aches and pains.

4.2 Posology and method of administration

Adults and children 12 years and over

Two caplets. Repeat every four hours as necessary. Do not take more than 8 caplets in 24 hours.

Do not exceed the stated dose.

Minimum dosing interval: 4 hours.

The lowest dose necessary to achieve efficacy should be used for the shortest duration of treatment.

Not to be given to children under 12 years except on medical advice.

Elderly

The normal adult dose may be taken.

Do not take continuously for more than 5 days without medical advice.

4.3 Contraindications

Known hypersensitivity to any of the ingredients.

Concomitant use of other sympathomimetic decongestants.

Phaeochromocytoma.

Closed angle glaucoma.

An enlargement of the prostate gland

Hepatic or severe renal impairment, hypertension, hyperthyroidism, diabetes, heart disease or those taking tricyclic antidepressants or beta-blocking drugs and those patients who are taking or have taken, within the last two weeks, monoamine oxidase inhibitors.

4.4 Special warnings and precautions for use

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

Concomitant use of decongestants and other cough and cold medicines should be avoided.

Medical advice should be sought before taking this product in patients with:

- Cardiovascular disease
- Occlusive vascular disease (e.g. Raynaud's Phenomenon)

- Glutathione depletion due to metabolic deficiencies
- Chronic cough such as occurs with smoking, asthma, chronic bronchitis or emphysema.

Use with caution in patients taking the following medications (see Interactions)

- vasoconstrictor agents such as ergot alkaloids (e.g. ergotamine and methysergide)
- digoxin and cardiac glycosides

Patients suffering from chronic cough or asthma should consult a physician before taking this product.

Patients should stop using the product and consult a health care professional if cough lasts for more than 5 days or comes back, or is accompanied by a fever, rash or persistent headache.

Do not take with a cough suppressant.

This product should not be used by patients taking other sympathomimetics (such as decongestants, appetite suppressants and amphetamine-like psychostimulants)

Keep out of the sight and reach of children.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactose deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular use of paracetamol with increased risk of bleeding. The hepato-toxicity of paracetamol may be potentiated by excessive intake of alcohol. The speed of absorption of paracetamol may be increased by metoclopramide or domperidone and absorption reduced by colestyramine. Pharmacological interactions involving paracetamol with a number of other drugs have been reported. These are considered to be of unlikely clinical significance in acute use at the dosage regimen proposed.

Phenylephrine should be used with caution in combination with the following drugs as interactions have been reported:

Monoamine oxidase inhibitors (including moclobemide)	Hypertensive interactions occur between sympathomimetic amines such as phenylephrine and monoamine oxidase inhibitors (see contraindications)..
Sympathomimetic amines	Concomitant use of phenylephrine with other sympathomimetic amines can increase the risk of cardiovascular side effects.
Beta-blockers and other antihypertensives (including debrisoquine, guanethidine, reserpine, methyl dopa)	Phenylephrine may reduce the efficacy of beta-blocking drugs and antihypertensive drugs. The risk of hypertension and other cardiovascular side effects may be increased.
Tricyclic antidepressants (e.g. amitriptyline)	May increase the risk of cardiovascular side effects with phenylephrine.
Ergot alkaloids (ergotamine and methylsergide)	Increased risk of ergotism
Digoxin and cardiac glycosides	Increase the risk of irregular heartbeat or heart attack
Warfarin and other coumarins	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.

If urine is collected within 24 hours of a dose of this product, a metabolite may cause a colour interference with laboratory determinations of 5 hydroxyindoleacetic acid (5-HIAA) and vanillylmandelic acid (VMA).

4.6 Pregnancy and lactation

This product should not be used during pregnancy without medical advice. 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. The safety of guaifenesin and phenylephrine during pregnancy has not been established.

Paracetamol and phenylephrine are excreted in breast milk but not in a clinically significant amount. This product should not be used in breast feeding without medical advice.

4.7 Effects on ability to drive and use machines

Patients should be advised not to drive or operate machinery if affected by dizziness.

4.8 Undesirable effects

Adverse events from historical clinical trial data are both infrequent and from small patient exposure. Events reported from extensive post-marketing experience at therapeutic/labelled dose and considered attributable are tabulated below by MedDRA System Organ Class. Due to limited clinical trial data, the frequency of these adverse events is not known (cannot be estimated from available data), but post-marketing experience indicates that adverse reactions to paracetamol are rare and serious reactions are very rare.

Body System	Undesirable effect
Blood and lymphatic system disorders	Thrombocytopenia Agranulocytosis These are not necessarily causally related to paracetamol
Immune system disorders	Very rare cases of serious skin reactions have been reported. Anaphylaxis Cutaneous hypersensitivity reactions including skin rashes and angiodema
Respiratory, thoracic and mediastinal disorders	Bronchospasm*
Hepatobiliary disorders	Hepatic dysfunction
Gastrointestinal disorders	Acute pancreatitis

* There have been cases of bronchospasm with paracetamol, but these are more likely in asthmatics sensitive to aspirin or other NSAIDs.

The following adverse events have been observed in clinical trials with phenylephrine and may therefore represent the most commonly occurring adverse events.

Body System	Undesirable effect
Psychiatric disorders	Nervousness, irritability, restlessness, and excitability
Nervous system disorders	Headache, dizziness, insomnia
Cardiac disorders	Increased blood pressure
Gastrointestinal disorders	Nausea, Vomiting, diarrhoea

Adverse reactions identified during post-marketing use are listed below. The frequency of these reactions is unknown but likely to be rare.

Eye disorders	Mydriasis, acute angle closure glaucoma, most likely to occur in those with closed angle glaucoma
Cardiac disorders	Tachycardia, palpitations
Skin and subcutaneous disorders	Allergic reactions (e.g. rash, urticaria, allergic dermatitis). Hypersensitivity reactions – including that cross-sensitivity may occur with other sympathomimetics.
Renal and urinary disorders	Dysuria, urinary retention. This is most likely to occur in those with bladder outlet obstruction, such as prostatic hypertrophy.

Guaifenesin

The frequency of these events is unknown but considered likely to be rare .

Body system	Undesirable effect
Immune system disorders	Allergic reactions, angioedema, anaphylactic reactions
Respiratory, thoracic and mediastinal disorders	Dyspnoea*
Gastrointestinal disorders	Nausea, vomiting, abdominal discomfort,
Skin and subcutaneous disorders	Rash, urticaria

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.

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 , Is on long term treatment with carbamazepine, phenobarbitone, 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 overdose 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, even if symptoms of overdose are not present. 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.

Phenylephrine

Symptoms and signs

Phenylephrine overdose is likely to result in effects similar to those listed under adverse reactions. Additional symptoms may include hypertension and possibly reflex bradycardia. In severe cases confusion, hallucinations, seizures and arrhythmias may occur. However the amount required to

produce serious phenylephrine toxicity would be greater than required to cause paracetamol-related toxicity.

Treatment

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

Guaifenesin

Symptoms and signs

Very large doses of guaifenesin cause nausea and vomiting.

Treatment

Vomiting would be treated by fluid replacement and monitoring of electrolytes if indicated.

5. Pharmacological properties

5.2 Pharmacokinetic properties

Paracetamol is readily absorbed from the gastrointestinal tract. It is metabolised in the liver and excreted in the urine, mainly as glucuronide and sulphate conjugates.

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

5.3 Preclinical safety data

Preclinical safety data on these active ingredients in the literature have not revealed any pertinent and conclusive findings which are of relevance to the recommended dosage and use of the product and which have not already been mentioned elsewhere in this SPC.

6. Pharmaceutical particulars

6.1 List of excipients

Povidone
Avicel PH 101
Stearic Acid Powder

6.2 Incompatibilities

None known.

6.3 Shelf life

Three years.

6.4 Special precautions for storage

Do not store above 30°C

6.5 Nature and contents of container

Blister of PVC/Aluminium foil containing 20 caplets

6.6 Special precautions for disposal and other handling

Not applicable.

7. Marketing authorisation holder

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