SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Corilief® Sinus and Allergy Relief

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Corilief Sinus Pain and Allergy Relief tablets contain Chlorpheniramine Maleate 2mg, 30mg Pseudoephedrine Hydrochloride and 500mg Paracetamol

3 PHARMACEUTICAL FORM

Tablets

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Corilief Sinus Pain and Allergy Relief is indicated for the symptomatic relief of conditions where congestion of the mucous membranes of the upper respiratory tract, especially nasal mucosa and sinuses, is accompanied by mild to moderate pain or pyrexia, e.g.: the common cold and influenza, sinusitis, nasopharyngitis, allergic rhinitis and vasomotor rhinitis.

4.2 Posology and method of administration

Adults and children aged 12 years and over: Oral. Two tablets every four to six hours, up to four times a day. Maximum daily dose: 8 tablets (i.e. 240 mg pseudoephedrine hydrochloride, 4 g paracetamol).

Not recommended for children under 12 years.

Elderly: There have been no specific studies of Corilief Sinus Pain and Allergy Relief in the elderly. Experience has indicated that normal adult dosage is appropriate. In the elderly the rate and extent of paracetamol absorption is normal but plasma half life is longer and paracetamol clearance is lower than in young adults. Hepatic dysfunction: Caution should be exercised when administering Corilief Sinus Pain and Allergy Relief to patients with severe hepatic impairment. Renal dysfunction: Caution should be exercised when administering Corilief Sinus Pain and Allergy Relief to patients with moderate to severe renal impairment. Do not exceed the stated

dose. Keep out of the reach and sight of children.

4.3 Contraindications

Corilief Sinus Pain and Allergy Relief is contraindicated in individuals with known hypersensitivity to the product or any of its components. Contraindicated in children under 6 months of age. Paracetamol should not be used in patients with severe liver and renal disease. Pseudoephedrine sould be avoided in patients undergoing inhalation anaesthesia. Not to be given concurrently with monoamine oxidase inhibitors (MAOI) for depression of or within 14 days of stopping such treatment. Contra-indicated in most types of cardiovascular disease including angina and hypertension, and also in hyperthyroidism, phaeochromocytoma, closed angle glaucoma and diabetes mellitus.

4.4 Special warnings and precautions for use

Although pseudoephedrine has virtually no pressor effects in normotensive patients, Corilief Sinus Pain and Allergy Relief should be used with caution in patients suffering from mild to moderate hypertension. As with other sympathomimetic agents Corilief Sinus Pain and Allergy Relief should be used with caution in patients with hypertension, heart disease, diabetes, hyperthyroidism, elevated intraocular pressure and prostatic enlargement. Care is advised in the administration of paracetamol to patients with severe renal or severe hepatic impairment. The hazards of overdose are greater in those with alcoholic liver disease. The following statements will appear on packs of this product. Do not store above 30ºC. Store in the original packaging. Warning: Do not exceed the recommended dose. Keep out of the reach and sight of children. If symptoms persist consult your doctor. Contains paracetamol. Causes no drowsiness. ‘Immediate medical advice should be sought in the event of an overdose, even if you feel well. (label). Immediate medical advice should be sought in the event of an overdose, even if you feel well, because of the risk of delayed, serious liver damage.’ (leaflet) Do not take with any other paracetamol-containing products.’ As with all medicines, if you are pregnant or currently taking any other medicine, consult your doctor or pharmacist before taking this product.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant use of Corilief Sinus Pain and Allergy Relief with tricyclic antidepressants, sympathomimetic agents (such as decongestants, appetite suppressants and amphetamine-like psychostimulants) or with monoamine oxidase inhibitors, which interferes with the catabolism of

sympathomimetic amines, may occasionally cause a rise in blood pressure, [See Contra-indications]. Because of the pseudoephedrine content, Corilief Sinus Pain and Allergy Relief may partially reverse the hypotensive action of drugs which interfere with sympathetic activity including bretylium, betanidine, guanethedine, debrisoquine, methyldopa, alpha- and beta-adrenergic blocking agents, [See Special Warnings and Special Precautions for Use]. Patients who have taken barbiturates, tricyclic antidepressants and alcohol may show diminished ability to metabolise large doses of paracetamol, the plasma half-life of which can be prolonged. Alcohol can increase the hepatotoxicity of paracetamol overdose and may have contributed to the acute pancreatitis reported in one patient who had taken an overdose of paracetamol. Chronic ingestion of anticonvulsants or oral steroid contraceptives induce liver enzymes and may prevent attainment of therapeutic paracetamol levels by increasing first pass metabolism or clearance. The speed of absorption of paracetamol may be increased by metoclopramide or domperidone and absorption reduced by colestyramine. The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular use of paracetamol with increased risk of bleeding; occasional doses have no significant effect.

4.6 Pregnancy and lactation

Pseudoephedrine. Although pseudoephedrine has been in widespread use for many years without apparent ill consequence, there are no specific data on its use during pregnancy. Caution should therefore be exercised by balancing the potential benefit of treatment to the mother against any possible hazards to the developing foetus. Systemic administration of pseudoephedrine, up to 50 times the human daily dosage in rats and up to 35 times the human daily dosage in rabbits, did not produce teratogenic effects. Pseudoephedrine is excreted in breast milk in small amounts but the effect of this on breast-fed infants is not known. It has been estimated that 0.5 to 0.7% of a single dose of pseudoephedrine ingested by a mother will be excreted in the breast milk over 24 hours. No studies have been conducted in animals to determine whether pseudoephedrine has the potential to impair fertility. There is no information of the effect of Corilief Sinus Pain and Allergy Relief on fertility. Paracetamol epidemiological studies in human pregnancy have shown no ill effects due to paracetamol used in the recommended dosage but patients should follow the advice of their doctor regarding its use. Paracetamol is excreted in breast milk but not in a clinically significant amount. Available published data do not contraindicate breast feeding.

4.7 Effects on ability to drive and use machines

None known

4.8 Undesirable effects

Pseudoephedrine Serious side effects associated with the use of pseudoephedrine are rare. Symptoms of central nervous system excitation may occur, including sleep disturbance and, rarely, hallucinations. Skin rashes, with or without irritation, have occasionally been reported with pseudoephedrine. Urinary retention has been reported occasionally in men receiving pseudoephedrine: prostatic enlargement could have been an important predisposing factor. Paracetamol has been widely used and, when taken at the usual recommended dosage, side effects are mild and infrequent and reports of adverse reactions are rare. Skin rash and other allergic reactions occur rarely. Most reports of adverse reactions to paracetamol relate to overdose with the drug. There have been reports of blood dyscrasias including thrombocytopenia and agranulocytosis, but these were not necessarily causality related to paracetamol. Chronic hepatic necrosis has been reported in a patient who took daily therapeutic dosages of paracetamol for about a year and liver damage has been reported after daily ingestion of excessive amounts for shorter periods. A review of a group of patients with chronic active hepatitis failed to reveal differences in the abnormalities of liver function in those who were long-term users of paracetamol nor was the control of their disease improved after paracetamol withdrawal. Nephrotoxic effects following therapeutic dosages of paracetamol are uncommon. Papillary necrosis has been reported after prolonged administration.

4.9 Overdose

Pseudoephedrine As with other sympathomimetic agents, symptoms and signs of pseudoephedrine overdosage include irritability, restlessness, tremor, convulsions, palpitations, hypertension and difficulty with micturition Measures should be taken to maintain and support respiration and control convulsions. Gastric lavage should be performed if indicated. Catheterisation of the bladder may be necessary. If desired, the elimination of pseudoephedrine can be accelerated by acid diuresis or by dialysis. 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, phenobarbital, 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 overdosage 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, haemorrhage, hypoglycaemia, cerebral oedema, coma and death. 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. Cardiac arrhythmias and pancreatitis have been reported. 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. Treatment with activated charcoal should be considered if the overdose has been taken within 1 hour. Plasma paracetamol concentration should be measured at 4 hours or later after ingestion (earlier concentrations are unreliable). Treatment with N-acetylcysteine may be used up to 24 hours after ingestion of paracetamol, however, the maximum protective effect is obtained up to 8 hours post-ingestion. The effectiveness of the antidote declines sharply after this time. If required the patient should be given intravenous N-acetylcysteine, in line with the established dosage schedule. If vomiting is not a problem, oral methionine may be a suitable alternative for remote areas, outside hospital.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pseudoephedrine

Pseudoephedrine has direct and indirect sympathomimetic activity and is an effective upper respiratory tract decongestant. Pseudoephedrine is substantially less potent than ephedrine in producing both tachycardia and elevation of systolic blood pressure and considerably less potent in causing stimulation of the central nervous system.

Paracetamol

Paracetamol has analgesic and antipyretic actions but only weak anti-inflammatory properties. This may be explained by presence of cellular peroxides at sites of inflammation which prevent inhibition of cyclooxygenase by paracetamol. At other sites associated with low levels of cellular perioxides, e.g. pain, fever, paracetamol can successfully inhibit prostaglandin biosynthesis.

Chlorpheniramine

Chlorphenamine is a potent antihistamine (H_1-antagonist).

Antihistamines diminish or abolish the actions of histamine in the body by competitive reversible blockade of histamine H_1-receptor sites on tissues. Chlorphenamine also has anticholinergic activity.

Antihistamines act to prevent the release of histamine, prostaglandins and leukotrienes and have been shown to prevent the migration of inflammatory mediators. The actions of chlorphenamine include inhibition of histamine on smooth muscle, capillary permeability and hence reduction of oedema and wheal in hypersensitivity reactions such as allergy and anaphylaxis.

5.2 Pharmacokinetic properties

Pseudoephedrine is partly metabolised in the liver by N-demethylation to norpseudoephedrine, an active metabolite. Pseudoephedrine and its metabolite are excreted in the urine: 55% to 75% of a dose is excreted unchanged. The rate of urinary excretion of pseudoephedrine is accelerated when the urine is acidified. Conversely as the urine pH increases, the rate of urinary excretion is slowed. Paracetamol Peak plasma paracetamol concentration usually occurs between 30 and 90 minutes after oral ingestion. Paracetamol is distributed uniformly throughout most body fluids and is only 15 to 25 per cent bound to plasma proteins. The plasma half-life of paracetamol after therapeutic doses is in the range of 1 to 3 hours. Chlorphenamine is well absorbed from the gastro-intestinal tract, following oral administration. The effects develop within 30 minutes, are maximal within 1 to 2 hours and last 4 to 6 hours. The plasma half-life has been estimated to be 12 to 15 hours. Chlorphenamine is metabolised to the monodesmethyl and didesmethyl derivatives. About 22% of an oral dose is excreted unchanged in the urine.

5.3 Preclinical safety data

The active ingredients of Corilief Sinus Pain and Allergy Relief are well known constituents of medicinal products and their safety profile is well documented. The results of pre-clinical studies do not add anything of relevance for therapeutic purposes.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Pregelatinised Maize Starch, Crospovidone, Povidone PVP K30, Croscarmellose Sodium, Sunset Yellow, Microcrystalline Cellulose, Stearic Acid and Magnesium Stearate

6.2 Incompatibilities

None known

6.3 Shelf life

2 years

6.4 Special precautions for storage

Do not store above 30ºC. Keep out of the reach of children

6.5 Nature and contents of container

PVC/Aluminium foil blister packs of 20s

20s in Polypropylene container with LPE container

7 PRINCIPAL AND MANUFACTURER

7. Applicant and Principal

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9. Registration number(s)

TBA

10. Category of Distribution

Pharmacy Only

11. Pharmacological Classification

R01BA52 – Nasal Preparations – Pseudoephedrine Combinations

12. Date of publication

September 2020