Professional Prescribing Information

SCHEDULING STATUS

S2

1. NAME OF THE MEDICINE

PAINAGON® SYRUP

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

PAINAGON® SYRUP

Each 5 ml of syrup contains:

Paracetamol	120, 0 mg
Codeine Phosphate	5, 0 mg
Promethazine	6, 5 mg

Preservative:

Methyl hydroxybenzoate	0, 10 % *m/v*.
Propyl hydroxybenzoate	0, 01 % *m/v*.
Alcohol	12,5 % *v/v*

Contains sugar:

Sucrose 1,825 g/ 5ml

Liquid glucose 2 g/ 5ml

Invert syrup 600 mg/ 5 ml

Contains sweeteners:

Saccharin sodium 1,5 mg/ 5ml

Sodium cyclamate 30 mg/ 5 ml

For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Syrup

Mauve to maroon-coloured clear syrup with a distinctive flavour of blackcurrant.

4. CLINICAL PARTICULARS

4.1 Therapeutic indication

For the relief of mild to moderate pain, associated with fever.

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4.2 Posology and Method of Administration

Posology:

2 To 5 years: One medicine measureful (5 ml) three times a day.

6 To 12 years: One to two medicine measuresful(s)

(5 to 10 ml) three times a day.

DO NOT EXCEED THE RECOMMENDED DOSES.

If symptoms persist consult your doctor

Method of Administration

For oral use

4.3 Contraindications

PAINAGON® SYRUP is contraindicated in:

- Hypersensitivity to **PAINAGON® SYRUP** or to any of the ingredients.listed in section 6.1
- Patients sensitive to one antihistamine may be sensitive to others.
- Patients with severe liver or kidney complications.
- Patients with obstructive airway disease, respiratory depression, especially in the presence of cyanosis and excessive bronchial secretion, and after operations on the

biliary tract. · .

- Acute alcoholism.
- Convulsive disorders.
- Head injuries and conditions in which intracranial pressure Is raised.
- Children under the age of two years.
- Pregnancy and lactation.
- Patients taking monoamine oxidase inhibitors or within 14 days of stopping such treatment

PAINAGON® SYRUP should not be given during an attack of bronchial asthma or in heart disease secondary to chronic lung disease.

Promethazine and codeine phosphate, as contained in **PAINAGON® SYRUP** should not be given to comatosed· patients.

4.4 Special warnings and precautions for use

- If the patient does not respond, a doctor should be consulted.
- Do not use continuously without consulting a doctor.

  - For pain: - for more than 10 days (adults).
  - for more than 5 days (children).
  - For fever: - for more than 3 days.
- This medicine may cause drowsiness and impaired (reduced) concentration, which may be increased by the simultaneous intake of alcohol or other central nervous system depressant (slowing down of the nervous system activity) agents. Patients should be warned against performing potentially hazardous activities/duties where loss of concentration may lead to accidents.
- Pigments should be examined periodically for abnormal skin pigmentation (discolourisation) or eye changes.
- Contra-indicated in patients receiving monoamine oxidase inhibitors

- Dosage in excess of those recommended may cause severe liver damage.
- Exceeding the prescribed dose, together with prolonged and continuous use of this medication, may lead to dependency and addiction

Paracetamol

PAINAGON® SYRUP contains paracetamol which may be. fatal in overdosage or suspected overdosage and not wlthstandlng the the fact that the person may be asymptomatic the nearest doctor, hospital or Poison Centre must be contacted immedlately.

- Dosages in excess of those recommended, may cause severe liver function damage.
- Patients suffering from hepatitis or alcoholism, or recovering from any form of liver disease should not take paracetamol. ·
- Use with caution in renal disease.
- Severe cutaneous adverse reactions (SCARs):

  Severe cutaneous adverse reactions (SCARs) such as toxic epidermal necrolysis (TEN), Steven-Johnson syndrome (SJS), acute generalized exanthematous pustulosis (AGEP), eosinophilia and systemic (DRESS)/Drug-induced hypersensitivity syndrome (DIHS) and fixed drug eruptions (FDE) have been reported in patients treated with paracetamol containing medicines. If a patient develops SCAR, treatment with **PAINAGON SYRUP** must immediately be discontinued and appropriate treatment instituted
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Codeine:

- Should be used with caution or in reduced doses in patients with adrenocortical insufficiency (failure of a part of the adrenal gland to produce adequate steroid hormones).
- Should be used with caution in patients with obstructive bowel disorders. Dosage should be reduced in debilitated (tired/weakened/run down) patients.

- Should be used with caution or reduced doses in patients with hypothyroidism (underactive thyroid gland).
- Should be used with caution in patients with liver impairment (decreased activity of the liver), myasthenia gravis (muscle disorder causing weakness), impaired renal function (decreased activity of the kidney) or shock

Promethazine:

- Should be used with caution in cardiovascular (heart and blood vessels) disease.
- Should be used with caution in patients with glaucoma (raised pressure in the eye).
- Should be used with caution in liver impairment (decreased function of the liver).
- Should be used with caution in patients with urinary retention. The positive results of a skin allergy test may be suppressed.

PAINAGON ® SYRUP contains sucrose.

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrose –isomaltase insufficiency should not take/be given **PAINAGON ® SYRUP.**

PAINAGON ® SYRUP contains liquid glucose

Patients with rare glucose-galactose malabsorption should not take this medicine

PAINAGON ® SYRUP contains invert syrup

Patients with rare hereditary problems of fructose intolerance or glucose-galactose malabsorption should not take this medicine

PAINAGON ® SYRUP contains propylene glycol.

Co-administration with any substrate for alcohol dehydrogenase such as ethanol may induce adverse effects in children less than 5 years old

While propylene glycol has not been shown to cause reproductive or development toxicity in animals or humans, it may reach the foetus and was found in milk. As a consequence, administration of propylene glycol to pregnant or lactating patients should be considered on a case to case basis

Medical monitoring is required in patients with impaired renal or hepatic functions because various adverse events attributed to propylene glycol have been reported such as renal dysfunction (acute tubular necrosis), acute renal failure and liver dysfunction

4.5 Interaction with other medicines and other forms of Interaction

The anticholinergic (to stop the passage of certain nerve impulses involving acetyl choline) effects of agents with anticholinergic (stop the passage of certain nerve impulses involving acetyl choline) properties may be enhanced. The depressant effects are aggravated by alcohol, anaesthetics (causes loss of sensation or pain, consciousness), hypnotics (causes sleep), sedatives (relaxation/calming effect), tricyclic antidepressants and phenothiazines. Monoamine oxidase inhibitors may enhance the anticholinergic (to stop the passage of certain nerve impulses involving acetyl choline) effects. The warning signs of damage caused by ototoxic agents (agents having toxic effects on the nerve of the ear) may be masked. May effect the activity of other medicines by delaying their absorption

4.6 Fertility, pregnancy and lactation

PAINAGON® SYRUP is contraindicated in pregnancy and lactation (see section 4.3)

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:

Patients should be advised, particularly at the initiation of therapy, against taking charge of vehicles or machinery or performing potentially hazardous tasks where loss of concentration could lead to accidents.

4.8 Undesirable effects

Paracetamol

System Organ Class	Frequency	Adverse reaction
Blood and lymphatic system disorders	Frequency unknown	Neutropenia,pancytopenia, leukopenia, thrombocytopenia, agranulocytosis, anaemia
Immune system disorder	Frequency unknown	Sensitivity (allergic) reactions resulting in skin rashes or blood disorders
Psychiatric disorders	Frequent	Confusion and hallucination,central effect includes euphoria.
Nervous system disorders	Frequent	Sedation varying from slight drowsiness to deep sleep including dizziness and incordination, Paradoxical CNS stimulation, occasional headaches
Ear and labyrinth Disorders	Frequency Unknown	Tinnitus
Vascular disorders	Frequency unknown	Hypotension,
Gastrointestinal	Frequent	Gastro-intestinal disturbances,

Disorders		nausea,vomiting diarrhoea or constipation,anorexia or increased appetite,epigastric pain,
Hepatobilary disorders	Frequency unknown	Hepatitis
Skin and subcutaneous tissue disorders	Frequency unknown	Dermatitis Risk of fixed drug eruptions anddrug-induced hypersensitivity syndrome
Musculoskeletal ,connective tissue and bone disorder	Frequency unknown	Muscle weakness
Renal and urinary disorders	Frequency unknown	Irreversible kidney damage with prolong excessive use,renal colic, renal failure,sterile pyuria
General disorders and administrative site conditions	Frequent	Lassitute

Promethaine Hydrochloride

System Organ Class	**Frequency**	**Adverse reaction**
Blood and lymphatic system disorders	Frequency unknown	agranulocytosis, leukopenia hemolytic anaemia

Nervous System Disorders	Frequency unknown	Epileptiform seizures with focal lesions of the cerebral cortex Extrapyrimadal symptoms with muscle spasms and dystonia
Eye Disorders	Frequency unknown	blurred vision
Cardiac disorders		In high doses,transient bradycardia followed by tachycardia with palpitations
Vascular disorders	Frequency unknown	flushing
Respiratory, thoracic and mediastinal disorders	Frequency unknown	Thickened respiratory tract secretion,dryness of the nose,tightness of the chest
Gastrointestinal Disorders	Frequency unknown	Dryness of the mouth and reduction in tone and motility of the gastrointestinal tract resulting in constipation and increased gastric reflux,
Hepatobilary disorders	Frequency unknown	Jaundice
Skin and subcutaneous tissue disorders	Frequency unknown	Photosensitivity, skin rashes,allergic dermatitis and thrombocytopaenic purpura
Renal and urinary disorders	Frequency unknown	Difficulty in micturition and dysuria

General disorders and administrative site conditions	Frequency unknown	Medicine fever

Codeine Phosphate

System Organ Class	**Frequency**	**Adverse reaction**
Psychiatric Disorders	Frequent	Confusion
	Frequency unknown	Abuse,restlessness,change in mood
Nervous System Disorders	Frequent	Drowsiness
	Frequency unknown	Raised intracrainial pressure
Eye Disorders	Frequency unknown	Miosis
Ear and Labyrinth disorder	Frequency unknown	Vertigo
Cardiac disorders		Bradycardia, palpitations
Vascular disorders	Frequency unknown	Facial flushing, orthostatic hypotension
Gastrointestinal Disorders	Frequentt	Nausea, vomiting, constipation

	Less frequent	Acute pancreatitis, increase risk of abdominal pain
	Frequency unknown	Dry mouth
Hepatobilary disorders	Frequency unknown	Biliary spasm, antidiuretic effect
Skin and subcutaneous tissue disorders	Frequency unknown	Urticaria, pruritus,contact dermatitis
Musculoskeletal connective tissue and bone disorder	Frequency unknown	Muscle rigidity
Renal and urinary disorders	Frequent	Micturition,uretic spasm,antidiuretic effect in ambulant and patients at rest in bed
General disorders and administrative site conditions	Frequent	Sweating
	Frequency unknown	Hypothermia

Post-marketing experience

Risk of fixed drug eruptions and drug-induced hypersensitivity syndrome associated with the use of paracetamol containing medicines

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions to SAHPRA via the **"6.04 Adverse Drug Reaction"**

Reporting Form", found online under SAHPRA's publications:

https://www.sahpra.org.za/Publications/Index/

4.9 Overdose

Paracetamol:

Prompt treatment is essential. In the event of an overdosage, consult a doctor immediately, or take the person directly to a hospital. 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 medicine 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.

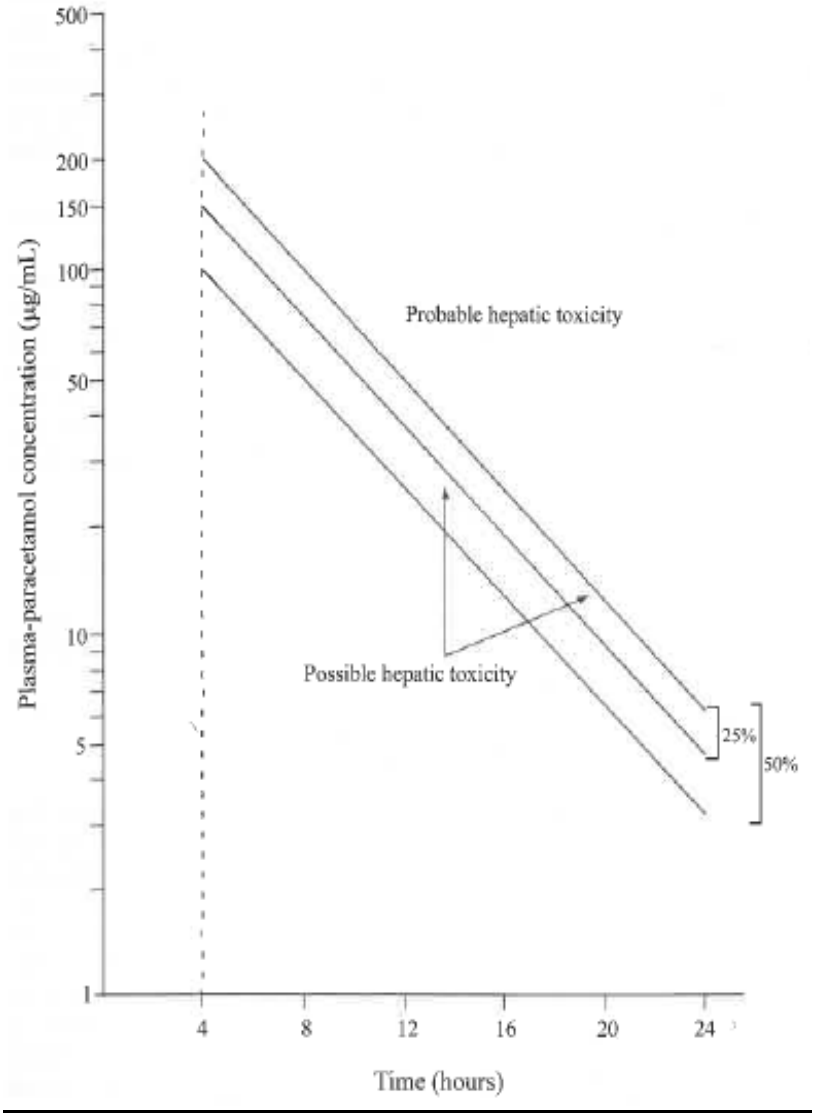
Liver damage may become apparent 12 to 48 hours, or later after ingestion, initially by elevation of the serum transaminase and lactic dehydrogenase activity, increased serum bilirubin concentration and prolongation of the prothrombin lime. Liver damage may lead to encephalopathy, coma and death.

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:

Although evidence is limited it is recommended that any adult person who has ingested 5 – 10 grams or more of paracetamol (or a chiId 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 a single dose of 50 g activated charcoal given via the lavage tube. Ingestion of amounts of paracetamol smaller than this may require treatment in patients susceptible to paracetamol poisoning. In patients who are stuperose or comatose endotracheal intubation should precede gastic lavage in order to avoid aspiration.

N-acetylcysteine should be administered to all cases of suspected overdose as soon as possible preferably within eight hours of overdosage, although treatment up to 36 hours after ingestion may still be of benefit, especially if more than 150 mg/kg of paracetamoI was taken. An initial dose of 150 mg/kg N-acetylcysteine in 200 ml dextrose injection given **intravenously** over 15 minutes, followed by an infusion of 50 mg/kg in 500 ml dextrose injection over the next four hours, and then 100 mg/kg in 1 000 ml dextrose injection over the next sixteen hours. **The volume of intravenous fluid should be modified for children.**



Those whose plasma paracetamol levels are above the “normal treatment line”, should continue N-acetylcysteine treatment with 100 mg/kg IV over sixteen hours repeated until recovery. Patients with increased susceptibility lo liver damage as identified above, should continue treatment if concentrations are above the "high risk treatment line”. Prothrombin index correlates best with survival.

Monitor all· patients with significant Ingestions for at least ninety-six hours.

Overdosage with promethazine causes a central excitatory effect which constitutes its greatest danger. Symptoms include drowsiness or paradoxical excitement, hallucinations,

ataxia, incoordination, athetosls and convulsions.

Fixed dilated pupils with a flushed face, sinus tachycardia, dyspnoea, urinary retention, dry mouth and fever can occur. Other symptoms Include a terminally, deepening coma with cardiorespiratory collapse. Children and the elderly are more likely to exhibit anticholinergic and central nervous system stimulant effects. The.eldertv 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

Respiratory depression Is the most important feature of **overdosage with codeine** containing preparations and it occurs with circulatory failure and a deepening coma.

Pinpoint" pupils, hypotention and hypothermia, excitement and convulslons; especially in children, and non-cardiogenic pulmonary oedema occur. Immediate attention should be given to maintaining adequate respiration:

Death may occur from respiratory failure. Naloxone should be given intravenously in a dose of 0,4 mg to 2 mg every 2 to 3 minutes until improvement occurs to a maximum of 10 mg. Children may be given 0,01 mg/kg initially followed by a dose of

0, 1 mg/kg.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties:

Pharmacotherapeutic group: A .2.8 Analgesic combination

Painagon syrup has analgesic (relief of pain), antipyretic (reduces fever) and antihistaminic (prevention or relief of symptoms associated with some types of allergies such as hayfever and runny nose) properties

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Other ingredients are

- Black currant colour LS 1904/18
- Citric acid anhydrous
- Essence of black currant No.1
- Ethanol 96 % *v/v*
- Invert syrup
- Liquid glucose
- Menthyl hydroxybenzoate
- Propyl hydroxybenzoate
- Propylene glycol
- Purified water
- Rasberry red H1227(Cl 14720)
- Saccharin sodium
- Sodium cyclamate
- Sucrose
- Vanilla flavour No.1

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 Months

6.4 Special precautions for storage

Store in a cool place at or below 25 ^{0}C.

Protect from light

6.5 Nature and contents of container

Amber PVC bottles containing 100 ml and 500 ml of syrup.

Amber glass bottles containing 100 ml of syrup.

H.D.P.E containers, containing 2,5 litre syrup.

6.6 Special precautions for disposal and other handling

None

7. HOLDER OF CERTIFICATE OF REGISTRATION

Ranbaxy Pharmaceuticals (Pty) Ltd

14 Lautre Road

Stormill Ext. 1

Roodepoort

1724

South Africa

8. REGISTRATION NUMBER(S)

S/2.8/29 (S.A

B9314915 Botswana)

NS1 90/2.8/00375 (Namibia) (100 ml, 500 ml, 2,5 L)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

28 February 1990

10.DATE OF REVISON OF THE TEXT

25 August 2023