Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Solpa-Sinus Film-coated Tablets Paracetamol 500mg Pseudoephedrine Hydrochloride 30mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

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

3 PHARMACEUTICAL FORM

Film coated tablet.
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

Solpa-Sinus is indicated in adults and in children and adolescents aged 12 years and over for the 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

Posology
Adults, including the elderly, and children 16 years and over:
Two tablets up to three times daily as required for relief of symptoms.
No more than 8 tablets should be taken in 24 hours

Elderly patients
Experience has indicated that normal adult dosage is usually appropriate. However, in frail, immobile, elderly subjects or in elderly patients with renal or hepatic impairment, a reduction in the amount or frequency of dosing may be appropriate.
The maximum daily dose should not exceed 60mg/kg/day (up to a maximum of 2g per day) in the following situations, unless directed by a physician:

- Weight less than 50kg
- Chronic alcoholism
- Dehydration
- Chronic malnutrition *Paediatric population Childrenaged 12 to 15 yearsold:*One tablet up to three times daily as required for relief of symptoms.Not to be used in children under 12 years of age. 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. Do not exceed the stated dose. Method of administration For oral use.The tablets should be taken with water.Do not exceed the recommended daily dosage or the specified number of doses because of the risk of liver damage (see section 4.4 and 4.9). Minimum dosing interval: 4 hours. If pain or fever persist for more than 3 days or get worse, or if any other symptoms occur, treatment should be discontinued, and a physician consulted (see section 4.4). *SpecialPopulations*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). Paracetamol and pseudoephedrine*Renal impairment*It is recommended, when giving paracetamol to patients with renal impairment, to reduce the dose and to increase the minimum interval between each administration to at least 6 hours unless directed otherwise by a physician. See Table below:

Glomerular filtration rate	Dose
10-50 ml/min	500mg every 6 hours
<10ml/min	500mg every 8 hours

Paracetamol
Hepatic impairment
In patients with hepatic impairment or Gilbert's Syndrome, the dose should be reduced or the dosing interval prolonged.

The daily dose should not exceed 2g/day unless directed by a physician.

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 Solpa-Sinus (see 4.5 Interaction with other medicinal products and other forms of interaction).

Not to be used by patients with the following conditions:

- Severe hypertension or uncontrolled hypertension
- Severe acute or chronic kidney disease/renal failure.
- Cardiovascular disease
- Hyperthyroidism
- Prostatic hypertrophy
- Glaucoma

Not to be used by patients currently receiving other sympathomimetics (such as decongestants, appetite suppressants and amfetamine-like psychostimulants).

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 anti-hypertensives (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.

Posterior reversible encephalopathy syndrome (PRES) and reversible cerebral vasoconstriction syndrome (RCVS)
Cases of PRES and RCVS have been reported with the use of pseudoephedrine-containing products (see section 4.8). The risk is increased in patients with severe or uncontrolled hypertension, or with severe acute or chronic kidney disease/renal failure (see section 4.3).
Pseudoephedrine should be discontinued and immediate medical assistance sought if the following symptoms occur: sudden severe headache or thunderclap headache, nausea, vomiting, confusion, seizures and/or visual disturbances. Most reported cases of PRES and RCVS resolved following discontinuation and appropriate treatment.

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

Caution is advised if paracetamol is administered concomitantly with flucloxacillin due to increased risk of high anion gap metabolic acidosis (HAGMA), particularly in patients with severe renal impairment, sepsis, malnutrition and other sources of glutathione deficiency (e.g. chronic alcoholism), as well as those using maximum daily doses of paracetamol. Close monitoring, including measurement of urinary 5-oxoproline, is recommended.

Ischaemic optic neuropathy
Cases of ischaemic optic neuropathy have been reported with pseudoephedrine.
Pseudoephedrine should be discontinued if sudden loss of vision or decreased visual acuity such as scotoma occurs.

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.

Sodium
This medicinal product contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

The co-administration of Solpa-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 Solpa-Sinus.

Caution should be taken when paracetamol is used concomitantly with flucloxacillin as concurrent intake has been associated with high anion gap metabolic acidosis, especially in patients with risks factors (see section 4.4)

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 Solpa- 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
Safe use of paracetamol-pseudoephedrine combination products in pregnancy has not been established despite widespread use over many years.
The product should be avoided during pregnancy, particularly during the first trimester, as defective closure of the abdominal wall (gastroschisis) has been reported very rarely in new-borns after first trimester exposure.
Animal studies are insufficient with respect to effects on pregnancy, embryonal/fetal development and postnatal development.
The use of Solpa-Sinus during pregnancy is therefore not recommended.
Breast-feeding
Pseudoephedrine is excreted in breast milk, in amounts leading to increased risk of effects in the infants even at therapeutic doses. May suppress lactation. This product should not be used whilst breastfeeding without medical advice.

Fertility
There are no data available regarding the influence of paracetamol and pseudoephedrine hydrochloride on fertility.

4.7 Effects on ability to drive and use machines

Dizziness is one of the most frequent adverse effects. This could effect 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
Not known: Posterior reversible encephalopathy syndrome (PRES) (see section 4.4), Reversible cerebral vasoconstriction syndrome (RCVS) (see section 4.4)

Eye disorders
Not known: Ischaemic optic neuropathy

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 HPRA Pharmacovigilance. Website: www.hpra.ie

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).
Paracetamol overdose can result in liver damage which may be fatal.
Symptoms generally appear within the first 24 hours and may comprise: nausea, vomiting, anorexia, pallor, and abdominal pain, or patients may be asymptomatic.
Overdose of paracetamol can cause liver cell necrosis likely to induce complete and irreversible necrosis, resulting in hepatocellular insufficiency, metabolic acidosis and encephalopathy which may lead to coma and death. Simultaneously, increased levels of hepatic transaminases (AST, ALT), lactate dehydrogenase and bilirubin are observed together with increased prothrombin levels that may appear 12 to 48 hours after administration.
Liver damage is likely in patients who have taken more than the recommended amounts of paracetamol. It is considered that excess quantities of toxic metabolite become irreversibly bound to liver tissue.
Some patients may be at increased risk of liver damage from paracetamol toxicity:

Risk factors include;
- Patients with liver disease
- Elderly patients
- Young children
- Patients receiving long-term treatment with carbamazepine, phenobarbitone, phenytoin, primidone, rifampicin, St John's Wort or other drugs that induce liver enzymes.
- Patients who regularly consume ethanol in excess of recommended amounts
- Patients with glutathione depletion e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia

Acute renal failure with acute tubular necrosis may also develop.
Cardiac arrhythmias and pancreatitis have also been reported.

Emergency Procedure:
Immediate transfer to hospital.
Blood sampling to determine initial paracetamol plasma concentration. In the case of a single acute overdose, paracetamol plasma concentration should be measured 4 hours post ingestion. Administration of activated charcoal should be considered if the overdose of paracetamol has been ingested within the previous hour.
The antidote N-acetylcysteine, should be administered as soon as possible in accordance with national treatment guidelines.
Symptomatic treatment should be implemented.

Pseudoephrine

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

Pharmacotherapeutic group: Other analgesics and antipyretics, anilides, ATC Code N02B E51

Solpa-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 is shrinkage of swollen nasal mucous membranes, reduction of nasal congestion and increase in nasal airway patency.

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.

A clinical study was conducted in patients with symptoms of cold and flu to assess relief of pain and nasal congestion. The study compared Solpa-Sinus (taken three times daily as required for three days) with paracetamol alone, pseudoephedrine alone and placebo. Results demonstrated that Solpa-Sinus gives significantly ($p<0.05$) greater pain relief than either placebo or pseudoephedrine and that Solpa-Sinus has a significantly ($p<0.05$) greater decongestant effect than either placebo or paracetamol. Solpa-Sinus demonstrated an additive effect for relief of pain and nasal congestion compared to paracetamol or pseudoephedrine. For a single dose of Solpa-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 saliva and plasma. Protein binding is low.

Biotransformation: 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.

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.

Biotransformation: 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 (Cmax, tmax) and extent (AUC0-6 hours) of absorption from Solpa-Sinus tablet is equivalent to those of paracetamol alone and of pseudoephedrine alone.

In the same study the median tmax values for the paracetamol and pseudoephedrine components of Solpa-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
Hypromellose E 464
Macrogol
Carnauba wax E 903
Indigo carmine E132

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 / PE PVdC) backed with aluminum foil. Blisters are packed into cartons and each carton contains2, 5, 6, 10, 12, 16, 18, 24, 30 or 32 tablets.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Chefaro Ireland DAC
The Sharp Building
Hogan Place
Dublin 2
Ireland

8 MARKETING AUTHORISATION NUMBER

PA1186/012/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 28 November 2003
Date of last renewal: 2 December 2012

10 DATE OF REVISION OF THE TEXT

April 2024