

Produktinformationen för Aspirin 500 mg brustablett, MTnr 18479, gäller vid det tillfälle då läkemedlet godkändes. Informationen kommer inte att uppdateras eftersom läkemedlet inte marknadsförs i Sverige. Av samma anledning finns inte någon svensk produktinformation. Den engelska produktinformationen kommer dock att uppdateras när Sverige är referensland för produkten.

Om läkemedelsnamnet i följande produktinformation inte stämmer med namnet på dokumentet, beror det på att läkemedlet i Sverige är godkänt under ett annat namn.

Summary of Product Characteristics

[country specific tradename]

1. NAME OF THE MEDICINAL PRODUCT

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[Aspirin Migraine] 500 mg effervescent tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each effervescent tablet contains 500 mg of acetylsalicylic acid.

Excipients: Each effervescent tablet contains 543 mg sodium. For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Effervescent tablet

White, round, flat effervescent tablets with Bayer cross embossed on one side

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For the symptomatic relief of headache associated with migraine.

4.2 Posology and method of administration

Adults:

1,000 mg as single dose.

If the attack persists the dose may be repeated at intervals of 4 - 8 hours.

A maximum daily dose of 3 g must not be exceeded.

[Aspirin Migraine] must not be taken for more than 3 days without consulting a physician. If migraine attacks occur frequently, if frequency of attacks increases or if symptoms persist, a physician should be consulted and an alternative treatment should be considered.

CHILDREN: [Aspirin Migraine] is not recommended for use in children below the age of 18 due to a lack of data in this population.

Method of administration

For oral use. Aspirin Migraine must be dissolved in a glass of water before taking.

4.3 Contraindications

- Active peptic ulcers;
- Haemorrhagic diathesis;
- Hypersensitivity to acetylsalicylic acid, to other salicylates, or to any of the excipients of the medicinal product;
- A history of asthma induced by the administration of salicylates or substances with a similar action, notably non-steroidal anti-inflammatory drugs;
- Severe hepatic failure;
- Severe renal failure;
- Severe uncontrolled cardiac failure;
- Combination with Methotrexate at doses of 15 mg/week or more (see section 4.5);
- Last trimester of pregnancy (see section 4.6).

4.4 Special warnings and precautions for use

- Concomitant treatment with anticoagulants;
- History of gastro-intestinal ulcers including chronic or recurrent ulcer disease or history of gastro-intestinal bleedings;
- Impaired renal function;
- Impaired hepatic function;
- Hypersensitivity to anti-inflammatory or antirheumatic drugs or other allergens.

Medicinal products containing acetylsalicylic acid should be used in children and adolescents with febrile diseases only after careful risk-benefit-evaluation because of the possibility of Reye's syndrome, a rare but serious illness.

Acetylsalicylic acid may precipitate bronchospasm and induce asthma attacks or other hypersensitivity reactions. Risk factors are present bronchial asthma, hay fever, nasal polyps, or chronic respiratory disease.

This applies also for patients showing allergic reactions (e.g. cutaneous reactions, itching, urticaria) to other substances.

Due to its inhibitory effect on platelet aggregation acetylsalicylic acid may lead to an increased bleeding tendency during and after surgical operations (including minor surgeries, e.g. dental extractions).

At low doses, acetylsalicylic acid reduces the excretion of uric acid. This can trigger gout in patients who already tend to have a low uric acid excretion.

Chronic intake of analgesics may cause headache which can lead to renewed dosing and thus to a continuation of headache.

Habitual use of analgesics (particularly combinations of different analgesic drugs) may permanently damage the kidneys (analgesic nephropathy).

The medicinal product contains 22.61 mmol (1086 mg) sodium per dose. To be taken into consideration by patients on a controlled sodium diet.

4.5 Interaction with other medicinal products 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, e.g. coumarin, heparin:
increased risk of bleeding via inhibition of platelet function, damage to gastroduodenal mucosa and displacement of oral anticoagulants from their plasma protein binding sites.
- Other non-steroidal anti-inflammatory drugs with salicylates at high doses ($\geq 3\text{g/day}$):
Increased risk of ulcers and gastrointestinal bleeding due to synergistic effect.
- Selective serotonin re-uptake inhibitors (SSRIs): Increased risk of upper gastrointestinal bleeding.
- Uricosurics such as benzbromarone, probenecid:
Decreased uricosurics effect (competition of renal tubular uric acid elimination).
- Antidiabetics, e.g. insulin, sulphonylureas: Increased hypoglycemic effect by high doses of acetylsalicylic acid via hypoglycaemic action of acetylsalicylic acid and displacement of sulfonylurea from its Plasma Protein binding.
- Thrombolytics / Other antiplatelet agents, e.g. ticlopidine: Increased risk of bleeding.
- Diuretics in combination with acetylsalicylic acid at doses of 3g/day or more: 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):
At doses of 3g/day and more, decreased glomerular filtration via inhibition of vasodilator 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 acetylsalicylic acid and alcohol.

4.6 Pregnancy and lactation

Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/fœtal 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. For acetylsalicylic acid overall the available epidemiological data suggest an increased risk of gastroschisis. Animal studies have shown reproductive toxicity (see section 5.3).

During the first and second trimester of pregnancy, acetyl salicylic acid should not be given unless clearly necessary. If acetyl salicylic acid is used by a woman attempting to conceive, or during the first and second trimester of pregnancy, the dose should be kept as low and duration of treatment 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;
- the mother and the child, at the end of pregnancy, to:
- possible prolongation of bleeding time, an anti-aggregating effect which may occur even after very low doses
 - inhibition of uterine contractions resulting in delayed or prolonged labour

Consequently, acetyl salicylic acid is contraindicated during the third trimester of pregnancy.

Fertility

There is some evidence that drugs which inhibit prostaglandin synthesis may cause impairment of female fertility by an effect on ovulation. This is reversible on withdrawal of treatment.

Lactation

Salicylates and its metabolites pass into breast milk in small quantities. Since no adverse effects on the infant have been observed so far after occasional use, interruption of breast-feeding is usually unnecessary. However, on regular use or on intake of high doses, breast feeding should be discontinued early.

4.7 Effects on ability to drive and use machines

Aspirin Migraine has no influence on the ability to drive and use machines.

4.8 Undesirable effects

Blood and lymphatic system disorders:

In very rare cases serious bleedings, such as cerebral haemorrhage (especially in patients with uncontrolled hypertension and/or on concomitant antihaemostatic agents), which in single cases may be potentially life-threatening, have been reported.

Bleeding syndromes (epistaxis, gingival bleeding, purpura, etc.) with prolonged bleeding time. This action may persist for 4 to 8 days after acetylsalicylic acid is stopped. It may result in the risk of bleeding during surgery.

Nervous system disorders:

Headache, vertigo, feelings of impaired hearing, tinnitus, which are usually indicating an overdose (see section 4.9).

Gastrointestinal disorders:

Gastro-duodenal ulcer and perforation.

Evident (hematemesis, melena) or occult gastro-intestinal bleeding which may cause iron deficiency anaemia. Such bleeding is commoner when the dosage is higher.

Abdominal pain, heartburn, nausea, vomiting.

Hepatobiliary Disorders:

Increase of transaminases

Skin and subcutaneous tissue disorders:

Skin reactions, e.g. Urticaria

Immune System disorders:

Hypersensitivity reactions (dyspnoea, anaphylactic reactions, severe skin reactions, asthma, Quincke oedema).

4.9 Overdose

Poisoning must be feared in the elderly and above all in young children (therapeutic overdose or frequent accidental poisoning) in whom it may be fatal.

Symptomatology:

Moderate poisoning:

Tinnitus, feeling of impaired hearing, headache, vertigo and mental confusion are observed in case of overdose and can be controlled by a dosage reduction.

Severe poisoning:

Fever, hyperventilation, ketosis, respiratory alkalosis, metabolic acidosis, coma, cardiovascular shock, respiratory failure, severe hypoglycaemia.

Emergency management:

immediate transfer to hospital specialist unit,

gastric lavage, administration of activated charcoal, check of acid-base balance,

alkaline diuresis so as to obtain a urine pH between 7.5 and 8, forced alkaline diuresis should be considered when the plasma salicylate concentration is greater than: 500 mg/litre (3.6 mmol/litre) in adults or 300 mg/litre (2.2 mmol/litre) in children,

possibility of hemodialysis in severe poisoning,

fluid losses should be replaced,

symptomatic treatment.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other analgesics and antipyretics; salicylic acid and derivatives
ATC-Code: N02BA01.

Acetylsalicylic acid belongs to the group of acidic nonsteroidal anti-inflammatory drugs 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 in oral doses of in general 0.5 to 1.0 g is used for the relief of mild to moderate pain and in minor febrile conditions, such as colds or influenza, for the reduction of temperature and relief of the joint and muscle pains.

It is also used in acute and chronic inflammatory disorders such as rheumatoid arthritis, osteoarthritis, and ankylosing spondylitis. Generally high doses of 4 to 8 g daily in divided doses are used for these disorders.

Acetylsalicylic acid also inhibits platelet aggregation by blocking thromboxane A₂ synthesis in platelets. Thus, it is used for various cardiovascular indications at doses of in general 75 to 100 mg daily.

The use of [Aspirin Migraine] is not recommended for platelet aggregation inhibition.

5.2 Pharmacokinetic properties

Following oral administration, acetylsalicylic acid is absorbed rapidly and completely from the gastro-intestinal tract. During and after absorption acetylsalicylic acid is converted into its main active metabolite salicylic acid. Maximal plasma levels are reached after 10 - 20 minutes for acetylsalicylic acid and after 0.3-2 hours for salicylic acid, resp.

Both acetylsalicylic acid and salicylic acid are extensively bound to plasma proteins and rapidly distributed to all body parts. Salicylic acid appears in breast milk and crosses the placenta.

Salicylic acid is mainly eliminated by hepatic metabolism; metabolites include salicyluric acid, salicyl phenolic glucuronide, salicyl acyl glucuronide, gentisic acid, and gentisuric acid.

The elimination kinetics of salicylic acid is dose-dependent, as the metabolism is limited by the capacity of liver enzymes. Thus, the elimination half-life varies between 2 to 3 hours after low doses 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 tests salicylates caused kidney damage but no other organic lesions.

Acetylsalicylic acid has been adequately tested for mutagenicity and carcinogenicity; no relevant evidence of a mutagenic or cancerogenic potential was found.

Salicylates have been found to have teratogenic effects in a number of animal species (e.g. cardiac and skeletal malformations, midline defects). There have been reports of implantation disturbance, embryotoxic and fetotoxic effects, and disturbance of learning capacity in the offspring after prenatal exposure.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Dihydrogen Citrate
Sodium Hydrogen Carbonate
Citric Acid, anhydrous
Sodium Carbonate, anhydrous

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

Do not store above 25° C
Store in the original package

6.5 Nature and contents of container

Strips (Paper / Polyethylene / Aluminium / Copolymer), each containing 2 effervescent tablets. Strips are packed into outer cartons in packs of 12 (6x2) and 24 (12x2) effervescent tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements

7. MARKETING AUTHORIZATION HOLDER

To be completed nationally.

8. MARKETING AUTHORIZATION NUMBER

To be completed nationally.

9. DATE OF FIRST AUTHORIZATION / DATE OF LAST RENEWAL

Date of first authorisation: January 29, 2003

Date of last renewal:

10. DATE OF REVISION OF THE TEXT

September 18, 2008