SCHEDULING STATUS

S0

1. NAME OF THE MEDICINE

GO PAIN ASPIRIN 300 mg tablets.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 300 mg aspirin.

Sugar free.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets.

A plain, white, round, convex tablet.

4. Clinical particulars

4.1 Therapeutic indications

GO PAIN ASPIRIN is indicated for the short-term use in the relief of mild to moderate pain and fever.

4.2 Posology and method of administration

Posology

Use the lowest effective dose for the shortest possible duration of treatment.

Adults and children 12 years and over:

300 – 1 000 mg as a single dose, to be repeated as needed after a minimum period of 4 hours.

A maximum daily dose of 4 000 mg must not be exceeded.

GO PAIN ASPIRIN must not be taken for more than 3 – 5 days without consulting a doctor. Excessive and prolonged use of this medicine may be dangerous.

Special populations

GO PAIN ASPIRIN should be used with caution in patients with abnormal hepatic or renal function (see section 4.4).

Paediatric population

GO PAIN ASPIRIN is recommended for children below 12 years only under doctor's supervision. In general, the daily dose of GO PAIN ASPIRIN in children is about 60 mg/kg, given as 4 to 6 divided doses, i.e., about 15 mg/kg every 6 hours or 10 mg/kg every 4 hours. In case of accidental administration or use in children, see section 4.4.

Method of administration

For oral use.

The tablets should preferably be taken after meals, with plenty of water.

4.3 Contraindications

GO PAIN ASPIRIN is contraindicated in:

- patients who are allergic (hypersensitive) to acetylsalicylic acid (aspirin) or other salicylates, or to the excipient in GO PAIN ASPIRIN (see section 6.1),
- patients with a history of asthma induced by the administration of aspirin (salicylates) or substances with a similar action, including non-steroidal anti-inflammatory drugs (NSAIDs),
- patients with a history of gastrointestinal perforation, ulceration, or bleeding (PUBs) related to previous use of NSAIDs, including GO PAIN ASPIRIN,
- patients with active or a history of recurrent ulcer / haemorrhage / perforations,
- acute gastrointestinal ulcers,
- haemorrhagic diathesis,
- haemophilia,
- patients taking anti-coagulants,
- severe liver failure,
- severe kidney damage,
- heart failure,
- combination with methotrexate at doses of 15 mg/week or more,
- last trimester of pregnancy (see section 4.6).

4.4 Special warnings and precautions for use

DO NOT USE CONTINUOUSLY FOR MORE THAN 3 – 5 DAYS WITHOUT CONSULTING A DOCTOR.

GO PAIN ASPIRIN should be administered with caution in the following cases:

- hypersensitivity to analgesics / anti-inflammatory medicines / anti-rheumatics and in the presence of other allergies,
- patients with impaired renal function or patients with impaired cardiovascular circulation (e.g., renal vascular disease, volume depletion, major surgery, sepsis, or major haemorrhagic events), since acetylsalicylic acid may further increase the risk of renal impairment and acute renal failure,
- in the presence of severe liver disease,
- impaired hepatic function,
- in patients with a history of gastrointestinal ulcers or a history of gastrointestinal bleeding,
- dyspepsia,
- anaemia,
- when the patient is dehydrated.

GO PAIN ASPIRIN may precipitate bronchospasm and induce asthma attacks or other hypersensitivity reactions. Risk factors are pre-existing asthma, hay fever, nasal polyps, or chronic respiratory disease. This also applies to patients exhibiting allergic reactions (e.g., cutaneous reactions, itching, urticaria) to other substances.

GO PAIN ASPIRIN should be withdrawn 1 week before surgery.

Due to its inhibitory effect on platelet aggregation which persists for several days after administration, GO PAIN ASPIRIN may lead to an increased bleeding tendency during and after surgical operations (including minor surgeries, e.g., dental extractions).

At low doses, GO PAIN ASPIRIN reduces the excretion of uric acid. This can possibly trigger gout attacks in predisposed patients.

Caution is required in patients with a history of hypertension and / or heart failure as fluid retention and oedema have been reported in association with GO PAIN ASPIRIN therapy.
In view of the medicine's inherent potential to cause fluid retention, heart failure may be precipitated in some compromised patients.

Elderly: The elderly have an increased frequency of adverse reactions to NSAIDs, including GO PAIN ASPIRIN, especially gastrointestinal perforation, ulceration and bleeding (PUBs) which may be fatal.

The risk of gastrointestinal perforation, ulceration, or bleeding (PUBs) is higher with increasing doses of GO PAIN ASPIRIN in patients with a history of ulcers, and the elderly.

Regular use of NSAIDs such as GO PAIN ASPIRIN during the third trimester of pregnancy, may result in premature closure of the foetal ductus arteriosus *in*

utero, and possibly, in persistent pulmonary hypertension of the new-born. The onset of labour may be delayed, and its duration increased.

When gastrointestinal bleeding or ulceration occurs in patients receiving GO PAIN ASPIRIN, treatment with GO PAIN ASPIRIN should be stopped.

GO PAIN ASPIRIN should be given with caution to patients with a history of gastrointestinal disease (e.g., ulcerative colitis, Crohn's disease, hiatus hernia, gastro-oesophageal reflux disease, angiodysplasia) as the condition may be exacerbated.

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis have been reported. GO PAIN ASPIRIN should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

In patients suffering from severe glucose-6-phosphatedehydrogenase (GP6PD) deficiency, GO PAIN ASPIRIN may induce haemolysis or haemolytic anaemia. Factors that may increase the risk of haemolysis are high dosage, fever, or acute infections.

Hypokalaemia and renal tubular acidosis: Severe hypokalaemia and renal tubular acidosis have been reported due to prolonged use of NSAIDs, as in GO PAIN ASPIRIN at higher than recommended doses. This risk is increased with the use of codeine/ aspirin as patients may become dependent on the codeine component.

Presenting signs and symptoms included reduced level of consciousness and generalised weakness. Aspirin-induced renal tubular acidosis should be considered in patients with unexplained hypokalaemia and metabolic acidosis.

Paediatric population

GO PAIN ASPIRIN should not be used in children and adolescents for viral infections with or without fever without consulting a doctor. In certain viral illnesses, especially influenza A, influenza B and varicella, there is a risk of Reye's syndrome, a very rare but possibly life-threatening illness requiring immediate medical action. The risk may be increased when GO PAIN ASPIRIN is given concomitantly. Should persistent vomiting occur with such diseases, this may be a sign of Reye's syndrome.

4.5 Interaction with other medicines and other forms of interaction

Contraindicated interactions:

Methotrexate used at doses of 15 mg/week or more (see section 4.3):

Increased haematological toxicity of methotrexate; decreased renal clearance of methotrexate by anti-inflammatory medicines in general and displacement of methotrexate from its plasma protein binding by salicylates.

Combinations requiring precautions for use:

Methotrexate used at doses of less than 15 mg/week:

Increased haematological toxicity of methotrexate (decreased renal clearance of methotrexate by anti-inflammatory medicines in general and displacement of methotrexate from its plasma protein binding by salicylates).

NSAIDs:

The use of two or more NSAIDs concomitantly could result in an increase in side effects. Other NSAIDs with salicylates increases the risk of ulcers and gastrointestinal bleeding due to a synergistic effect.

Corticosteroids:

Increased risk of gastrointestinal ulceration or bleeding (PUBs).

Systemic glucocorticoids, except hydrocortisone, used as replacement therapy in Addison's disease:

Decreased blood salicylate levels during corticosteroid treatment and risk of salicylate, after this treatment is stopped, via increased elimination of salicylates by corticosteroids.

Anticoagulants:

GO PAIN ASPIRIN may enhance the effects of anticoagulants such as warfarin.

Anti-platelet medicines and selective serotonin reuptake inhibitors (SSRIs):

Increased risk of gastrointestinal bleeding.

Digoxin:

Plasma concentrations of digoxin are increased due to a decrease in renal excretion.

Antidiabetic medicines, e.g., oral antidiabetic preparations, insulin, sulphonylurea: Increased hypoglycaemic effect by high doses of GO PAIN ASPIRIN via hypoglycaemic action of GO PAIN ASPIRIN and displacement of sulphonylurea from its plasma protein binding sites.

Diuretics in combination with GO PAIN ASPIRIN:

Decreased glomerular filtration via decreased renal prostaglandin synthesis.

Angiotensin converting enzyme inhibitors (ACEI) in combination with GO PAIN ASPIRIN:

Decreased glomerular filtration via inhibition of vasodilatory prostaglandins. Furthermore, decreased antihypertensive effect.

Valproic acid:

Increased toxicity of valproic acid due to displacement from protein binding sites.

Alcohol:

Increased damage to gastro-intestinal mucosa and prolonged bleeding time due to additive effects of GO PAIN ASPIRIN and alcohol.

Uricosurics such as benzbromarone, probenecid, sulphinpyrazone:

Decreased uricosuric effect of antigout preparations (competition of renal tubular uric acid elimination).

Sulphonamides:

GO PAIN ASPIRIN may enhance the activity of sulphonamides.

Sedatives:

Barbiturates and other sedatives may mask the respiratory symptoms of GO PAIN ASPIRIN overdosage and have been reported to enhance its toxicity.

4.6 Fertility, pregnancy and lactation

Pregnancy

Safety in pregnancy has not been established.

Inhibition of prostaglandin synthesis may adversely affect the pregnancy and / or the embryo / foetal development. Data from epidemiological studies raise concern about an increased risk of miscarriage and of malformations after the use of a prostaglandin synthesis inhibitor in early pregnancy. The risk is believed to increase with dose and duration of therapy.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the foetus to:

- cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension)
- renal dysfunction, which may progress to renal failure with oligo-hydroamniosis.

Prostaglandin synthesis inhibitors may expose both the mother and the child at the end of pregnancy to:

- possible prolongation of bleeding time / increased INR, an anti-aggregating effect which may occur even after very low doses.
- inhibition of uterine contractions resulting in delayed or prolonged labour.

Consequently, GO PAIN ASPIRIN is contraindicated during the third trimester of pregnancy (see section 4.3).

Lactation

Safety and efficacy during lactation have not been established.

GO PAIN ASPIRIN and its metabolites pass into breast milk in small quantities.

Fertility

Based on the limited published data available, the studies in humans showed no consistent effect of GO PAIN ASPIRIN on impairment of fertility and there is no conclusive evidence from animal studies.

4.7 Effects on ability to drive and use machines

People who experience dizziness should refrain from driving or operating machinery.

4.8 Undesirable effects

The following side-effects may occur and the frequency of occurrence is unknown (cannot be established from the available data):

System organ class	Side effect
Blood and lymphatic system disorders	Blood dyscrasias. Haemorrhage may result in haemorrhagic anaemia / iron-deficiency anaemia (due to e.g., occult microbleeding) with respective laboratory and clinical signs and symptoms, such as asthenia, pallor and hypoperfusion.
Immune system disorders	Hypersensitivity, allergic angioedema, allergic reaction, anaphylactic / anaphylactoid reaction, anaphylactoid / anaphylactic shock, rash and urticaria.
Metabolism and nutrition disorders	Hypokalaemia
Ear and labyrinth disorders	Dizziness and tinnitus have been reported, which may be indicative of an overdose.
Cardiac disorders	Oedema, hypertension and cardiac failure.
Vascular disorders	Oedema, hypertension.
Gastrointestinal disorders	The most commonly observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation or gastrointestinal bleeding, sometimes fatal. Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain.
Hepato-biliary disorders	Transient hepatic impairment with increase in liver transaminases.
Skin and subcutaneous tissue disorders	Bullous reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis.

Renal and urinary disorders	Renal impairment and acute kidney injury, renal papillary necrosis, renal tubular acidosis
General disorders and administration site conditions	Some persons, asthmatics, those with chronic urticaria or chronic rhinitis, may exhibit notable sensitivity to GO PAIN ASPIRIN which may provoke various hypersensitivity reactions which may include skin eruptions, urticaria, angioedema, paroxysmal bronchospasm and dyspnoea.
Investigations	GO PAIN ASPIRIN may produce falsely increased results for blood creatinine, urate (low dose aspirin) and urea. Falsely decreased results may be obtained for blood thyroxine and urate (> 4 g / day aspirin) and for urinary 5-HIAA (with nitrosonapthol method). Urinary VMA (HMMA) levels may be falsely increased or decreased depending on the method of analysis. Urinary glucose oxidase: GO PAIN ASPIRIN may cause a false negative test in the presence of glycosuria.

Description of Selected Adverse Reactions

Renal tubular acidosis and hypokalaemia have been reported in the post-marketing setting typically following prolonged use of the NSAID component at higher than recommended doses, usually due to dependence on the codeine component of a co-formulation.

Paediatric population

In certain viral illnesses, especially influenza A, influenza B and varicella, there is a risk of Reye's syndrome, a very rare but possibly life-threatening illness requiring immediate medical action. The risk may be increased when GO PAIN ASPIRIN is given concomitantly. Should persistent vomiting occur with such diseases, this may be a sign of Reye's syndrome.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of GO PAIN ASPIRIN is important. It allows continued monitoring of the benefit / risk balance of GO PAIN ASPIRIN. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA online:

https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose

IN THE EVENT OF OVERDOSAGE AND NOT WITHSTANDING THE FACT THAT THE PERSON MAY BE ASYMPTOMATIC, THE NEAREST DOCTOR, HOSPITAL OR POISON CONTROL CENTRE MUST BE CONTACTED IMMEDIATELY. DO NOT EXCEED THE RECOMMENDED DAILY DOSE.

Salicylate toxicity may result from chronic, therapeutically acquired intoxication, and from potentially life-threatening, acute intoxications (overdose), ranging from accidental ingestions in children to incidental intoxications.

Chronic salicylate intoxication

Chronic salicylate poisoning can be insidious as signs and symptoms are non-specific. Mild chronic salicylate intoxication, or salicylism, usually occurs only after repeated use of large doses.

Symptoms include dizziness, vertigo, tinnitus, deafness, sweating, nausea and vomiting, headache and mental confusion, and may be controlled by reducing the dosage. Tinnitus can occur at plasma concentrations of 150 to 300 micrograms/ml. More serious adverse events occur at concentrations above 300 micrograms/ml.

Prolonged use at higher than recommended doses may result in severe hypokalaemia and renal tubular acidosis. Symptoms may include reduced level of consciousness and generalised weakness (see section 4.4 and section 4.8).

Acute salicylate intoxication

The principal feature of acute intoxication is severe disturbance of the acid-base balance, which may vary with age and severity of intoxication. The most common presentation for a child is metabolic acidosis. In children serious signs of overdosage may develop rapidly.

The severity of poisoning cannot be estimated from plasma concentration alone. Absorption of acetylsalicylic acid can be delayed due to reduced gastric emptying, formation of concretions in the stomach, or as a result of ingestion of enteric-coated preparations.

Management of GO PAIN ASPIRIN intoxication is determined by its extent, stage and clinical symptoms and according to standard poisoning management techniques. Predominant measures should be the accelerated excretion of the medicine as well as the restoration of the electrolyte and acid-base metabolism.

Due to the complex pathophysiologic effects of salicylate poisoning, signs and symptoms / investigational findings may include:

Signs and Symptoms	**Investigational findings**	**Therapeutic measures**
Mild-to- moderate intoxication		Gastric lavage, repeated administration of activated charcoal, forced alkaline diuresis
Tachypnoea, hyperventilation, respiratory alkalosis	Alkalaemia, alkaluria	Fluid and electrolyte management
Diaphoresis		
Nausea, vomiting		
Moderate–to-severe intoxication		Gastric lavage, repeated administration of activated charcoal, forced alkaline diuresis, haemodialysis in severe cases
Respiratory alkalosis with compensatory metabolic acidosis	Acidaemia, aciduria	Fluid and electrolyte management

Hyperpyrexia, fever		Fluid and electrolyte management
Respiratory: ranging from hyperventilation, non-cardiogenic pulmonary oedema to respiratory arrest, hypoxia		
Cardiovascular: ranging from dysrhythmias, hypotension to cardiovascular arrest	e.g., Blood pressure, ECG alteration	
Fluid and electrolyte loss: dehydration, oliguria to renal failure	e.g., Hypokalaemia, hypernatraemia, hyponatraemia, altered renal function	Fluid and electrolyte management
Impaired glucose metabolism, ketosis	Hyperglycaemia, hypoglycaemia (especially in children), increased ketone levels	
Tinnitus, vertigo, deafness		
Gastrointestinal: GI bleeding		
Haematologic: ranging from platelet inhibition to coagulopathy	e.g., PT prolongation / increased INR, hypo-prothrombinaemia	
Neurologic: Headache,		

restlessness, toxic encephalopathy and CNS depression with manifestations ranging from lethargy, confusion to coma and seizures		

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 2.9 Other Analgesics

Pharmacotherapeutic group: Other analgesics and antipyretics

ATC code: N02BA01

Mechanism of action:

Acetylsalicylic acid (aspirin) has analgesic, antipyretic and anti-inflammatory actions.

Acetylsalicylic acid belongs to the group of acidic nonsteroidal anti-inflammatory drugs (NSAIDs) with analgesic, antipyretic and anti-inflammatory properties. Its mechanism of action is based on irreversible inhibition of cyclo-oxygenase enzymes involved in prostaglandin synthesis.

Acetylsalicylic acid inhibits platelet aggregation by blocking thromboxane A_2 synthesis in platelets.

5.2 Pharmacokinetic properties

Absorption

Following oral administration, acetylsalicylic acid is well and completely absorbed from the gastrointestinal tract. During and after absorption acetylsalicylic acid is converted into its main active metabolite, salicylic acid. Maximal plasma levels are reached after 18 – 30 minutes for acetylsalicylic acid and after 0,72 - 2 hours for salicylic acid, respectively.

Distribution

Both acetylsalicylic acid and salicylic acid are extensively bound to plasma proteins and are rapidly distributed throughout the body.
Salicylic acid passes into breast milk and crosses the placenta.

Metabolism

Acetylsalicylic acid is converted into its main metabolite salicylic acid. The acetyl group of acetylsalicylic acid begins to split off hydrolytically even during passage through the intestinal mucosa but mainly this process takes place in the liver. Its metabolites are salicyluric acid, salicylic phenolic glucuronide, salicylacyl glucuronide, gentisic acid and gentisuric acid.

Excretion

The elimination kinetics of salicylic acid is dose-dependent, as metabolism is limited by liver enzyme capacity. The elimination half-life therefore varies from 2 to 3 hours after low doses to up to about 15 hours at high doses. Salicylic acid and its metabolites are excreted mainly via the kidneys.

5.3 Preclinical safety data

The preclinical safety profile of acetylsalicylic acid is well documented.

In animal studies, salicylates caused kidney damage at high dosages but no other organic lesions. Acetylsalicylic acid has been extensively studied *in vitro* and *in vivo* for mutagenicity; no relevant evidence of a mutagenic potential was found. The same applies to carcinogenicity studies.

Salicylates have exhibited teratogenic effects in animal studies and a number of different species. Implantation disorders, embryotoxic and fetotoxic effects and impairment of learning ability in the offspring after prenatal exposure have been described.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Starch.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store at or below 25 °C, in a cool, dry place.

Protect from light.

6.5 Nature and contents of container

PVC/aluminium foil blister, packed in a cardboard carton containing 10 or 20 tablets.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Pharmacorp (Pty) Ltd

29 Victoria Link

Route 21 Corporate Park

Irene, 0178

South Africa

8. REGISTRATION NUMBER

J/2.9/0006

9. DATE OF FIRST AUTHORISATION

15 July 1976

10. DATE OF REVISION OF THE TEXT

31 October 2023