PACKAGE INSERT FOR SINU-FLU TABLETS

SCHEDULING STATUS:

S2

PROPRIETARY NAME (AND DOSAGE FORM):

SINU-FLU (Tablets)

COMPOSITION:

Each tablet contains paracetamol 400 mg, phenylephrine hydrochloride 5 mg and mepyramine maleate 5 mg.

Preservative: nipastat 0,62 mg.

PHARMACOLOGICAL CLASSIFICATION:

A 5.8 Preparations for the common cold, including nasal decongestants and antihistaminics.

PHARMACOLOGICAL ACTION:

Paracetamol has analgesic and antipyretic properties and acts predominantly by the inhibition of prostaglandin synthesis.

Phenylephrine hydrochloride mainly acts by directly affecting adrenergic receptors. It has predominantly alpha-adrenergic activity and does not

significantly stimulate the central nervous system at usual doses. Its pressor activity is weaker than that of ephedrine.

Mepyramine is a histamine H_1-receptor antagonist with antimuscarinic and central sedative properties.

INDICATIONS:

SINU-FLU tablets relieve the symptoms associated with sinus congestion, colds and flu, including pain and fever.

CONTRA-INDICATIONS:

SINU-FLU is contra-indicated in patients:

- With hypersensitivity to any of the ingredients.
- With severe liver impairment.
- Who are receiving monoamine oxidase inhibitor treatment, or within 14 days of its termination.
- Who are pregnant, since safety has not been established. It is also not recommended in lactation.
- Who are sensitive to other antihistamines due to the possibility of cross-sensitivity.
- Who suffer from severe hyperthyroidism, since the phenylephrine hydrochloride in **SINU-FLU** may induce tachycardia or reflex bradycardia.

WARNINGS:

In the event of overdosage or suspected overdose and notwithstanding the fact that the person may be asymptomatic, the nearest doctor, hospital or poison centre must be contacted immediately.

Paracetamol administration in excess of the recommended dosage may cause severe liver damage.

1. Consult a doctor if pain or fever persists or gets worse, if new symptoms occur or if redness or swelling is present, as these could be signs of a serious condition.

   Do not use this product continuously without consulting a doctor:

   - For pain – for more than 10 days.
   - For fever – for more than 3 days.

2. **In the event of overdosage or suspected overdosage, prompt medical attention is critical for adults and children, even if there are no obvious signs or symptoms. The nearest doctor, hospital or poisons control centre must be contacted immediately.**

   Dosages in excess of those recommended may cause severe liver damage. A doctor should be consulted if no relief is obtained from the recommended dosage. Patients who suffer from hepatitis or alcoholism, or who are recovering from liver disease, should not take paracetamol and therefore

also not **SINU-FLU**. To avoid accidental overdosage, **SINU-FLU** should be stored in a safe place, out of reach of children.

3. Use with caution in renal disease.
4. This medicine may lead to **drowsiness and impaired concentration**, which may be aggravated by simultaneous intake of alcohol or other central nervous system depressants, e.g., sedatives and tranquillisers. Caution should be used when driving a motor vehicle or operating machinery or performing potentially dangerous tasks, where loss of concentration may lead to accidents.
5. Caution should be used when the following medical conditions exist: prostatic hypertrophy, narrow angle glaucoma, emphysema or chronic bronchitis, porphyria, and severe ischaemic heart disease.
6. Paradoxical hyperexcitability, nervousness and insomnia may occur in children and the elderly taking antihistamines. Elderly patients are especially susceptible to dizziness, sedation, confusion, hypotension, and to anticholinergic effects, such as dry mouth and urinary retention.

INTERACTIONS:

Phenylephrine hydrochloride:

SINU-FLU tablets may reverse the action of antihypertensive agents and special care is therefore advised in patients receiving antihypertensive therapy. Interactions with alpha- and beta-blocking agents may be complex. Interactions

are also possible with guanethidine, reserpine, tricyclic antidepressants, digoxin and alpha-methyldopa.

Mepyramine maleate:

All sedatives, including alcohol, will potentiate the depressant effects of antihistamines on the central nervous system.

Antihistamines, and therefore **SINU-FLU** tablets, may also potentiate the effects of medications tending to cause extrapyramidal reactions and those with anticholinergic effects. These include tricyclic antidepressants, maprotiline and monoamine oxidase inhibitors.

Antihistamines, and therefore **SINU-FLU** tablets, may suppress positive skin test results and should be stopped several days before the test.

PREGNANCY AND LACTATION:

SINU-FLU tablets are contra-indicated during pregnancy and lactation (see **"CONTRA-INDICATIONS"**).

DOSAGE AND DIRECTIONS FOR USE:

Adults and children over 12 years:

The usual dose is two tablets every 6 hours while symptoms persist, not to exceed four doses in 24 hours.

Children 9 to 12 years:

The usual dose is one tablet every 6 hours while symptoms persist, to a maximum of four doses per 24 hours, for not longer than 5 days.

SIDE-EFFECTS AND SPECIAL PRECAUTIONS:

SIDE-EFFECTS:

Paracetamol:

Blood and lymphatic system disorders:

Less frequent: Agranulocytosis, anaemia and thrombocytopenia.

The following side-effects have been reported and frequencies are unknown:

Leucopenia, pancytopenia, and neutropenia have been reported.

Immune system disorders:

Less frequent: Allergic dermatitis.

The following side-effects have been reported and frequencies are unknown:

Pancreatitis, skin rashes and other allergic reactions may occur. The rash is usually erythematous or urticarial, but sometimes more serious and accompanied by fever and mucosal lesions.

Hepatobiliary system disorders:

Less frequent: Hepatitis.

Skin and subcutaneous tissue disorders:

Less frequent: Dermatitis.

Renal and urinary system disorders:

Less frequent: Renal colic, renal failure and sterile pyuria have occurred.

Phenylephrine hydrochloride:

Metabolism and nutrition disorders:

The following side-effects have been reported and frequencies are unknown:

Altered metabolism, including disturbances of glucose metabolism, and sweating have been reported.

Neuropsychiatric system disorders:

The following side-effects have been reported and frequencies are unknown:

Fear, anxiety, restlessness, tremor, insomnia, confusion, irritability, weakness and psychotic states have been reported. Headache is also common.

Ear and labyrinth disorders:

The following side-effects have been reported and frequencies are unknown:

Tinnitus.

Cardiovascular system disorders:

The following side-effects have been reported and frequencies are unknown:

Vasoconstriction with resultant hypertension has been reported. The rise in blood pressure may produce cerebral haemorrhage and pulmonary oedema. There may also be a reflex bradycardia, but stimulation of β_1-adrenergic receptors of the heart may produce tachycardia and cardiac arrhythmias, anginal pain, palpitations and cardiac arrest. Hypotension with dizziness and fainting and flushing may occur.

Respiratory system disorders:

The following side-effects have been reported and frequencies are unknown:

Dyspnoea.

Gastrointestinal system disorders:

The following side-effects have been reported and frequencies are unknown:

Appetite may be reduced and nausea and vomiting may occur. Hypersalivation has been reported.

Renal and urinary system disorders:

The following side-effects have been reported and frequencies are unknown:

Difficulty in micturition and urinary retention have been reported.

Mepyramine maleate:

Blood and lymphatic system disorders:

The following side-effects have been reported and frequencies are unknown:

Blood dyscrasias, including agranulocytosis, leucopenia, haemolytic anaemia, and thrombocytopenia, have been reported.

Neuropsychiatric system disorders:

The following side-effects have been reported and frequencies are unknown:

Sedation, drowsiness, nervousness, fatigue, dizziness, tremors, incoordination, insomnia, confusion, hallucinations, convulsions, and headache have been reported. Extrapyramidal

effects with muscle spasms and dystonia may also occur. Anticholinergic effects include ataxia, flushing, blurred vision, dryness of the mouth and nose, thickening of mucus, urinary retention or frequency, dysuria, and reduction in tone and motility of the gastrointestinal tract, resulting in constipation and increased gastric reflux.

Cardiovascular system disorders:

The following side-effects have been reported and frequencies are unknown:

Hypotension, tachycardia.

Gastrointestinal system disorders:

The following side-effects have been reported and frequencies are unknown:

Gastrointestinal disturbances, such as nausea, vomiting, diarrhoea or epigastric pain have occurred with antihistamines.

Skin and subcutaneous tissue disorders:

The following side-effects have been reported and frequencies are unknown:

Photosensitivity and skin rash, allergic dermatitis.

General disorders:

The following side-effects have been reported and frequencies are unknown:

Drug fever.

Special Precautions:

Phenylephrine hydrochloride, and therefore **SINU-FLU** tablets, should be used with caution in patients with:

- Hyperthyroidism (see **"CONTRA-INDICATIONS"**).
- Cardiovascular disease, such as ischaemic heart disease, arrhythmias or tachycardia.
- Occlusive vascular disorders, including arteriosclerosis, hypertension or aneurisms.
- Diabetes mellitus.
- Closed-angle glaucoma.

Phenylephrine hydrochloride may precipitate anginal pains in patients with angina pectoris.

Phenylephrine hydrochloride, and therefore **SINU-FLU** tablets, should be avoided or used with caution in patients undergoing anaesthesia with cyclopropane, halothane or other halogenated anaesthetics as ventricular fibrillation may be induced.

An increased risk of arrhythmias may occur if phenylephrine hydrochloride (and therefore **SINU-FLU** tablets) is administered to patients receiving cardiac glycosides, quinidine or tricyclic antidepressants.

Antihistamines, and therefore **SINU-FLU** tablets, should be used with care in patients with pyloroduodenal obstruction, epilepsy and severe cardiovascular disorders.

Effects on the ability to drive and use machines:

SINU-FLU tablets may cause drowsiness. Patients should be advised not to drive or operate machines in the event of feeling sleepy or tired.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

Paracetamol:

Prompt treatment is essential. In the event of an overdosage, consult a doctor immediately, or take the person to a hospital immediately. A delay in starting treatment may mean that antidote is given too late to be effective. Evidence of liver damage is often delayed until after the time for effective treatment has lapsed.

Susceptibility to paracetamol toxicity is increased in patients who have taken repeated high doses (greater than 5 – 10 g/day) of paracetamol for several days, in chronic alcoholism, chronic liver disease, AIDS, malnutrition, and with the use of medicines that induce liver microsomal oxidation, such as barbiturates, isoniazid, rifampicin, phenytoin and carbamazepine.

Symptoms of paracetamol overdosage in the first 24 hours include pallor, nausea, vomiting, anorexia and possibly abdominal pain. Mild symptoms during the first two days of acute poisoning do not reflect the potential seriousness of the overdosage.

Liver damage may become apparent 12 to 48 hours, or later, after ingestion, initially by elevation of the serum transaminase and lactic dehydrogenase levels, increased serum bilirubin concentration and prolongation of the prothrombin time. Liver damage may lead to encephalopathy, coma and death.

Acute renal failure with acute tubular necrosis may develop even in the absence of severe liver damage. Abnormalities of glucose metabolism and metabolic acidosis may occur. Cardiac arrhythmias have been reported.

Treatment for paracetamol overdosage:

Any adult person who has had about 7.5 grams of paracetamol (or a child who has had more than 140 mg/kg within the preceding four hours) should have the

stomach emptied by lavage (emesis may be adequate for children) and should receive a single dose of 50 g activated charcoal via the lavage tube.

N-acetylcysteine should be administered to all cases of suspected overdose as soon as possible, but preferably within eight hours of overdosage. However, treatment up to 36 hours after ingestion may still be of benefit, especially if more than 150 mg/kg of paracetamol was taken.

An initial dose of 150 mg/kg N-acetylcysteine in 200 ml glucose injection given **intravenously** over 15 minutes, should be followed by an infusion of 50 mg/kg in 500 ml glucose injection over the next four hours, and then by 100 mg/kg in 1000 ml glucose injection over the next sixteen hours. The volume of intravenous fluid should be modified for children.

Orally (not the treatment of choice): 140 mg/kg as a 5 % solution initially, followed by 70 mg/kg every four hours for seventeen doses. N-acetylcysteine is more likely to be effective if administered within 8 hours of overdosage.

A plasma paracetamol level should be determined four hours after ingestion in all cases of suspected overdosage. Levels done before four hours, unless high, may be misleading. Patients at risk of liver damage, and hence requiring continued treatment with N-acetylcysteine, can be identified according to their plasma paracetamol level.

If N-acetylcysteine is not available, methionine 2.5 g may be given immediately, followed by 2.5 g every four hours for three doses. Patients should, however, preferably be transferred to a facility where N-acetylcysteine can be given.

Monitor all patients with significant ingestions for at least ninety six hours.

Mepyramine maleate:

Central excitatory effects constitute the greatest danger in overdose. Symptoms include drowsiness or paradoxical excitement, hallucinations, ataxia, incoordination, athetosis, convulsions, fixed dilated pupils with a flushed face, sinus tachycardia, dyspnoea and urinary retention, dry mouth and fever. Terminally deepening coma and cardiorespiratory collapse may develop. Children and the elderly are more likely to exhibit anticholinergic as well as central nervous system stimulant effects. The elderly are prone to hypotension.

The stomach should be emptied by emesis or lavage. There is no specific antidote and treatment is symptomatic and supportive. It may be necessary to treat extrapyramidal reactions with barbiturates or diphenhydramine.

IDENTIFICATION:

Pink and white mottled, biconvex tablet.

PRESENTATION:

20 tablets in a white, plastic securitainer with a white plastic lid.

STORAGE INSTRUCTIONS:

Store at or below 25 °C.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:

C739 (Act 101/1965)

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

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