SUMMARY OF PRODUCT CHARACTERISTICS

VCs FLUMED SYRUP

1. Name of the medicinal product

VCs FLUMED SYRUP

2. Qualitative and quantitative composition

Each 5 ml (teaspoonful) contains: 120 mg Paracetamol BP, 2.5 mg Phenylephrine HCl BP, 2 mg Dextromethorphan HBr BP, 0.5 mg Chlorpheniramine maleate BP in a pleasant cherry base. Preserved with 0.1 % m/v Methylhydroxybenzoate.and 0.01 %m/v Propylhydroxybenzoate

3. Pharmaceutical form

A pink syrup with a pleasant cherry flavour.

4. Clinical particulars

4.1 Therapeutic indications

Short-term symptomatic relief of colds, chills and influenza

4.2 Posology and method of administration

Given preferably after food.
6 months – 1 year; 2.5 ml (half a teaspoonful).
1 year – 3 years: 5 ml (one teaspoonfuls).
Over 3 years: 10 ml (two teaspoonfuls).
The dose may be repeated every 4 to 6 hours as necessary.
Do not exceed four doses in 24 hours unless directed by your doctor.

4.3 Contraindications

Impaired liver and renal functions. Epilepsy

4.4 Special warnings and precautions for use

The use of this medicine leads to drowsiness which is aggravated by the simultaneous intake of alcohol. Do not use continuously for more than ten days without consulting your doctor.

Special label warnings

Do not take with any other paracetamol-containing products. Do not take with other allergy, flu, cold or decongestant products.

Immediate medical advice should be sought in the event of an overdose, even if you feel well.

Special leaflet warnings

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.

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, methyldopa)	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

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 vanillymandelic acid (VMA).

Concurrent use of chlorpheniramine and hypnotics or anxiolytics may cause an increase in sedative effects, therefore medical advice should be sought before taking chlorpheniramine concurrently with these medicines.

Chlorpheniramine inhibits phenytoin metabolism and can lead to phenytoin toxicity.

The anticholinergic effects of chlorpheniramine are intensified by MAOIs

The concomitant use of a dextromethorphan-containing product and monoamine oxidase inhibitors can occasionally result in symptoms such as hyperpyrexia, hallucinations, gross excitation or coma.

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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 chlorpheniramine and phenylephrine during pregnancy has not been established.

Paracetamol and phenylephrine are excreted in breast milk but not in a clinically significant amount.

Although dextromethorphan has been in widespread use for many years without apparent ill consequence, there is insufficient information on the effects of administration during human pregnancy. In addition, it is not known whether dextromethorphan or its metabolites are excreted in breast milk. This product should not be used in pregnancy and breast feeding without medical advice.

4.7 Effects on ability to drive and use machines

The anticholinergic properties of chlorpheniramine and dextromethorphan may cause drowsiness, dizziness, blurred vision and psychomotor impairment, which can seriously hamper the patients' ability to drive and use machinery.

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	Anaphylaxis

	Cutaneous hypersensitivity reactions including skin rashes, angiodema and Stevens Johnson syndrome
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.

<u>Chlorpheniramine</u>

Specific estimation of the frequency of adverse events for OTC products is inherently difficult (particularly numerator data). Adverse reactions which have been observed in clinical trials and which are considered to be common (occurring in ≥1% to <10% of subjects) or very common (occurring in ≥10% of subjects) are listed below by MedDRA Sytem Organ Class. The frequency of other adverse reactions identified during post-marketing use is unknown..

Body system	**Undesirable effect**
Blood nd lymphatic system disorders	Unknown: haemolytic anaemia, blood dyscrasias
Immune system disorders	Unknown: allergic reaction, angioedema, anaphylactic

	reactions
Metabolism and nutritonal disorders	Unknown: anorexia
Psychiatric disorders	Unknown: confusion*, excitation*, irritability*, nightmares*, depression
Nervous system disorders	Very common: sedation, somnolence Common: disturbance in attention, abnormal coordination, dizziness headache
Eye Disorders	Common: blurred vision
Ear and labyrinth disorders	Unknown: tinnitus
Cardiac disorders	Unknown: palpitations, tachycardia, arrythmias
Vascular disorders	Unknown: Hypotension
Respiratory, thoracic and mediastinal disorders	Unknown: thickening of bronchial secretions
Gastrointestinal disorders	Common: nausea, dry mouth Unknown: vomiting, abdominal pain, diarrhoea, dyspepsia
Hepatobiliary disorders	Unknown: hepatitis, including jaundice
Skin and subcutaneous disorders	Unknown: exfoliative dermatitis, rash, urticaria, photosensitivity
Musculoskeletal and connective tissue disorders	Unknown: muscle twitching, muscle weakness
Renal and urinary disorders	Unknown: urinary retention
General disorders and administration site conditions	Common: fatigue Unknown: chest tightness

Dextromethorphan
Side effects attributed to dextromethorphan are uncommon; occasionally dizziness, nausea, vomiting, or gastro-intestinal disturbance may occur

4.9 Overdose

Paracetamol

Liver damage is possible in adults who have taken 10g or more of paracetamol. Ingestion of 4g 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, 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 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 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 overdosage is likely to result in effects similar to those listed under adverse reactions. Additional symptoms may include hypertension and possibly reflux 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.

Chlorpheniramine

Symptoms and signs

The estimated lethal dose of chlorpheniramine is 25 to 50mg/kg body weight. Symptoms and signs include sedation, paradoxical excitation of the CNS, toxic psychosis, convulsions, apnoea, anticholinergic effects, dystonic reactions and cardiovascular collapse including arrhythmias. . However the amount required to produce serious Chlorpheniramine toxicity would be greater than required to cause paracetamol-related toxicity.

Treatment

Symptomatic and supportive measures should be provided with special attention to cardiac, respiratory, renal and hepatic functions and 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 arrhythmias vigorously. CNS convulsions may be treated with i.v. diazepam. Haemoperfusion may be used in severe cases.

Dextromethorphan

Symptoms and signs

The effects of acute toxicity from dextromethorphan overdose may include drowsiness, lethargy, nystagmus, ataxia, respiratory depression, nausea, vomiting, hyperactivity.

Treatment
Treatment should be symptomatic and supportive. Gastric lavage may be of use. Naloxone has been used successfully as a specific antagonist to dextromethorphan toxicity in children.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacological Classification: ATC Code: R05DA20 - Cough Suppressants, Excl. Combinations With Expectorants

Paracetamol is an analgesic and antipyretic.

Chlorpheniramine Maleate is a potent antihistamine (H1-antagonist)

Phenylephrine Hydrochloride is a sympathomimetic decongestant.

The active ingredients Chlorpheniramine Maleate causes sedation.

Dextromethorphan is a non-opioid antitussive drug. It exerts its antitussive activity by acting on the cough centre in the medulla oblongata, raising the threshold for the cough reflex. The onset of antitussive effects are realised within 15 to 30 minutes of oral administration, lasting for approximately 3 to 6 hours.

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.

Chlorpheniramine is well absorbed from the gastro-intestinal 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. Chlorpheniramine is metabolised to the monodesmethyl and didesmethyl derivatives. About 22% of an oral dose is excreted unchanged 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.

Dextromethorphan is rapidly absorbed from the gastrointestinal tract with peak plasma concentrations reached in approximately 2 to 2.5 hours. and is widely distributed in the human body.
Dextromethorphan and its active metabolite, dextrorphan, are actively taken up and concentrated in brain tissue. It is not known if dextromethorphan or dextrorphan are excreted in breast milk or cross the placenta.
MetabolismDextromethorphan undergoes rapid and extensive first-pass metabolism in the liver after oral administration. As the hepatic metabolism of dextromethorphan is genetically determined, individuals vary in their ability to metabolise dextromethorphan and have been classified as either poor or extensive metabolisers. Dextromethorphan undergoes O-demethylation via CYP2D6 to dextrorphan; N-demethylation to 3-methoxymorphinan via CYP3A4/3A5; which is further metabolised to 3-hydroxy-morphinan via CYP2D6.
Excretion
Dextromethorphan is primarily excreted via the kidney as unchanged parent drug and its active metabolite, dextrorphan. Dextrorphan and 3-hydroxy-morphinan are further metabolised by glucuronidation and are eliminated via the kidneys.
The elimination half-life of the parent compound is between 1.4 to 3.9 hours; dextrorphan is between 3.4 to 5.6 hours. The half-life of dextromethorphan in poor metabolisers is extremely prolonged, in the range of 45 hours.

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

Ethanol 96% BP
Propylene glycol BP
Sucrose BP
Saccharin sodium BP
Methylparaben BP
Propylparaben BP
Liquid Raspberry Flavour R101
Raspberry red H1227
Sodium hydroxide BP
Purified Water USP

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

VC_s Flumed® Syrup is available in 100 ml HDPE containers.

6.6 Special precautions for disposal and other handling

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

7. Principal and Manufacturer

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8. Registration number(s)

TBA

9. Category of Distribution

Pharmacy Only

10. Pharmacological Classification

R05D - Cough Suppressants, Excl. Combinations With Expectorants

11. Date of revision of the text
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