# SUMMARY OF PRODUCT CHARACTERISTICS

**Product Summary**

## 1. Name of the Medicinal Product

Panadol Cold & Flu

## 2. Qualitative and Quantitative Composition

Each Panadol Cold & Flu tablet contains Paracetamol 500 mg, pseudoephedrine hydrochloride 30 mg, chlorpheniramine maleate 2mg

For a full list of excipients, see section 6.1

## 3. Pharmaceutical Form

Tablet.

## 4. Clinical Particulars

### 4.1 Therapeutic Indications

Panadol Cold & Flu is indicated for temporary relief of sinus and headache pain, nasal decongestion associated with sinusitis or due to cold, hay fever or other upper respiratory allergies. It also temporarily relieves runny nose, sneezing, itching of nose and throat and itchy, watery eyes due to hayfever or other upper respiratory allergies.

### 4.2 Posology and Method of Administration

For oral use.

**Adults, including the elderly and children 12 years and over:**

Two tablets up to four times daily as required for relief of symptoms. The dose should not be repeated more frequently than every four hours nor should more than four doses be given in any 24 hour period.

### 4.3 Contraindications

Hypersensitivity to paracetamol, pseudoephedrine, chlorpheniramine or any of the other constituents.

Not to be used by patients taking monoamine oxidase inhibitors (MAOI's) or for two weeks after stopping the MAOI drug.

## 4.4 Special Warning and Precautions for Use

Care is advised in the administration of Panadol Cold & Flu to patients with renal or hepatic impairment, cardiovascular disease, hypertension, hyperthyroidism, prostatic hypertrophy, diabetes mellitus or glaucoma, breathing difficulties such as emphysema or chronic bronchitis, epilepsy or thyrotoxicosis. Do not exceed the stated dose. Chlorpheniramine may cause drowsiness, dizziness, blurred vision and psychomotor impairment, which can seriously hamper the patients' ability to drive and operate machinery.

Patients should be advised not to take other paracetamol-containing products or sympathomimetic agents concurrently. Patients should be advised to consult their doctor if their cold or flu symptoms persist

Keep all medicines safely away from children.

## 4.5 Interaction with Other Medicinal Products and Other Forms of Interaction

The co-administration of Panadol Cold & Flu with tricyclic antidepressants, sympathomimetic agents (such as decongestants, appetite suppressants and amphetamine-like psychostimulants), or with monoamine oxidase inhibitors (MAOI's) (or within two weeks of stopping MAOI's) which interfere with the catabolism of sympathomimetic agents, may occasionally cause a rise in blood pressure and may lead to hypertensive crisis in the case of MAOI's.

Because of its pseudoephedrine content, this product may partially reverse the hypotensive action of drugs which interfere with sympathetic activity including alpha- and beta- adrenergic blocking agents and methyldopa.

Drowsiness caused by Chlorpheniramine can be exacerbated by concomitant use of alcohol, sedatives and tranquilizers. Chlorpheniramine inhibits phenytoin metabolism and can lead to phenytoin toxicity

The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular daily use of Panadol Cold & Flu with increased risk of bleeding; occasional doses have no significant effect.

## 4.6 Pregnancy and Lactation

Do not use Panadol Cold & Flu if pregnant or breast-feeding without medical advice.

## 4.7 Effects on Ability to Drive and Use Machines

Chlorpheniramine can cause drowsiness, if affected patients should not drive or operate machinery

## 4.8 Undesirable Effects

Adverse effects of Panadol Cold & Flu are rare but a variety of allergic cutaneous reactions, with or without systemic features, have been reported. Hypersensitivity including skin rash, angioedema have also been reported rarely. There have been very rare reports of blood dyscrasias including thrombocytopenia and agranulocytosis but these were not necessarily causally related to Panadol Cold & Flu. Dizziness, dry mouth, insomnia, nervousness, agitation and restlessness have also been

reported but these are usually mild. Urinary retention can occur in those patients with prostatic enlargement. Hallucinations have been reported rarely.

### 4.9 Overdose

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. Gastric lavage or 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 after the overdose. Antidotes such as N acetylcysteine (NAC) and methionine protect the liver if administered within 12 hours of overdose. NAC is effective up to and possibly beyond 24 hours. General supportive measures must be available.

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, coma and death. Acute renal failure with acute tubular necrosis may develop even in the absence of severe liver damage. Cardiac arrhythmias and pancreatitis have been reported. Liver damage is possible in adults who have taken 10g or more of paracetamol. It is considered that excess quantities of a toxic metabolite (usually adequately detoxified by glutathione when normal doses of paracetamol are ingested) become irreversibly bound to liver tissue.

As with other sympathomimetics pseudoephedrine overdose will result in symptoms due to central nervous system and cardiovascular stimulation e.g. excitement, irritability, restlessness, tremor, hallucinations, hypertension, palpitations, arrhythmias and difficulty with micturition. In severe cases, psychosis, convulsions, coma and hypertensive crisis may occur. Serum potassium levels may be low due to extracellular to intracellular shifts in potassium.

Treatment should consist of standard supportive measures. Beta-blockers should reverse the cardiovascular complications and the hypokalaemia.

Symptoms and signs of chlorpheniramine overdose include sedation, paradoxical stimulation of CNS, toxic psychosis, seizures, apnoea, convulsions, anticholinergic effects, dystonic reactions and cardiovascular collapse including arrhythmias. 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 should include gastric lavage or induced emesis. Following these measures activated charcoal and cathartics may be administered to minimise absorption. Treat hypotension and arrhythmias vigorously. CNS convulsions may be treated with i.v. diazepam or phenytoin. Haemoperfusion may be used in severe cases.

## 5. Pharmacological Properties

### 5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: Paracetamol combinations excluding psycholeptics, ATC code:N02BE51The analgesic and antipyretic actions of paracetamol are believed to be due, at least

in part, to inhibition of prostaglandin synthesis in the central nervous system. Paracetamol 1 g has been shown to be an effective analgesic and antipyretic.

Pseudoephedrine is predominantly an indirect-acting sympathomimetic amine. Pseudoephedrine 60 mg has been shown to be an effective nasal decongestant, as measured by nasal airflow, in patients with the common cold and rhinitis.

At therapeutic doses, pseudoephedrine has no clinically significant effect on blood pressure in normotensive patients. Studies in patients with controlled hypertension have demonstrated that pseudoephedrine 60 mg has no, or minimal, effect on blood pressure and does not have sedative effects.

Chlorpheniramine produces a dose-dependent inhibition of histamine-induced wheal and flare in healthy subjects . Following a single dose of chlorpheniramine 4 mg, the effect is apparent within one hour and lasts at least 12 hours . Chlorpheniramine produces sedation in man although the effect is variable and tolerance develops . The anti-cholinergic properties of chlorpheniramine have been demonstrated in man. These anticholinergic properties are relevant clinically in conditions associated with rhinorrhoea since the seromucosal glands of the nose are under anticholinergic control.

## 5.2 Pharmacokinetic Properties

Paracetamol is rapidly and completely absorbed from the gastro-intestinal tract with peak plasma levels occurring about 0.25-2 hours after dosing. The absolute bioavailability is about 80% and is independent of dose in normal therapeutic doses (5-20 mg/kg). It is not bound to plasma proteins. The volume of distribution is about 0.9 l/kg. The plasma half-life ranges from 1-3 hours and is largely unaffected by age. It is metabolised in the liver and excreted in the urine as the glucuronide and sulphate conjugates. In overdose situations, saturation of the detoxification of a minor metabolite, N-acetyl-p-benzoquinoneimine, by conjugation with glutathione occurs and this leads to its accumulation and resultant liver damage.

Pseudoephedrine is rapidly and completely absorbed from the gastrointestinal tract after oral administration, with no presystemic metabolism. Peak plasma levels are achieved after 1-2 hours. No protein binding data are available. The volume of distribution ranges from 2.64 to 3.51 l/kg in both single and multiple dose studies. The plasma half-life varies from 4.3-7.0 hours in adults. There is little metabolism of pseudoephedrine in man with approximately 90% being excreted in the urine unchanged. Approximately 1% is eliminated by hepatic metabolism, by N-demethylation to norpseudoephedrine.

As a weak base, the extent of renal excretion is dependent on urinary pH . At low urinary pH, tubular resorption is minimal and urine flow rate will not influence clearance of the drug. At high pH (>7.0), pseudoephedrine is extensively reabsorbed in the renal tubule and renal clearance will depend on urine flow rate.

Hepatic disease is unlikely to affect the pharmacokinetics of pseudoephedrine. Renal impairment will result in increased plasma levels.

Chlorpheniramine has relatively low oral bioavailability (25-50%) indicating extensive first pass metabolism in the liver. Administration with food reduces bioavailability. Peak plasma levels occur 2-3 hours following administration of immediate release and 6-8 hours following administration of immediate release formulations. The drug is extensively metabolised via demethylation in the liver to mono and didesmethyl derivatives and by deamination to polar alcoholic and acidic derivatives. There is considerable inter-subject variation in the half-life of the drug: the overall mean from a range of studies in adults was 20.4 hours with a range from 3-43 hours. The half-life of the d-isomer is approximately 60% longer than that of the l-isomer suggesting stereoselective metabolism. The half-life in children appears shorter. Chlorpheniramine is primarily excreted via the kidneys. At steady state, approximately 34% of chlorpheniramine is excreted as the parent drug. Since chlorpheniramine is a weak base, renal excretion will vary with urinary pH

### 5.3 Preclinical Safety Data

Preclinical safety data on paracetamol, pseudoephedrine and chlorpheniramine in the literature have not revealed findings which are of relevance to the recommended dosage and use of the product and which have not been mentioned elsewhere in the summary.

## 6. Pharmaceutical Particulars

### 6.1 List of Excipients

silicon dioxide, stearic acid, sodium benzoate, povidone, pregelatinised starch, maize starch, talc

### 6.2 Incompatibilities

None known.

### 6.3 Shelf life

Three years.

### 6.4 Special Precautions for Storage

Do not store above 25°C.

### 6.5 Nature and Contents of Container

Opaque blister strips (12s) of PVC (200 microns) backed with aluminium foil.

### 6.6 Special precautions for disposal and other handling

Not applicable.

**Administrative data**

## 7. Marketing Authorisation Holder

GlaxoSmithkline Export Limited
980 Great West Road,
Brentford,
Middlesex TW8 9GS,
England

## 8. Marketing Authorisation Number

MA575/00101

## 9. Date of First Authorisation / Renewal of the Authorisation

9th February 2007

## 10. Date of Revision of the text