SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Panadol Cold & Sinus 500mg / 30mg Film-Coated Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Paracetamol 500 mg and pseudoephedrine hydrochloride 30mg.
For excipients see Section 6.1

3 PHARMACEUTICAL FORM

Form: Film coated tablet.
Description:
A bilayer (white/blue) film coated capsule shaped tablet. The tablet is debossed with the number 2 in a circle on one face.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
Symptomatic relief of nasal congestion when combined with fever and/or pain such as, sore throat, sinus pain or headache in the common cold or influenza.

4.2 Posology and method of administration

For oral use.
Adults, including the elderly, and children 16 years and over:  
Two tablets up to three times daily as required for relief of symptoms.  
Children aged 12 to 15 years old:  
One tablet up to three times daily as required for relief of symptoms. The dose should not be repeated more frequently than every four hours nor should more than three doses be given in any 24 hour period.  

Not to be used in children under 12 years of age.  

Patients should be advised not to use this product for more than 5 days and to seek medical advice if symptoms persist.  
Do not exceed the stated dose.  
The tablets should be taken with water.  

Special Populations  
Pseudoephedrine is primarily excreted renally. Pseudoephedrine should not be used by those with severe renal impairment (see Contraindications) and should be used with caution in those with moderate renal impairment (see 4.4 Special warnings and precautions for use and 5.2 Pharmacokinetics).  

4.3 Contraindications  
Hypersensitivity to paracetamol, pseudoephedrine, sympathomimetics or any of the other constituents.  
Not to be used by patients taking moclobemide or monoamine oxidase inhibitors (MAOI’s) or for two weeks after stopping the MAOI drug.  
The antibiotics furazolidone and linezolid should not be taken with Panadol Cold & Sinus (see 4.5 Interaction with other medicinal products and other forms of interaction).  
Not to be used by patients with the following conditions:  
- Hypertension.  
- Cardiovascular disease  
- Hyperthyroidism  
- Prostatic hypertrophy  
- Glaucoma  
- Severe renal impairment  

Not to be used by patients currently receiving other sympathomimetics (such as decongestants, appetite suppressants and amphetamine-like psycho-stimulants).  
Not to be used by patients taking beta-blockers (see 4.5 Interaction with other medicinal products and other forms of interaction).  
Not to be used in children under 12 years of age.
4.4 Special warnings and precautions for use
Use with caution in patients with hepatic impairment or mild to moderate renal impairment, diabetes mellitus, arrhythmias or phaeochromocytoma.

Use with caution in patients taking antihypertensives (see 4.5 Interaction with other medicinal products and other forms of interaction).

The hazard of overdose is greater in those with non-cirrhotic alcoholic liver disease.

Patients should be advised not to take other paracetamol-containing products concurrently.

This product may give rise to insomnia and nervousness.

There have been rare cases of posterior reversible encephalopathy (PRES) / reversible cerebral vasocostriction syndrome (RCVS) reported with sympathomimetic drugs, including pseudoephedrine. Symptoms reported included sudden onset of severe headache, nausea, vomiting, and visual disturbances. Most cases improved or resolved within a few days following appropriate treatment. Psuedoephedrine should be discontinued immediately and medical advice sought if signs/ symptoms of PRES/RCVS develop.

Care is advised in the administration of Panadol Cold & Sinus to patients who will be undergoing general anaesthesia within a few days.

If you are taking medication, or are under medical care consult your doctor or pharmacist.

Keep all medicines safely out of sight and reach of children.

4.5 Interaction with other medicinal products and other forms of interaction
The co-administration of Panadol Cold & Sinus with tricyclic antidepressants, the antidepressant moclobemide 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 moclobemide or MAOI’s.

The antibiotic furazolidone is a monoamine oxidase inhibitor and the antibiotic linezolid is a reversible non-selective MAOI with weak MAO-inhibitory properties. Therefore neither should be taken with Panadol Cold & Sinus.

Pseudoephedrine may antagonize the effect of certain classes of antihypertensives (e.g., beta-blockers, methyl-dopa, reserpine, debrisoquine,
guanethidine) (see 4.3 Contraindications and 4.4 Special warnings and precautions for use).

The rate of paracetamol absorption may be reduced by colestyramine. The interaction can be avoided by delaying administration of colestyramine by one hour, in order to maintain maximal analgesic effects.

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

Sodium bicarbonate alkalinizes the urine and may reduce the renal elimination of pseudoephedrine, a reduction in dose may be necessary.

The speed of absorption of paracetamol may be increased by metoclopramide or domperidone.

4.6  Fertility, Pregnancy and lactation

Pregnancy:
The safe use of the combination paracetamol and pseudoephedrine has not been fully established. Animal studies are insufficient with respect to effects on pregnancy, embryonal/fetal development and postnatal development. The use of Panadol Cold & Sinus during pregnancy is therefore not recommended.

Lactation:
Pseudoephedrine is excreted in breast milk in amounts leading to increased risk of effects in the infant even at therapeutic doses. Treatment with Panadol Cold and Sinus is not recommended during breastfeeding.

4.7  Effects on ability to drive and use machines

Dizziness is one of the most frequent adverse effects. This could affect driving or using machines.

4.8  Undesirable effects

The following adverse reactions have been reported with products containing paracetamol and/or pseudoephedrine.

Blood and the lymphatic system:

Very Rare (<1/10,000): blood dyscrasia, including thrombocytopenia and agranulocytosis

Immune System disorders:

Rare (>1/10,000, <1/1,000): hypersensitivity*

Psychiatric disorders:
Common (>1/100, <1/10): nervousness, insomnia
Uncommon (>1/1,000, <1/100): agitation, restlessness
Rare (>1/10,000, <1/1,000): hallucinations
Nervous system disorders:
Common (>1/100, <1/10): dizziness
Gastrointestinal disorders:
Common (>1/100; <1/10): dry mouth, nausea, vomiting
Skin and subcutaneous tissue disorders:
Rare (>1/10,000, <1/1,000): rash, dermatitis allergic*
Renal and urinary disorders:
Uncommon (>1/1,000, <1/100): urinary retention**
Cardiovascular disorders:
Uncommon (>1/1,000, <1/100): minor tachycardia
Rare (>1/10,000, <1/1,000): cardiac arrhythmias
Rare (>1/10,000, <1/1,000): hypertension
Hepatic disorders:
Very Rare (<1/10,000): Hepatic dysfunction
Respiratory disorders:
Very Rare (<1/10,000): Bronchospasm is more likely in patients sensitive to aspirin or NSAIDs.

*A variety of allergic skin reactions, with or without systemic features such as bronchospasm, angioedema have been reported following use of pseudoephedrine. Hypersensitivity reactions, including skin rashes, Stevens Johnson Syndrome, Toxic Epidermal Necrolysis, angioedema and anaphylaxis have been reported very rarely with paracetamol.

**Urinary retention is most likely to occur in those with bladder outlet obstruction such as prostatic hypertrophy.

**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. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard

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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:
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 usually occur within the first 24 hours and are pallor, nausea, vomiting, anorexia and abdominal pain.

Simultaneously, increased levels of hepatic transaminases (AST, ALT), lactate dehydrogenase and bilirubin are observed together with increased prothrombin time that may appear 12 to 48 hours after administration. Abnormalities of glucose metabolism and metabolic acidosis may occur. Clinical symptoms of liver damage are usually evident initially after 2 days, and reach a maximum after 4 to 6 days.

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. Other non-hepatic symptoms that have been reported following paracetamol overdosage include myocardial abnormalities and pancreatitis.

In severe poisoning, hepatic failure may progress to encephalopathy, haemorrhage, hypoglycaemia, cerebral oedema, and death.

**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.

Paracetamol concentrations in blood should be measured not less than 4 hours after overdose in order to be able to assess the risk of developing liver damage (using the paracetamol overdose nomogram). However, N-acetylcysteine (NAC) treatment should be started immediately when massive overdose is suspected.

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.

Intravenous (IV) infusion (or oral administration if IV infusion is not possible) of the antidote N-acetylcysteine should be started if possible before the 8th hour. The effectiveness of the antidote declines sharply after this time. N-acetylcysteine can, however, give some degree of protection even after 8 hours, and up to 24 hours, but in these cases prolonged treatment is given. If vomiting is not a problem, oral methionine may be a suitable alternative for remote areas, outside hospital.
Symptomatic treatment should be implemented.

**Pseudoephedrine**

*Symptoms*
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.

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

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
ATC Code N02BE51
Panadol Cold & Sinus is a mild to moderate analgesic, antipyretic and decongestant.

The 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 acts on the alpha adrenergic receptors in the mucosa of the respiratory tract producing vasoconstriction which results in shrinkage of swollen nasal mucous membranes, reduction of nasal congestion and increase in nasal airway patency.

Pseudoephedrine 60mg 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 60mg has no, or minimal, effect on blood pressure and does not have sedative effects.

GlaxoSmithKline has conducted a clinical study in patients with symptoms of cold and flu to assess relief of pain and nasal congestion. The study compared
Panadol Cold & Sinus (taken three times daily as required for three days) with paracetamol alone, pseudoephedrine alone and placebo. Results demonstrated that Panadol Cold & Sinus gives significantly (p<0.05) greater pain relief than either placebo or pseudoephedrine and that Panadol Cold & Sinus has a significantly (p<0.05) greater decongestant effect than either placebo or paracetamol. Panadol Cold & Sinus demonstrated an additive effect for relief of pain and nasal congestion compared to paracetamol or pseudoephedrine. For a single dose of Panadol Cold & Sinus there was significantly greater (P<0.05) relief of pain and nasal congestion (nasal airflow) compared to placebo at one hour post dose.

5.2 Pharmacokinetic properties

Paracetamol:

Absorption: The absorption of paracetamol by the oral route is rapid and complete. Maximum plasma concentrations are reached 30 to 60 minutes following ingestion.

Distribution: Paracetamol is distributed rapidly throughout all tissues. Concentrations are comparable in blood salivary and plasma. Protein binding is low.

Metabolism: Paracetamol is metabolised mainly in the liver, following two major metabolic pathways: Glucuronic acid and sulfuric acid conjugates. The latter route is rapidly saturated at doses higher than the therapeutic dosages. A minor route, catalyzed by the Cytocrome P 450 (mostly CYP2E1), results in the formation of an intermediate reagent (N-acetyl-p-benzoquinoneimine) which under normal conditions of use, is rapidly detoxified by glutathione and eliminated in the urine, after conjugation with cysteine and mercapturic acid.

Conversely, when massive intoxication occurs, the quantity of this toxic metabolite is increased.

Elimination: Elimination is essentially through the urine. 90% of the ingested dose is eliminated via the kidneys within 24 hours, principally as glucuronide (60-80%) and sulphate conjugates (20-30%). Less than 5% is eliminated in unchanged form.

Elimination half life is about 2 hours.

Physiopathological variations

Renal Insufficiency: In cases of severe renal insufficiency (creatinine clearance lower than 10ml/min) the elimination of paracetamol and its metabolites is delayed.

Elderly subjects: Conjugation capacity is not modified.

Pseudoephedrine:

Absorption: 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.
**Distribution:** Pseudoephedrine is rapidly distributed throughout the body. 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.

**Metabolism:** 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.

**Elimination:** The plasma half-life varies from 4.3-7.0 hours in adults. As a weak base the extent of renal excretion is dependent on urinary pH. At low 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.

**Renal Insufficiency:** Renal impairment will result in increased plasma levels.

**Elderly subjects:** Elimination capacity is not modified.

A steady state pharmacokinetic interaction study in healthy volunteers has demonstrated that the rate (C_{max}, t_{max}) and extent (AUC_{0-6-hours}) of absorption from Panadol Cold & Sinus tablet is equivalent to those of paracetamol alone and of pseudoephedrine alone.

In the same study the median t_{max} values for the paracetamol and pseudoephedrine components of Panadol Cold & Sinus were 0.7 hours and 1.2 hours, respectively.

5.3 **Preclinical safety data**

There are no preclinical data considered relevant to clinical safety beyond data included in other sections of the SPC.

6 **PHARMACEUTICAL PARTICULARS**

6.1 **List of excipients**

Cellulose microcrystalline E 460
Silica, Colloidal anhydrous E 551
Stearic acid E 570
Magnesium stearate E 572
Starch pregelatinised
Povidone
Crospovidone
Croscarmellose sodium E 468
Hyromellose E 464
Macrogol
6.2 **Incompatibilities**  
Not applicable

6.3 **Shelf life**  
3 years

6.4 **Special precautions for storage**  
Do not store above 25°C

6.5 **Nature and contents of container**  
Opaque blister strips of PVC (250 microns)/ PE (25 or 30 microns)/ PVdC 90g/m²) backed with aluminium foil. Blisters are packed into cartons and each carton contains 2, 5, 6, 10, 12, 16, 18, 24, 30 or 32 tablets (not all pack sizes may be marketed).

6.6 **Special precautions for disposal**  
No special requirements

7 **MARKETING AUTHORISATION HOLDER**

Omega Pharma Ltd.  
1st Floor  
32 Vauxhall Bridge Road  
LONDON, SW1V 2SA  
United Kingdom

8 **MARKETING AUTHORISATION NUMBER(S)**
PL 02855/0076
DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORITY
06/11/2012

DATE OF REVISION OF THE TEXT
17/01/2017