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SCHEDULING STATUS

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1. NAME OF THE MEDICINE

Bayer Aspirin 300 mg Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

300 mg acetylsalicylic acid per tablet.

For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Tablets.

A round white biconvex tablet with the Bayer cross on one side and Aspirin 0.3 on the other.

4. CLINICAL PARTICULARS

4.1. Therapeutic Indications

Bayer Aspirin is indicated for short-term use in the relief of mild to moderate pain and fever.

4.2. Posology and method of administration

Posology

Bayer Aspirin must not be taken for more than 3 – 5 days without consulting a doctor.

Adults and children 12 years and over:

300 – 1000 mg as a single dose, to be repeated as needed after a minimum period of 4 hours.

A maximum daily dose of 4000 mg must not be exceeded.

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

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Special populations

- **Patients with hepatic impairment**

  Bayer Aspirin should be used with caution in patients with abnormal hepatic function (See section 4.4).

- **Patients with renal impairment**

  Bayer Aspirin should be used with caution in patients with abnormal renal function (See section 4.4).

Paediatric population

Bayer Aspirin is recommended for children below 12 years only under physician's supervision. In general, the daily dose of Bayer 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 "Special warnings and precautions for use".

Method of administration

For oral use.

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

4.3. Contraindications

Bayer Aspirin must not be used in the following cases:

- hypersensitivity to acetylsalicylic acid or other salicylates, or to any other components of Bayer Aspirin,
- acute gastrointestinal ulcers,
- haemorrhagic diathesis,
- severe renal impairment,
- patients receiving oral anti-coagulant therapy,
- severe hepatic failure,
- a history of asthma induced by the administration of aspirin (salicylates) or substances with a similar action, including non-steroidal anti-inflammatory drugs,

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- heart failure,
- combination with methotrexate at doses of 15 mg/week or more,
- last trimester of pregnancy (see section 4.6),
- history of gastrointestinal perforation, ulceration or bleeding related to previous NSAIDs use, including Bayer Aspirin,
- active or history of recurrent ulcer/haemorrhage/perforation.

4.4. Special warnings and precautions for use

If symptoms persist a doctor should be consulted. Bayer Aspirin should not be used continuously for more than 3 – 5 days without consulting a doctor.

Bayer Aspirin should be administered with caution in the following cases:

- hypersensitivity to analgesics / anti-inflammatory agents / anti-rheumatic and in the presence of other allergies,
- patients with impaired renal function or patients with impaired cardiovascular circulation (e.g. renal vascular disease, congestive heart failure, volume depletion, major surgery, sepsis or major hemorrhagic events), since acetylsalicylic acid may further increase the risk of renal impairment and acute renal failure,
- in the presence of severe liver disease,
- in patients with a history of gastrointestinal ulcers including chronic or recurrent ulcer disease or a history of gastrointestinal bleeding,
- concomitant treatment with anticoagulants (See section 4.5)
- impaired hepatic function

Bayer 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.

Bayer Aspirin should be withdrawn 1 week before surgery.

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

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

In view of the medicine's inherent potential to cause fluid retention, heart failure may be precipitated in some compromised patients.

Bayer 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 Bayer Aspirin is given concomitantly. Should persistent vomiting occur with such diseases, this may be a sign of Reye's syndrome.

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 Bayer Aspirin therapy.

In patients suffering from severe glucose-6-phosphatedehydrogenase (GP6PD) deficiency, Bayer Aspirin may induce hemolysis or hemolytic anemia. Factors that may increase the risk of hemolysis are high dosage, fever, or acute infections.

Elderly: the elderly have an increased frequency of adverse reactions to NSAIDs, especially gastrointestinal bleeding and perforation (PUBs) which may be fatal. The risk of gastrointestinal bleeding or perforation (PUBs) is higher with increasing doses of Bayer Aspirin in patients with a history of ulcer and the elderly. When gastrointestinal bleeding or ulceration occurs in patients receiving Bayer Aspirin, treatment with Bayer Aspirin should be stopped.

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

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

4.5. Interaction with other medicines and other forms of interaction

Contra-indicated interactions:

Methotrexate used at doses of 15 mg/week or more:

Increased haematological toxicity of methotrexate (decreased renal clearance of methotrexate by anti-inflammatory agents in general and displacement of methotrexate from its plasma protein binding by salicylates), (see section 4.3).

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 agents in general and displacement of methotrexate from its plasma protein binding by salicylates).

Anticoagulants, thrombolytics/other inhibitors of platelet aggregation/haemostasis:

Increased risk of bleeding.

Bayer Aspirin may enhance the effects of anti-coagulants such as warfarin.

Other non-steroidal anti-inflammatory drugs with salicylates

Increased risk of ulcers and gastrointestinal bleeding due to synergistic effect.

Selective Serotonin Re-uptake Inhibitors (SSRIs):

Increased risk of upper gastrointestinal bleeding due to a possible synergistic effect.

Digoxin:

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

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Antidiabetic Medicines, e.g. insulin, sulphonylureas:

Increased hypoglycaemic effect by high doses of Bayer Aspirin via hypoglycaemic action of Bayer Aspirin and displacement of sulphonylurea from its plasma protein binding sites.

Diuretics in combination with Bayer Aspirin

Decreased glomerular filtration via decreased renal prostaglandin synthesis.

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

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

Angiotensin converting enzyme inhibitors (ACE) in combination with acetylsalicylic acid

Decreased glomerular filtration via inhibition of vasodilatory prostaglandins. Further-more, 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 Bayer Aspirin and alcohol.

Uricosurics such as benzbromarone, probenecid:

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

NSAIDs

The use of two or more NSAIDs concomitantly could result in an increase in side effects.

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4.6. Fertility, pregnancy and lactation

Safety in pregnancy has not been established.

Pregnancy:

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 first and second trimester of pregnancy, Bayer Aspirin should not be given. If Bayer Aspirin is used by a woman attempting to conceive, or during the first and second trimesters of pregnancy, the dose should be kept as low, and the duration of treatment kept as short, as possible.

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, Bayer Aspirin is contraindicated during the third trimester of pregnancy (see 4.3).

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Lactation:

Salicylates and their 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 Bayer Aspirin on impairment of fertility and there is no conclusive evidence from animal studies.

4.7. Effects on ability to drive and use machines

No effects on ability to drive and use machines have been observed.

4.8. Undesirable effects

The side effects listed below are based on spontaneous post-marketing reports. Thus, an organization by categories of frequency is not pertinent (frequency = unknown).

Blood and the lymphatic system disorders

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.

Ear and labyrinth disorders

Dizziness and tinnitus have been reported, which may be indicative of an overdose.

Gastrointestinal disorders

Upper and lower gastrointestinal tract disorders such as common signs and symptoms of dyspepsia, gastrointestinal and abdominal pain, gastrointestinal inflammation and gastrointestinal

ulcer, hemorrhage and perforation, with the Respective laboratory and clinical signs and symptoms, intestinal diaphragm disease with frequency not known (especially in long-term treatment).

Hepato-biliary disorders

Transient hepatic impairment with increase in liver transaminases has been reported.

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.

General disorders and administrative site conditions

Some persons, asthmatics, those with chronic urticaria or chronic rhinitis, may exhibit notable sensitivity to Bayer Aspirin which may provoke various hypersensitivity reactions which may include skin eruptions, urticaria, angioedema, paroxysmal bronchospasm and dyspnoea.

Interference with laboratory tests:

Salicylates 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: Aspirin may cause a false negative test in the presence of glycosuria.

Reporting of suspected adverse reactions

Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "6.04 Adverse Drug Reactions Reporting Form", found under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

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4.9. Overdose

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 salicylic 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 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.

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. 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 Bayer 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:

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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, hemodialysis in severe cases
Respiratory alkalosis with compensatory metabolic acidosis,	Acidaemia, aciduria	Fluid and electrolyte management
Hyperpyrexia		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, deafness		
Gastrointestinal: GI bleeding		

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Haematologic: ranging from platelet inhibition to coagulopathy	e.g. PT prolongation / increased INR, hypo-prothrombinaemia	
Neurologic: Toxic encephalopathy and CNS depression with manifestations ranging from lethargy, confusion to coma and seizures		

5. PHARMACOLOGICAL PROPERTIES

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

5.1. Pharmacodynamic properties

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.

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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

Cellulose powder

Maize starch

6.2. Incompatibilities

None Known

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6.3. Shelf life

48 months

6.4. Special precautions for storage

Store at or below 25 ºC. Keep out of reach of children

6.5. Nature and contents of container

300 mg tablets in blister packs of 10, 20, 30, 50, 100 and 1000.

6.6. Special precautions for disposal and other handling

Return all unused medicine to your pharmacist.

Do not dispose of unused medicines in drains or sewerage (e.g. toilets)

7. HOLDER OF CERTIFICATE OF REGISTRATION

Bayer (Pty) Ltd

27 Wrench Road

Isando, 1600

1968/011192/07

8. REGISTRATION NUMBER

C/2.7/166

9. DATE OF FIRST AUTHORISATION

22 February 1971

10. DATE OF REVISION OF THE TEXT

07 January 2021

ZIMBABWE – E 98/2.2.1/3304 Pharmacological classification: 2.1 Analgesics and antipyretics
NAMIBIA – 90/2.7/00354
BOTSWANA – BOT0400714

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