NALIS® PARACETAMOL SYRUP

(Paracetamol 125 mg/5 ml)

SUBMITTED BY: NALIS PHARMACEUTICALS LTD

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SUMMARY OF PRODUCT CHARACTERISTICS

(SmPC).

1 NAME OF THE MEDICINAL PRODUCT:

Nalis Paracetamol Syrup

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

A red-coloured syrup.
Each 5 ml contains:
Paracetamol BP……**125 mg**
Excipients……qs

3. PHARMACEUTICAL FORM

Oral Syrup

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Nalis® Paracetamol syrup, a para-aminophenol derivative has analgesic and antipyretic properties and weak anti-inflammatory activity. It is used in the management of mild to moderate pain and may also be used as an adjunct to opioids in the management of severe pain such as cancer pain. It's the pr**eferred choice for pain in children because of its** association of aspirin with Reye's syndrome in this age-**group.**

4.2 Posology and method of administration

For oral administration.

Dosage:

3 months to 1 year	**- ½ teaspoonful (2.5ml) – 1 teaspoonful (5ml)**
1 to 5 years	**- 1 teaspoonful (5ml) – 2 teaspoonfuls (10ml)**
6 to 12 years	**- 2 teaspoonfuls (10ml) – 4 teaspoonfuls (20ml)**

These doses are to be given every 4 to 6 hours, if necessary, up to a maximum of 4 doses in 24 hours.

4.3 Contraindications

Nalis® Paracetamol syrup is usually contraindicated in patients having impaired kidney or liver function, caloric undernutrition, patients in shock, and patients having acute inflammation of the liver due Hepatitis C virus.

4.4 Special warnings and precautions for use

Paracetamol should be given with care to patients with impaired kidney or liver function. It is recommended that large doses should be avoided in patients with hepatic impairments. It should also be given with care to patients with alcohol dependence.

4.5 Interaction with other medicinal products

The risk of paracetamol toxicity may be increased in patients receiving other potentially hepatotoxic drugs or drugs that induce liver microsomal enzymes. The absorption of paracetamol may be accelerated by drugs such as metoclopramide. Excretion may be affected and plasma concentrations altered when given with probenecid. Colestyramine reduces the absorption of paracetamol if given within 1 hour of paracetamol. The plasma paracetamol concentrations should be halved in patients receiving enzyme-inducing drugs such as rifampicin.

4.6 Pregnancy and lactation

Paracetamol is generally considered to be analgesic of choice in pregnant patients. However, the frequent use of paracetamol (daily use) in third trimester may be associated with an increased risk of persistent wheezing in the infant which may persist into childhood. Infrequent intake of paracetamol should remain the analgesic of choice in pregnancy.

4.7 Effects on ability to drive and use machines

None

4.8 Undesirable effects

Side effects of Nalis® Paracetamol syrup are rare and usually mild, although haematological reactions including neutropenia and agranulocytosis have been reported. Skin rashes and other hypersensitivity reactions occur occasionally.

4.9 Overdose

Paracetamol overdose may cause liver failure which can lead to liver transplant or death. Acute pancreatitis has been observed, usually with hepatic dysfunction and liver toxicity. There is a risk of poisoning with paracetamol particularly in elderly subjects, young children, patients with liver disease, cases of chronic alcoholism and in patients with chronic malnutrition. Overdosing may be fatal in these cases. 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 in a single administration in adults or children can cause liver cells 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 adults who have taken more than the recommended amounts of paracetamol. It is considered that excess quantities of toxic metabolite (usually adequately detoxified by glutathione when normal doses of paracetamol are ingested), become irreversibly bound to liver tissue. Some patients may be at increased risk of liver damage from paracetamol toxicity.

Risk Factors include: If the patient;
- **Is on long-term treatment with carbamazepine, phenobarbitone, phenytoin, primidone, rifampicin, St John's Wort**
- **or other drugs that induce liver enzymes.**
- **Regularly consumes ethanol in excess of recommended amounts**
- **Is likely to be glutathione depleted e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia**

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 >150mg/kg paracetamol has been taken within 1 hour. The antidote N-acetylcysteine, should be administered as soon as possible in accordance with National treatment guidelines Symptomatic treatment should be implemented.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Paracetamol has analgesic and antipyretic actions based on the inhibition of prostaglandin biosynthesis. It has no other significant pharmacodynamic properties.

5.2 Pharmacokinetic properties

Paracetamol is readily absorbed from the gastrointestinal tract and peak plasma concentrations occur about 10 to 60 minutes after oral doses. Paracetamol is distributed into most body tissues. It crosses the placenta and is present in breast milk. Plasma-protein binding is negligible at usual therapeutic concentrations but increases with increasing concentrations. The elimination half-life of paracetamol varies from about 1 to 3 hours.
Paracetamol is metabolized mainly in the liver and excreted in the urine mainly as the glucuronide and sulphate conjugates. Less than 5% is excreted as unchanged paracetamol. A minor hydroxylated metabolite is usually produced in very small amounts to cytochrome P450 isoenzymes (mainly CYP2E1 and CYP3A4) in the liver and kidney. It is usually detoxified by conjugation with glutathione but may accumulate after paracetamol overdosage and cause tissue damage.

5.3 Preclinical safety data

Mutagenicity
The results of a range of tests suggest that neither diphenhydramine or menthol have mutagenic potential.

Carcinogenicity
There is insufficient information to determine the carcinogenic potential of diphenhydramine or menthol, although such effects have not been associated with these drugs in animal studies.

Teratogenicity
The results of a number of studies suggest that the administration of either diphenhydramine or menthol does not produce any statistically significant teratogenic effects in rats, rabbits and mice.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium CMC, Propylene Glycol, Methyl Paraben, Propyl Paraben, Glycerine, Xanthan Gum, Sugar, Strawberry Flavour, Carmoisine Red, Treated Water

6.2 Incompatibilities
None stated except as in 'Interactions with other medicaments'.

6.3 Shelf life
36 months

6.4 Special precautions for storage
Do not store above 30°C.
Keep away from light

6.5 Nature and contents of container

60ml Pet bottles with ROPP caps.
100 by 60ml in a carton.

6.6 Special precautions for disposal and other handling
None

7. APPLICANT/HOLDER OF CERTIFICATE OF PRODUCT REGISTRATION

Nalis Pharmaceuticals Ltd

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8. DRUG PRODUCT MANUFACTURER

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9. NAFDAC REGISTRATION NUMBER(S)

A11-0842