

Summary of Product Characteristics

1. NAME OF THE MEDICINAL PRODUCT

Coldrex HotRem

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5.0 g sachet of powder for oral solution contains:

Active Constituents:

Paracetamol	750.00 mg
Phenylephrine Hydrochloride	10.00 mg
Ascorbic acid	60.00 mg

Excipients with known effect:

Sucrose 2904.42 mg
Sodium 138.11 mg

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Powder for oral solution with lemon flavor.

Pale yellow to yellow crystalline powder with a characteristic lemon odor.

The powder dissolves in hot water to form a yellow solution with a characteristic lemon odor and flavor.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the short-term relief of the symptoms of cold & influenza, such as;

- Increased body temperature
- nasal and sinus congestion
- minor aches and pains, such as sore throat, headache, muscle ache and sinus pain

4.2 Posology and Method of Administration

Posology

Adults (including the elderly) and children aged 12 years and over:

One sachet to be taken every four to six hours as required.
Maximum daily dose - five sachets in any 24 hour period.
Minimum dosing interval: 4 hours.
Not recommended for children under the age of 12 years.

Maximum duration of use without medical advice: 7 days.

Do not exceed the stated dose.

The lowest effective dose and shortest duration of treatment should be considered.

Method of administration

For oral administration only. Empty the contents of the sachet into a glass, fill with hot water, stir until dissolved. Add cold water as necessary.

4.3 Contraindications

This product is contraindicated in patients with:

- Hypersensitivity to paracetamol, phenylephrine, ascorbic acid or any of the excipients;
- Who are taking, or have taken, within the last two weeks, monoamine oxidase inhibitors, which typically are used to treat depression;
- Pheochromocytoma;
- Closed-angle glaucoma;
- Hepatic or severe renal insufficiency;
- Hypertension;
- Hyperthyroidism;
- Diabetes
- Heart disease
- Taking beta-blockers and tricyclic antidepressants.

Do not take simultaneously with other sympathomimetic decongestants.

4.4 Special Warnings and Precautions for Use

Contains paracetamol. Do not use with any other paracetamol-containing products, decongestants (medicines for the relief congestion or blocked nose) or cold and flu medicines. The concomitant use with other products containing paracetamol may lead to an overdose. Paracetamol overdose may cause liver failure which can lead to liver transplant or death.

Cases of hepatic dysfunction/failure have been reported in patients with depleted glutathione levels, such as those who are severely malnourished, anorexic, have a low body mass index or are chronic heavy users of alcohol or sepsis.

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.

A doctor should be consulted, in these cases:

- Liver and kidney impairment
- Reduced weight or depletion
- Regular use of alcohol. You may need to avoid the use of the medicine or limit the number of received paracetamol.
- Glutathione depleted states the use of paracetamol may increase the risk of metabolic acidosis. Immediately consult the doctor if you have the following symptoms of metabolic acidosis: deep, rapid, difficult breathing; feeling sick (nausea), vomiting; loss of appetite

- Heart disease, prostatic hypertrophy (prostate problems or difficulty urinating), occlusive vascular disease (such as Raynaud's syndrome, which can manifest as numbness, tingling and discoloration (white, blue, then red) of the fingers and toes after hypothermia)
- If you are taking the following medicines:
 - pressure control drugs (antihypertensives)
 - digoxin or similar drugs for heart diseases
 - warfarin or similar blood thinners
 - other sympathomimetics, such as decongestants, appetite suppressants, amphetamine-like psychostimulants
 - ergot alkaloids, such as ergotamine and methysergide, which are used to treat acute migraine headache
 - other medicinal products.

Contains 2904.42 mg sucrose per dose. This should be taken into account in patients with diabetes. Patients with rare congenital fructose intolerance or glucose-galactose malabsorption or sucrose-isomaltose deficiency should not take this drug.

Contains 138.11 mg / dose of sodium. This should be taken into account in patients on a low-sodium diet.

If symptoms worsen, persist for more than 7 days or are accompanied by high body temperature, skin rash or persistent headache, contact your doctor.

Keep out of reach of children.

Always read and follow the label.

4.5 Interaction with Other Medicinal Products and Other Forms of Interaction

Potentially clinically significant drug interactions are listed below (see Contraindications and Warnings and Precautions).

Monoamine oxidase inhibitors (including moclobemide):	Hypertensive interactions occur between sympathomimetic amines such as phenylephrine and monoamine oxidase inhibitors
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
Digoxin and cardiac glycosides	Concomitant use of phenylephrine may increase the risk of irregular heartbeat or heart attack
Ergot alkaloids (e.g. ergotamine and methysergide)	Concomitant use of phenylephrine may cause 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 increased risk of bleeding; occasional doses have no significant effect.

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).

4.6 Pregnancy and Lactation

Pregnancy

This product should not be used during pregnancy unless the expected benefit to the mother justifies the potential risk to the fetus. This product should not be used during pregnancy without medical advice. The lowest effective dose and shortest duration of treatment should be considered.

Lactation

This product should not be used while breast feeding unless the expected benefit to the mother justifies the potential risk to the newborn. This product should not be used while breast feeding without medical advice.

Phenylephrine may be excreted in breast milk.

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

Paracetamol

Adverse reactions from historical clinical trial data are both infrequent and from small patient exposure. Adverse reactions reported from extensive post-marketing experience at therapeutic/labelled dose and considered attributable are listed below by System Organ Class. As these reactions, have been reported voluntarily from a population of uncertain size, the frequency of these reactions is unknown but considered likely to be very rare (<1/10000):

- Blood and lymphatic system disorders: Thrombocytopaenia, agranulocytosis.
- Immune system disorders: Anaphylaxis, cutaneous hypersensitivity reactions including, among others, skin rashes, angioedema, Stevens Johnson syndrome and Toxic Epidermal Necrolysis.
- Respiratory, thoracic and mediastinal disorders: Bronchospasm in patients sensitive to aspirin and other NSAIDs
- Hepatobiliary disorders: Hepatic dysfunction
- Metabolic and nutrition disorders: 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.

Phenylephrine

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

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 (rare or very 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: Hypersensitivity, allergic reactions (e.g. urticaria, allergic dermatitis, rash)
- Renal and urinary disorders: Dysuria, urinary retention. This is most likely to occur in those with bladder outlet obstruction such as prostatic hypertrophy

While taking this drug, you may experience: headache, dizziness, nervousness, insomnia, increased blood pressure, nausea, vomiting.

Stop taking the drug and consult your doctor if you have;

- Allergic reactions, such as skin rash or itching, sometimes with difficult breathing or swelling of lips, tongue, throat or face;
- Rash, peeling of the skin or an ulcer in the mouth;
- You have already had breathing problems when taking aspirin or other nonsteroidal anti-inflammatory drugs, as well as similar reactions when taking this drug;
- Bruising or bleeding for unexplained reasons;
- Heart palpitations, excessive increases in heart rate, or excessively fast irregular heartbeats;
- Blurred vision that may be associated with abnormally high blood pressure in the eyes. This reaction occurs very rarely and is more likely to occur in patients with glaucoma;
- Problem with urination. The occurrence of this reaction is more likely in patients with prostatic hyperplasia.
- These reactions are rare or very rare.

4.9 Overdose

If you have taken the drug more than recommended, consult a doctor immediately because of the risk of liver failure, even if you have no symptoms.

Paracetamol

Symptoms and Signs

Paracetamol overdose may cause liver failure which can lead to liver transplant or lead to death. Acute pancreatitis has been observed, usually with hepatic dysfunction and liver toxicity.

Treatment

Immediate medical management is required in the event of overdose, even if symptoms of overdose are not present. Administration of N-acetylcysteine or methionine may be required.

Phenylephrine

Symptoms and Signs

Phenylephrine overdosage is likely to result in effects similar to those listed under adverse reactions. Additional symptoms may include irritability, restlessness, hypertension and possibly reflux brachycardia. 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 liver toxicity.

Treatment

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

Ascorbic Acid

Symptom and Signs

High doses of ascorbic acid (>3000mg) may cause transient osmotic diarrhoea and gastrointestinal effects such as nausea and abdominal discomfort. Effects of overdose of ascorbic acid would be subsumed by serious liver toxicity caused by paracetamol overdose.

5. PHARMACOLOGICAL PROPERTIES

ATC code: N02B E51

Pharmacotherapeutic group: Other analgesics and antipyretics, paracetamol, combinations excluding psycholeptics.

5.1 Pharmacodynamic Properties

Paracetamol is an analgesic and antipyretic. Its mechanism of action is believed to include inhibition of prostaglandin synthesis, primarily within the central nervous system.

Paracetamol is, therefore, particularly suitable for patients with a history of disease or on concomitant medication, where peripheral prostaglandin inhibition would be undesirable (such as, for example, those with a history of gastrointestinal bleeding or the elderly).

Phenylephrine hydrochloride is a sympathomimetic agent with mainly direct effects on adrenergic receptors (predominantly alpha-adrenergic activity) producing nasal decongestion.

Ascorbic Acid (Vitamin C) is usually included in the combination of anti-cold components, compensating for the loss of vitamin C that occurs during the initial stages of viral diseases, including the common cold.

5.2 Pharmacokinetic Properties

Paracetamol is rapidly and almost completely absorbed from the gastrointestinal tract and is distributed in most tissues of the body. Binding to plasma proteins is minimal at therapeutic concentrations. It is metabolised in the liver and excreted in the urine mainly as glucuronide and sulphate conjugates. Less than 5% is excreted as unmodified paracetamol.

Phenylephrine is irregularly absorbed from the gastrointestinal tract. It undergoes first-pass metabolism by monoamine oxidases in the gut and liver; orally administered phenylephrine

thus has reduced bioavailability. It is excreted in the urine almost entirely as the sulphate conjugate.

Ascorbic Acid is rapidly absorbed from the gastrointestinal tract and is widely distributed throughout the body. It is 25% bound to plasma proteins. Ascorbic acid in excess of the body's needs is eliminated in the urine as metabolites.

5.3 Preclinical Safety Data

Preclinical safety data on paracetamol, phenylephrine and ascorbic acid in the literature have not revealed findings which are of relevance to the recommended dosage and use of the product.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Sucrose
Citric acid (anhydrous)
Saccharin sodium
Sodium Citrate
Quinoline yellow (E 104)
Lemon tetraaroma 100%
Lemon flavour 52293/TP05.51

6.2 Incompatibilities

Not applicable

6.3 Shelf-life

3 years. Do not use after the expiration date indicated on the package.

6.4 Special Precautions for Storage

Store below 25°C. Keep out of the sight and reach of children.

6.5 Nature and Contents of Container

Powder for oral solution with lemon flavor. Each laminated sachet (paper/ polyethylene /aluminum foil/ polyethylene) contains 5g of powder. 10 sachets are packed in one carton box with patient information leaflet.

6.6 Special precautions for disposal

None.

7. MANUFACTURING SITE

SmithKline Beecham SA, Ctra. de Ajalvir, Km 2,500, Alcalá de Henares, 28806 Madrid, Spain.

8. MARKETING AUTHORISATION HOLDER

STADA Arzneimittel AG, Stadastrasse 2-18, 61118 Bad Vilbel, Germany.

9. DATE OF REVISION OF THE TEXT