SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

SNIP 325mg/15mg/1mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each SNIP 325mg/15mg/1mg tablet contains 325 mg of paracetamol, 15 mg of pseudoephedrine hydrochloride and 1 mg of chlorphenamine maleate.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

White, round, flat, scored tablets embossed SNIP.
The score line is not intended for breaking the tablet.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

SNIP is indicated for:
Relief of symptoms associated with cold and flu, such as:

- Cough
- Nasal congestion
- Rhinitis
- Sneeze
- Fever
- Light to severe pain of different origin

Additional, for alleviating symptoms of hay fever and other allergies of upper respiratory tract associated with fever.

4.2 Posology and method of administration

Posology

Adults

1-2 tablets every 4-6 hours as needed up to maximum 12 tablets per day.

Adolescents (over 12 years old):

1-2 tablets every 6 hours as needed up to maximum 8 tablets per day

Paediatric population

For children 6 to 11 years old

1 tablet every 4 to 6 hours, not to exceed 6 tablets per day. For children between 6 to 8 years old the maximum recommended dose is 5 tablets per day.

Children under 6 years old:

As with any antihistamine-containing product, use of Snip tablets in children under 6 years of age should be only under the advice and supervision of a physician.

Renal/hepatic impairment

Consideration should be given to a reduced total daily dosage in patients with hepatic or renal impairment.

Elderly

There is evidence of prolonged half life in the elderly, so reduction in dosage should be considered.

Method of administration

For oral use.

4.3 Contraindications

- Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.
- Severe hypertension or uncontrolled hypertension.
- Severe acute or chronic kidney disease/renal failure.
- Snip is contraindicated in individuals who are taking or have taken monoaminoxidase inhibitors within the preceding two weeks.
- Patients with severe heart, kidney and liver diseases, diabetes, glaucoma, high blood pressure, bronchial asthma should not use this medicine.

- The concomitant use of pseudoephedrine and SNIP may occasionally cause a rise in blood pressure, so it should be avoided.

4.4 Special warnings and precautions for use

Ischaemic colitis

Some cases of ischaemic colitis have been reported with pseudoephedrine. Pseudoephedrine should be discontinued and medical advice sought if sudden abdominal pain, rectal bleeding or other symptoms of ischaemic colitis develop.

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.

Severe Skin reactions

Severe skin reactions such as acute generalized exanthematous pustulosis (AGEP) may occur with pseudoephedrine-containing products. This acute pustular eruption may occur within the first 2 days of treatment, with fever, and numerous, small, mostly non-follicular pustules arising on a widespread oedematous erythema and mainly localized on the skin folds, trunk, and upper extremities. Patients should be carefully monitored. If signs and symptoms such as pyrexia, erythema, or many small pustules are observed, administration of Snip should be discontinued and appropriate measures taken if needed.

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.

Risks of abuse

Pseudoephedrine carries the risk of abuse. Increased doses may ultimately produce toxicity. Continuous use can lead to tolerance resulting in an increased risk of overdosing. The recommended maximum dose and treatment duration should not be exceeded (see section 4.2).

Other warnings and precautions

Patients should be advised not to exceed the recommended dose and to avoid alcohol.
Individuals that have glaucoma, high blood pressure, heart disease, thyroid disease, diabetes, prostate hypertrophy, bladder neck obstruction, stenosing peptic ulcer, emphysema or chronic bronchitis, epilepsy or thyrotoxicosis should ask for medical advice before taking this medicine.
In addition, a doctor should be consulted in case of concurrent administration with sedatives or tranquilizers, muscle relaxants, antidepressants or other CNS depressant drugs; patients should be advised of the additive depressant effects of these combinations.
Excitability may occur due to chlorpheniramine, especially in children.

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.

Chlorpheniramine may cause drowsiness, dizziness, blurred vision and psychomotor impairment, which can seriously hamper the patients' ability to drive and operate machinery.

Anginal pain may be precipitated in angina pectoris.

SNIP should not be taken with any other paracetamol-containing products.
SNIP should not be taken with any other flu, cold or decongestant products.

Patients should be advised to consult their doctor if their cold or flu symptoms persist.
Overdosage may damage the liver, due predominantly to the accumulation of intermediate metabolites of paracetamol which cause hepatic necrosis. Immediate medical advice should be sought in the event of an overdose, even if the patient feels well, because of the risk of delayed,

serious liver damage. Compared to the general population, the hazards of overdose are greater in those with non-cirrhotic alcoholic liver disease.
SNIP should be administered with caution to patients with hepatic or renal impairment since higher serum concentrations or delayed elimination may occur.

4.5 Interaction with other medicinal products and other forms of interaction

Drug interactions:
Absorption of paracetamol is increased by drugs, which increase gastric emptying e.g. metoclopramide and domperidone and decreased by drugs, which decrease gastric emptying e.g. tricyclic antidepressants, narcotic analgesics. The likelihood of paracetamol toxicity may be increased by the concomitant use of enzyme inducing agents such as alcohol and anticonvulsants.
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 Snip with increased risk of bleeding; occasional doses have no significant effect.
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).
Anticonvulsants (including phenytoin, barbiturates, carbamazepine) that induce hepatic microsomal enzymes may increase paracetamol-induced liver toxicity because of increased conversion of the drug to hepatotoxic metabolites. The patients are at risk especially in case of concomitant ingestion of anticonvulsant with larger than recommended doses of paracetamol. Rate and extent of absorption of orally administered paracetamol may be reduced by concomitant administration of caffeine, propantheline, methoclopramide, and cholestiramine.
Concomitant use of Snip tablets with tricyclic antidepressants, sympathomimetic agents (such as decongestants, appetite suppressants and amphetamine-like psychostimulants) or with monoaminoxidase inhibitors (MAOI's) (or within two weeks of stopping MAOI's), which interferes with catabolism of sympathomimetic amines, 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, Snip tablets may partially reverse the hypotensive action of drugs, which interfere with sympathetic activity including bretylium bethanidine, guanethidine, debrisoquine, methyldopa, alpha and beta-adrenergic blocking agents.
Alcohol may reduce the capacity of the liver to metabolise paracetamol.

Chronic use of paracetamol enhanced the effects of anticoagulants.
Concurrent use of paracetamol with NSAIDs may increase the risk of adverse renal effects. The prolonged combined use of these compounds may increase the risk of renal damage.

Drug-lab modifications:
Chlorphenamine may interfere with the interpretation of the pulmonary function tests after a methacholine bronchial challenge test. Although the mechanism is not totally clear, it is presumed that chlorphenamine changes the responsiveness of the airway to methacholine therefore, if possible, Snip tablets should be discontinued for 48 hours prior to a methacholine challenge test.

4.6 Fertility, pregnancy and lactation

Pregnancy
Safety in pregnancy has not been established relative to possible adverse effects on foetal development. Withdrawal symptoms in neonates have been reported following use during pregnancy. Therefore, SNIP tablets should not be used in pregnant women unless, in the judgement of the physician, the potential benefits outweigh the possible hazards.

Breast-feeding
Nursing mothers: Paracetamol is excreted in breast milk but not in a clinically significant amount. Available published data do not contraindicate breast feeding. It has been estimated that 0.5-0.7% of a single dose of pseudoephedrine ingested by a mother will be excreted in breast milk over 24 hours.
The physician should decide either the mother to stop breastfeeding or to cease the administration of the product, considering its necessity for the mother.

4.7 Effects on ability to drive and use machines

SNIP tablets may cause drowsiness and impaired performance in tests of auditory vigilance. Patients should not drive a vehicle or operate machinery until they have determined their own response.

4.8 Undesirable effects

The frequencies of the adverse reactions are defined as follows: Very common (≥11/10); Common (≥11/100 to <1/10); Uncommon (≥11/1,000 to <1/100); Rare (≥11/10,000 to <1/1,000); Very rare (<1/10,000); Not known (cannot be estimated from the available data).

Adverse effects of Snip are rare but a variety of allergic cutaneous reactions, with or without systemic features, have been reported.

Blood and lymphatic system disorders

Very rare: There have been very rare reports of blood dyscrasias including thrombocytopenia and agranulocytosis but these were not necessarily causality related to Snip.

Psychiatric disorders

Rare: Hallucinations have been reported rarely.

Not known: nervousness

Nervous system disorders

Not known: dizziness, insomnia, agitation and restlessness have also been reported but these are usually mild, drowsiness.

- 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.

Cardiac disorders

Not known: tachycardia.

Vascular disorders

Not known: hypertension.

Gastrointestinal disorders

Not known: Ischaemic colitis, dry mouth.

Skin and subcutaneous tissue disorders

Rare: Hypersensitivity including skin rash, angioedema have also been reported rarely.

Very rare: Very rare cases of serious skin reactions have been reported.
Not known: Severe skin reactions, including acute generalized exanthematous pustulosis (AGEP).

Renal and urinary disorders
Not known: Urinary retention can occur in those patients with prostatic enlargement.

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 to:
The Medicines Authority,
Post-Licensing Directorate,
203 Level 3, Rue D'Argens, GŻR-1368 Gżira
website: www.medicinesauthority.gov.mt
e-mail: postlicensing.medicinesauthority@gov.mt

4.9 Overdose

The effects of acute toxicity from SNIP tablets may include drowsiness, lethargy, dizziness, ataxia, weakness, hypotonicity, respiratory depression, dryness of the skin and mucous membranes, tachycardia, hypertension, hyperpyrexia, hyperactivity, irritability, convulsions and difficulty with micturition.

PARACETAMOL
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, 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.
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. 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.

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.

CHLORPHENIRAMINE

Symptoms

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.

Management

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 without psycholeptics.

ACT code: N02BE51

The product possesses analgesic, antipyretic, antihistamine and reducing the edema of the mucosa of the upper respiratory tract effect, which is owed to the active substances.
Paracetamol is clinically proven analgesic and antipyretic. The analgesia is performed by increasing the pain threshold; the antipyretic effect is performed by influencing the centre of thermoregulation in the hypothalamus.
Pseudoephedrine has a direct and indirect sympathomimetic activity and is an orally effective upper respiratory tract decongestant. Pseudoephedrine is substantially less potent than ephedrine in producing both tachycardia and elevation in systolic blood pressure and considerably less potent in causing stimulation of the central nervous system.
Chlorphenamine is a propylamine derivative antihistamine of the alkylamine class. This agent specifically blocks the H1 receptor, which inhibits the action of histamine. Chlorphenamine blocks the effect histamine has on smooth muscle, including the gastrointestinal and respiratory tract, this agent prevents vasodilatation induced by histamine, and suppresses capillary permeability resulting in reduction of oedema or wheal formation.

5.2 Pharmacokinetic properties

Paracetamol is rapidly and almost completely absorbed from the GI tract following oral administration and for immediate- release paracetamol preparations, peak plasma concentrations are attained within 10–60 minutes. Plasma paracetamol concentrations of 2.1 mcg/mL, occur at 6 hours following administration of a single 500-mg conventional tablet. Paracetamol is rapidly distributed into the body and 25% is bound to plasma protein. Plasma half life of paracetamol is 1.5-3 hours and 80-85% of the dose undergoes glucurono- or sulfo-conjugation. Approximately 85% of a dose of paracetamol is excreted in urine as free and conjugated paracetamol within 24 hours after ingestion.

Pseudoephedrine is rapidly and completely absorbed after oral administration. After an oral dose of 180 mg to man, peak plasma concentrations of 500-900 ng/ml were obtained about 2 hours post dose. The plasma half life was approximately 5.5 hours and was increased in subjects with alkaline urine and decreased in subjects with acid urine. The only metabolism was n-demethylation which occurred to a small extent. Excretion was mainly via the urine.

In common with other antihistamines, chlorphenamine maleate is rapidly absorbed, peak plasma levels being observed 2 hours after an oral dose, metabolised in the liver and excreted, mainly as

metabolites in the urine, only 3-18% being excreted as unchanged drug. The plasma half life is approximately 20 hours. The elimination half life is decreased in elderly and in children.

5.3 Preclinical safety data

There are no preclinical data of relevance to the prescriber in addition to that summarised in other sections of the Summary of Product Characteristics.
Conventional studies using the currently accepted standards for the evaluation of toxicity to reproduction and development are not available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline cellulose 101
Microcrystalline cellulose 105
Croscarmellose sodium
Powdered cellulose
Magnesium stearate

Pregelatinized starch
Corn starch
PVP K-30
Stearic Acid
Sodium Starch Glycolate

6.2 Incompatibilities

Not applicable.

6.3 Shelf-life

5 years.

6.4 Special precautions for storage

Store below 25ºC, in the original packaging in order to be protected from light and moisture.

6.5 Nature and contents of container

PVC/Alu blisters of 10 tablets. Each carton box contains 10, 20 or 30 tablets and a patient information leaflet.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements for disposal.

7. MARKETING AUTHORISATION HOLDER

MEDOCHEMIE LTD, 1-10 Constantinoupoleos street, 3011 Limassol, Cyprus

8. MARKETING AUTHORISATION NUMBER(S)

MA032/06401

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 22/03/2007

10. DATE OF REVISION OF THE TEXT

07/2024