SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Coldrex Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Paracetamol Ph Eur 500 mg, Caffeine Ph Eur 25 mg, Phenylephrine hydrochloride Ph Eur 5 mg, Terpin Hydrate BPC 20 mg, Ascorbic Acid 30 mg.

3 PHARMACEUTICAL FORM

Tablet

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the relief of symptoms of colds and influenza.

4.2 Posology and method of administration

Adults, the elderly and adolescents 16 years and over:

2 tablets every 4 to 6 hours, if you need to, up to 4 times in any 24 hours. Do not take more than 8 tablets in any 24 hours.

Children and adolescents aged 12 to 15 years:

1 tablet every 4 to 6 hours, if you need to, up to 4 times in any 24 hours. Do not take more than 4 tablets in any 24 hours.

These doses should not be repeated more frequently than every four hours. Do not take continuously for more than 7 days without medical advice.

Do not use in children under the age of 12 years.

Method of Administration

Oral.

4.3 Contraindications

Hypersensitivity to paracetamol, caffeine, phenylephrine hydrochloride, terpin hydrate, ascorbic acid or any of the other constituents.

Hepatic or severe renal impairment, hypertension, hyperthyroidism, diabetes, heart disease, angle closure glaucoma or phaeochromocytoma.

Patients taking tricyclic antidepressants, 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

Medical advice should be sought before using this product in patients with these conditions:
Cardiovascular disease
An enlargement of the prostate gland
Occlusive vascular disease (e.g. Raynaud's phenomenon)

This product should not be used by patients taking other sympathomimetics (such as decongestants, appetite suppressants and amphetamine-like psychostimulants) (see section 4.5).

Use with caution in patients taking other antihypertensives (see section 4.5).

Concomitant use of other flu, cold or decongestant medicines, or other paracetamol-containing medicines should be avoided. Care is advised in the administration of paracetamol to patients with severe renal or severe hepatic impairment. The hazard of overdose is greater in those with non-cirrhotic alcoholic liver disease.

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.

Excessive intake of tea or coffee should be avoided while taking this product. If symptoms persist consult your doctor.
Do not exceed the stated dose.

Keep out of the reach and sight of

children. Pack Label:

Immediate medical advice should be sought in the event of an overdose, even if you feel well. Do not take with any other paracetamol-containing products.

Patient Information Leaflet:

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 speed of absorption of paracetamol may be increased by metoclopramide or domperidone and absorption reduced by colestyramine. 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. These interactions are considered unlikely to be of clinical significance in acute use at the dosage regimen proposed.

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 acidisis, especially in patients with risks factors (see section 4.4).

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

Monoamine oxidase inhibitors	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.
Ergot alkaloids (ergotamine and methylsergide)	Increased risk of ergotism

Digoxin and cardiac glycosides	Increase the risk of irregular heartbeat or heart attack

4.6 Fertility, Pregnancy and lactation

This product is not recommended for use during pregnancy due to the possible increased risk of spontaneous abortion associated with caffeine consumption.

This product should not be used while breast-feeding without medical advice.

Phenylephrine may be excreted in breast milk. Caffeine in breast milk may potentially have a stimulating effect on breast fed infants but significant toxicity has not been observed.

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 events from historical clinical trial data are both infrequent and from small patient exposure. Accordingly, events reported from extensive post-marketing experience at therapeutic/labelled dose and considered attributable are tabulated below by system class. The frequency of these adverse events is not known (cannot be estimated from available data).

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/toxic epidermal necrolysis
Respiratory, thoracic and mediastinal disorders	Bromchospasm *
Hepatobiliary disorders	Hepatic dysfunction

Metabolism and nutrition	High anion gap metabolic acidosis

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

Phenylephrine

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

Caffeine

Body System	**Undesirable effect**
Central nervous system	Nervousness Dizziness

When the recommended paracetamol-caffeine-codeine dosing regimen is combined with dietary caffeine intake, the resulting higher dose of caffeine may increase the potential for caffeine-related adverse effects such as insomnia, restlessness, anxiety, irritability, headaches, gastrointestinal disturbances and palpitations.

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

Skin and subcutaneous disorders	Hypersensitivity reactions including cross-sensitivity with other sympathomimetics may occur

Description of selected adverse reactions

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.

4.9 Overdose

Paracetamol

Liver damage is possible in adults who have taken 10 g or more of paracetamol. Ingestion of 5 g 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 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 arrythmias 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 the 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 24 h from ingestion should be discussed with the NPIS or a liver unit.

Caffeine

Symptoms and signs

Overdose of caffeine may produce nervousness, restlessness, insomnia, excitement, diuresis, facial flushing, muscle twitching, GI disturbance, tachycardia or cardia arrhythmia, "rambling" flow of thought and speech, psychomotor agitation or periods of inexhaustibility.

It must be noted that for clinically significant symptoms of caffeine overdose to occur with this product, the amount ingested would be associated with serious paracetamol-related liver toxicity

Management

Patients should receive general supportive care (e.g. hydration and maintenance of vital signs). The administration of activated charcoal may be beneficial when performed within one hour of the overdose, but can be considered for up to four hours of the overdose. The CNS effects of the overdose may be treated with intravenous sedatives.

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 bradycardia. In severe cases confusion, hallucinations, seizures and arrythmias 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.

Ascorbic acid

Symptoms and signs

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

Terpin Hydrate

Overdosage may cause gastrointestinal effects such as nausea, vomiting and abdominal pain.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Paracetamol is an analgesic and antipyretic.

Caffeine is a potent stimulator of the CNS.

Ascorbic acid is a common ingredient of cold and influenza combination products included to compensate for Vitamin C losses which occur in the initial stages of acute viral infections.

Phenylephrine hydrochloride is a sympathomimetic decongestant.

Terpin hydrate has been stated to increase bronchial secretion directly and is used as an expectorant.

The active ingredients are not known to cause sedation.

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.

Caffeine - is absorbed readily after oral administration, maximal plasma concentrations are achieved within one hour and the plasma half-life is about 3.5 hours. 65-80% of administered caffeine is excreted in the urine as 1-methyluric acid 1-methylxanthine.

Ascorbic acid - is readily absorbed from the gastro-intestinal tract and is widely distributed in the body tissues, 25% bound to plasma proteins. Ascorbic acid in excess of the body's needs is eliminated in the urine as metabolites.

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

No relevant pharmacokinetic data are available for terpin hydrate.

5.3 Preclinical safety data

Pre-clinical 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 Summary.

The toxicity of paracetamol has been extensively studied in numerous animal species. Pre-clinical studies in rats and mice have indicated single dose oral LD_{50} values of 3.7 g/kg and 338 mg/kg, respectively. Chronic toxicity in these species at large multiples of the human therapeutic dose, occurs as degeneration and necrosis of hepatic, renal and lymphoid tissue, and blood count changes. The metabolites believed responsible for these effects have also been demonstrated in man.

Paracetamol should not, therefore, be taken for long periods of time, and in excessive doses. At normal therapeutic doses, paracetamol is not associated with genotoxic or carcinogenic risk. There is no evidence of embryo- or foeto-toxicity from paracetamol in animal studies.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize starch, soluble starch, talc, stearic acid, polyvinyl pyrollidone, potassium sorbate, sodium lauryl sulphate, sunset yellow.

6.2 Incompatibilities

None.

6.3 Shelf life

4 years

6.4 Special precautions for storage

Store in a dry place

6.5 Nature and contents of container

PVC blister strips are packed into cardboard cartons. Each pack contains 12 or 24 tablets.

6.6 Special precautions for disposal

None stated

7 MARKETING AUTHORISATION HOLDER

Omega Pharma Ltd., Wrafton, Braunton, Devon, EX33 2DL, UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 02855/0269

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

23/02/2011

10 DATE OF REVISION OF THE TEXT

06/03/2026