SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the Medicinal Product

SILAPEN NIGHT SYRUP (Paracetamol and Diphenhydramine Syrup)

2. Qualitative and Quantitative Composition

Each 5 mL contains

Paracetamol BP	125 mg
Diphenhydramine Hydrochloride BP	7 mg

3. Pharmaceutical Form

Oral Suspension

4. Clinical Particulars

4.1 Therapeutic Indications

For the treatment of mild to moderate pain in infants and children, including teething pain, headache, sore throat, aches and pains and for the symptomatic relief of influenza, feverishness and feverish colds. Controls excessive mucous secretion and eases nasal irritation. Also helps restful sleep

4.2 Posology and Method of Administration

For Oral Administration

Dosage:

3 months – under 1 year: 2.5 mL to 5 mL three to four times daily

1 year – under 6 years: 5 mL – 10 mL three to four times daily

6 years – 12 years: 10 mL – 20 mL three times daily

4.3 Contraindications

Hypersensitivity to Paracetamol, Diphenhydramine Hydrochloride or to any of the constituents of the formulation. Large doses of antihistamines may precipitate seizures in epileptics.

Silapen is contraindicated in individuals with chronic or persistent cough such as that which occurs with asthma or where cough is accompanied by excessive secretions unless directed by a doctor

Silapen should not be administered to patients currently receiving monoamine oxidase inhibitors (MAOIs) or those patients who have received treatment with MAOIs within last two weeks

4.4 Special Warnings and Precautions for use

Do not give this medication to babies under 3 months unless under the direction of a doctor. Do not give with any other paracetamol-containing products. Dose should not be repeated more frequently than four hour intervals. Not more than 4 doses should be taken in 24 hours. Dosage should not be continued for more than three days without consulting a doctor. 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 (non-cirrhotic) alcoholic liver disease. Patients with moderate to severe renal or hepatic dysfunction or urinary retention should exercise caution when using this product. Immediate medical advice should be sought in the event of overdose, even if the child seems well, because of the risk of delayed serious liver disease. Diphenhydramine should not be taken by patients with narrow-angle glaucoma or symptomatic prostatic hypertrophy unless directed by a doctor. Alcohol or other potential sedating medicines should not be used concurrently with Silapen. Patients with rare hereditary problems of fructose intolerance should not take this medicine. Children should be supervised while on this medication. Do not exceed the recommended dose. If symptoms persist consult your doctor. Keep out of the reach and sight of children.

Special label warnings Do not give with any other paracetamol-containing products. Immediate medical advice should be sought in the event of an overdose, even if the child seems well.

Special leaflet warnings Immediate medical advice should be sought in the event of an overdose, even if the child seems well, because of the risk of delayed, serious liver damage. If you have been told by your doctor that your child has an intolerance to some sugars, contact your doctor before giving this medicinal product.

4.5 Interactions with other medicinal products and other forms of interactions

The speed of absorption of paracetamol may be increased by metoclopramide or domperidone and absorption reduced by colestyramine. The anti-coagulant 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. Chronic alcohol intake 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. Acute alcohol intake may diminish an individual's ability to metabolise large doses of paracetamol, the plasma half-life of which can be prolonged. The use of drugs that induce hepatic microsomal enzymes, such as anticonvulsants and oral contraceptives, may increase the extent of metabolism of paracetamol, resulting in reduced plasma concentrations of the drug and a faster elimination rate. Diphenhydramine may potentiate the effect of alcohol, codeine, antihistamines and other CNS depressants. The effects of anticholinergics e.g. some psychotropic drugs and atropine may be potentiated by diphenhydramine giving rise to tachycardia, mouth dryness, gastrointestinal disturbances e.g. colic, urinary retention and headache.

4.6 Fertility, Pregnancy and Lactation

Safety in pregnancy has not been established. Pregnant or lactating patients should not take this medication unless it is considered essential by a doctor. 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. Diphenhydramine hydrochloride crosses the placenta and is excreted in breast milk.

4.7 Effects on ability to drive and use machines

May cause drowsiness, dizziness or blurred vision. If affected do not drive or operate machinery. Avoid alcoholic drink.

4.8 Undesirable Effects

Adverse effects of paracetamol are rare, but hypersensitivity including skin rash may occur. There have been reports of blood dyscrasias including thrombocytopenia and agranulocytosis, but these were not necessarily causally related to paracetamol. Most reports of adverse

Silapen is contraindicated in individuals with chronic or persistent cough such as that which reported in a patient who took daily therapeutic doses 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 the disease improved after paracetamol withdrawal. Nephrotoxicity following therapeutic doses of paracetamol is uncommon, but papillary necrosis has been reported after prolonged administration. Diphenhydramine may cause drowsiness, dizziness, gastrointestinal disturbance, dry mouth, nose and throat, difficulty in urination or blurred vision. Less frequently it may cause palpitations, tremor, convulsions or paraesthesiae. Hypersensitivity reactions to diphenhydramine have been reported, in particular, skin rashes, erythema, urticaria and angiodema.

4.9 Overdose

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.

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 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, 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. Symptoms of diphenhydramine overdose include drowsiness, hyperpyrexia and anticholinergic effects. In children, CNS excitation, including hallucinations and convulsions may appear; with larger doses, coma or cardiovascular collapse may follow.

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. Management of patients who present with serious hepatic dysfunction beyond 24h from ingestion should be discussed with a liver unit.

5. Pharmacological Properties

5.1 Pharmacodynamic Properties

Paracetamol (ATC Code: NO2B E01) is an antipyretic analgesic with a mechanism of action that is not fully elucidated. Diphenhydramine hydrochloride (ATC Code: RO6A A02) is an antihistamine with anticholinergic, anti-emetic, anti-allergic and sedative effects.

5.2 Pharmacokinetics

Paracetamol and diphenhydramine hydrochloride are both readily absorbed from the gastrointestinal tract. Both are widely distributed throughout the body, metabolised in the liver and excreted in the urine. As Silapen is an oral solution, the active ingredients are absorbed rapidly following ingestion.

5.3 Pre-Clinical Safety Data

Paracetamol and Diphenhydramine Hydrochloride are well established drug substances whose pre-clinical profiles have been investigated and are thoroughly established.

6 Pharmaceutical Particulars

6.1 List of Excipients

Sucrose BP

Sodium Methylparaben BP

Sodium Propylparaben BP

Product Name: SILAPEN NIGHT SYRUP (Paracetamol and Diphenhydramine Syrup)

Sorbitol Solution 70% BP

Croscarmellose Sodium BP

Polysorbate BP

Colloidal Anhydrous Silica BP

Citric Acid Monohydrate BP

Flavoring Agent

Purified Water BP

6.2 Incompatibilities

Not Applicable

6.3 Shelf Life

36 months from the Date of Manufacture

6.4 Special precautions for Storage

Store below 30°C. Store reconstituted suspension in a refrigerator

6.4 Nature and contents of Container

100 mL bottle packed in a monocarton along with Pack Insert

6.5 Special precautions for disposal

7 Marketing Authorization Holder

Richygold International Ltd.(Pharmaceutical formulations)
103c Amuwo-Odofin Industrial Scheme Oshodi Apapa Express Way, Lagos
Nigeria
.

8 Marketing Authorisation Numbers

NA

Product Name: SILAPEN NIGHT SYRUP (Paracetamol and Diphenhydramine Syrup)