SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Acetylsalicylic acid Bluefish 75 mg tablets
Acetylsalicylic acid Bluefish 160 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 75 mg acetylsalicylic acid.
Each tablet contains 160 mg acetylsalicylic acid.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet.

75 mg: White to off-white, clear to mottled, 6.5 mm round, biconvex, uncoated tablets plain on both sides.

160 mg: White to off-white, clear to mottled, 8.5 mm round, biconvex, uncoated tablets with score line on one side and plain on the other side.
The score line is not meant for dividing the tablet into equal doses, but to facilitate swallowing.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Acute myocardial infarction. Prophylaxis of cardiovascular complications after acute myocardial infarction and for unstable coronary syndromes (unstable angina pectoris, completed non-Q-wave myocardial infarction) and stable angina pectoris.

Secondary prophylaxis against recurrence of cerebrovascular disease such as TIA (transient ischemic attacks) and RIND (reversible ischemic neurological defect).

4.2 Posology and method of administration

Posology
Acute myocardial infarction: Initially a loading dose of 150-500 mg is given. The loading dose is given as soon as possible after the onset of symptoms.

Prophylaxis of cardiovascular complications after acute myocardial infarction, unstable coronary syndrome (unstable angina pectoris, completing non-Q-wave myocardial infarction), stable angina pectoris: 1 tablet of 75 mg per day.

Prophylaxis of recurrence of cerebrovascular disease: 1 tablet of 75 mg per day.

Elderly
In general, acetylsalicylic acids should be used with caution in elderly patients who are more prone to adverse events. The usual adult dose is recommended in the absence of severe renal or hepatic insufficiency (see sections 4.3 and 4.4). Treatment should be reviewed at regular intervals.

Paediatric population
Acetylsalicylic acid should not be administered to children and adolescents younger than 16 years, except on medical advice where the benefit outweighs the risk (see section 4.4).

4.3 Contraindications

- Hypersensitivity to salicylic acid compounds or prostaglandin synthetase inhibitors (e.g. certain asthma patients who may suffer an attack or faint) or to any of the excipients listed in section 6.1;
- Active, or history of recurrent peptic ulcer and/or gastric/intestinal haemorrhage, or other kinds of bleeding such as cerebrovascular haemorrhages;
- Haemorrhagic diathesis; coagulation disorders such as haemophilia and thrombocytopenia;
- Severe hepatic impairment;
- Severe renal impairment;
- Gout;
- Doses >100 mg/day during the third trimester of pregnancy (see section 4.6);
- Methotrexate used at doses >15mg/week (see section 4.5).

4.4 Special warnings and precautions for use

Acetylsalicylic acid Bluefish is not suitable for use as an anti-inflammatory/analgesic/antipyretic.

Recommended for use in adults and adolescents from 16 years of age. This medicinal product is not recommended for use in adolescents/children under 16 years unless the expected benefits outweigh the risks. Acetylsalicylic acid may be a contributory factor in the causation of Reye's Syndrome in some children.

There is an increased risk of haemorrhage particularly during or after operative procedures (even in cases of minor procedures, e.g. tooth extraction). Use with caution before surgery, including tooth extraction. Temporary discontinuation of treatment may be necessary.

Acetylsalicylic acid Bluefish is not recommended during menorrhagia where it may increase menstrual bleeding.

Acetylsalicylic acid Bluefish is to be used with caution in cases of hypertension and when patients have a past history of gastric or duodenal ulcer or haemorrhagic episodes or are undergoing therapy with anticoagulants.

Patients should report any unusual bleeding symptoms to their physician. If gastrointestinal bleeding or ulceration occurs the treatment should be withdrawn.

Acetylsalicylic acid should be used with caution in patients with moderately impaired renal or hepatic function (contraindicated if severe), or in patients who are dehydrated since the use of NSAIDs may result in deterioration of renal function. Liver function tests should be performed regularly in patients presenting slight or moderate hepatic insufficiency.

Acetylsalicylic acid may promote bronchospasm and asthma attacks or other hypersensitivity reactions. Risk factors are existing asthma, hay fever, nasal polyps or chronic respiratory diseases. The same applies for patients who also show allergic reaction to other substances (e.g. with skin reactions, itching or urticaria).

Serious skin reactions, including Steven-Johnsons syndrome, have rarely been reported in association with the use of acetylsalicylic acid (see section 4.8). Acetylsalicylic acid Bluefish should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Elderly patients are particularly susceptible to the adverse effects of NSAIDs, including acetylsalicylic acid especially gastrointestinal bleeding and perforation which may be fatal (see section 4.2). Where prolonged therapy is required, patients should be reviewed regularly.

Concomitant treatment with Acetylsalicylic acid Bluefish and other drugs that alter haemostasis (i.e. anticoagulants such as warfarin, thrombolytic and antiplatelet agents, anti-inflammatory drugs and selective serotonin reuptake inhibitors) is not recommended, unless strictly indicated, because they may enhance the risk of haemorrhage (see section 4.5). If the combination cannot be avoided, close observation for signs of bleeding is recommended.

Caution should be advised in patients receiving concomitant medications which could increase the risk of ulceration, such as oral corticosteroids, selective serotonin-reuptake inhibitors and deferasirox (see section 4.5).

Acetylsalicylic acid should be avoided in late pregnancy and generally during breast feeding (see section 4.6).

Acetylsalicylic acid in low doses reduces uric acid excretion. Due to this fact, patients who tend to have reduced uric acid excretion may experience gout attacks (see section 4.5).

The risk of hypoglycaemic effect with sulfonylureas and insulins may be potentiated with Acetylsalicylic acid Bluefish taken at over dosage (see section 4.5).

4.5 Interaction with other medicinal products and other forms of interaction

Contraindicated combinations
Methotrexate (used at doses >15 mg/week):
The combined drugs, methotrexate and acetylsalicylic acid, enhance haematological toxicity of methotrexate due to the decreased renal clearance of methotrexate by acetylsalicylic acid. Therefore, the concomitant use of methotrexate (at doses >15 mg/week) with Acetylsalicylic acid Bluefish is contraindicated (see section 4.3).

Not recommended combinations
Uricosuric agents, e.g. probenecid
Salicylates reverse the effect of probenecid. The combination should be avoided.

Combinations requiring precautions for use or to be taken into account
Anticoagulants e.g. coumarin, heparin, warfarin
Increased risk of bleeding due to inhibited thrombocyte function, injury of the duodenal mucosa and displacement of oral anticoagulants from their plasma protein binding sites. The bleeding time should be monitored (see section 4.4).

Anti-platelet agents (e.g clopidogrel and dipyridamole) and selective serotonin reuptake inhibitors (SSRIs; such as sertraline or paroxetine)
Increased risk of gastrointestinal bleeding (see section 4.4).

Antidiabetics, e.g. sulphonylureas
Salicylics may increase the hypoglycaemic effect of sulphonylureas.

Digoxin and lithium
Acetylsalicylic acid impairs the renal excretion of digoxin and lithium, resulting in increased plasma concentrations. Monitoring of plasma concentrations of digoxin and lithium is recommended when initiating and terminating treatment with acetylsalicylic acid. Dose adjustment may be necessary

Diuretics and antihypertensives
NSAIDs may decrease the antihypertensive effects of diuretics and other antihypertensive agents. As for other NSAIDs concomitant administration with ACE-inhibitors increases the risk of acute renal insufficiency.
Diuretics: Risk of acute renal failure due to the decreased glomerual filtration via decreased renal prostaglandin synthesis. Hydrating the patient and monitoring renal function at the start of the treatment is recommended.

Carbonic anhydrase inhibitors (acetazolamide)
May result in severe acidosis and increased central nervous system toxicity

Systemic corticosteroids
The risk of gastrointestinal ulceration and bleeding may be increased when acetylsalicylic acid and corticosteroids are co-administered (see section 4.4).

Methotrexate (used at doses <15 mg/week):
The combined drugs, methotrexate and acetylsalicylic acid, may increase haematological toxicity of methotrexate due to decreased renal clearance of methotrexate by acetylsalicylic acid. Weekly blood count checks should be done during the first weeks of the combination. Enhanced monitoring should take place in the presence of even mildly impaired renal function, as well, as in elderly.

Other NSAIDs
Increased risk of ulcerations and gastrointestinal bleeding due to synergistic effects.

Ibuprofen
Experimental data suggest that ibuprofen may inhibit the effect of low dose acetylsalicylic acid on platelet aggregation when they are dosed concomitantly. However, the limitations of these data and the uncertainties regarding extrapolation of ex vivo data to the clinical situation imply that no firm conclusions can be made for regular ibuprofen use, and no clinically relevant effect is considered to be likely for occasional ibuprofen use (see section 5.1).

Metamizole
Metamizole may reduce the effect of acetylsalicylic acid on platelet aggregation, when taken concomitantly. Therefore, this combination should be used with caution in patients taking low dose acetylsalicylic acid for cardio protection.

Cyclosporin, tacrolimus
Concomitant use of NSAIDs and cyclospoin or tacrolimus may increase the nephrotoxic effect of ciclosporin and tacrolimus. The renal function should be monitored in case of concomitant use of these agents and acetylsalicylic acid.

Antacids
The excretion of acetylsalicylic acid is increased by alkaline urine, which can occur with some antacids.

Alcohol
Concomitant administration of alcohol and acetylsalicylic acid increases the risk of gastrointestinal bleeding.

4.6 Fertility, pregnancy and lactation

Pregnancy
Low doses (up to and including 100 mg/day):
Clinical studies indicate that doses up to 100 mg/day for restricted obstetrical use, which require specialized monitoring, appear safe.

Doses of above 100 mg/day and up to 500 mg/day:
There is insufficient clinical experience regarding the use of doses above 100 mg/day up to 500 mg/day. Therefore, the recommendations below for doses of 500 mg/day and above apply also for this dose range.

Doses of 500 mg/day and above:
Inhibition of prostaglandin synthesis may affect pregnancy in a negative way. Data from epidemiological studies suggest an increased risk of miscarriage and risk of cardiac malformation and gastroschisis after use of a prostaglandin synthesis inhibitor in early pregnancy. The absolute risk of cardiovascular malformation increased from less than 1% to about 1.5%. The risk is believed to increase with increased dose and duration of therapy. In animals, the administration of prostaglandin synthesis inhibitors has been shown to result in increased pre- and post-implantation losses and embryo / fetal death. In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals exposed to a prostaglandin synthesis inhibitor during the period of organogenesis. During the first and second trimester of pregnancy, acetylsalicylic acid should only be used when absolutely necessary. If acetylsalicylic acid is used by a woman trying to conceive or is given during the first and second trimester of pregnancy, the dose should be kept as low and duration of treatment as short as possible.

From the 20th week of pregnancy onward, Acetylsalicylic acid Bluefish use may cause oligohydramnios resulting from foetal renal dysfunction. This may occur shortly after treatment initiation and is usually reversible upon discontinuation. In addition, there have been reports of ductus arteriosus constriction following treatment in the second trimester, most of which resolved after treatment cessation. Therefore, during the first and second trimester of pregnancy, Acetylsalicylic acid Bluefish should not be given unless clearly necessary. If Acetylsalicylic acid Bluefish 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. Antenatal monitoring for oligohydramnios and ductus arteriosus constriction should be considered after exposure to Acetylsalicylic acid Bluefish for several days from gestational week 20 onward. Acetylsalicylic acid Bluefish should be discontinued if oligohydramnios or ductus arteriosus constriction are found.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the foetus to:
- cardiopulmonary toxicity (premature constriction/closure of the ductus arteriosus and pulmonary hypertension);
- renal dysfunction (see above),

the mother and the neonate, at the end of pregnancy, to:
- possible prolongation of bleeding time, an anti-aggregation effect which may occur even at very low doses;
- inhibition of uterine contractions resulting in delayed or prolonged labor.

Consequently, acetylsalicylic acid at doses higher than 100 mg/day is contraindicated during the third trimester of pregnancy (see sections 4.3). Doses up to and including 100 mg/day may only be used under strict obstetric monitoring.

Breast-feeding
Low quantities of salicylates and their metabolites are excreted in breast milk. Short-term use of therapeutic doses does not require interruption of breastfeeding since no side effects in nursing infants have been reported. For long-term use and / or treatment with high doses breastfeeding should be discontinued.

Fertility
Treatment with Acetylsalicylic acid Bluefish can lead to reduced fertility in women and is not recommended for women attempting to conceive. Discontinuation of the drug should be considered in women who have difficulty conceiving or are undergoing fertility investigation.

4.7 Effects on ability to drive and use machines

Acetylsalicylic acid Bluefish has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The most common side effect is dyspeptic symptoms, approximately 2-6%. The increased risk of haemorrhage, especially from the gastrointestinal tract, is rarely symptomatic.

Adverse reactions are listed below by system organ class and frequency.

Common (≥1/100 to <1/10)
Blood and lymphatic system disorders: increased bleeding tendencies.
Gastrointestinal disorders: Dyspepsia.

Uncommon (≥1/1,000 to <1/100)
Immune system disorders: Allergic reactions (urticaria, rhinitis, asthma).

Rare (≥1/10,000 to <1/1,000)
Gastrointestinal disorders: Severe gastrointestinal bleeding.
Nervous system disorders: Intracranial bleeding.
Skin and subcutaneous tissue disorders: Severe skin reactions (such as Stevens-Johnson syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms (DRESS syndrome)).
Renal and urinary disorders: Renal disorders.

People with known allergy or asthma are at increased risk of hypersensitivity reactions. Minor blood losses may in rare cases lead to anemia. Severe gastrointestinal bleeding occurs only at higher doses and at regular use.

Dizziness and tinnitus can be symptoms of overdose, especially in children and the elderly.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.*

4.9 Overdose

Toxicity
Children under 3 years are particularly susceptible. 150 mg / kg leads to mild, 150-300 mg / kg leads to mild-moderate and more than 300 mg / kg leads to severe intoxication. The level of salicylate in blood is valuable for the assessment but must always be related to the time factor and the clinical

presentation. (Above 2.5 mmol / l may be mild, 3.5-4.5 mmol / l moderate, 4.5-6.0 mmol / l serious and > 6.0 mmol / l very severe intoxication; note that these are approximate initial levels, at a later stage the level of salicylate can be relatively low during severe intoxication.) 0.9-5 g to 3 months-3 year olds gave moderate-severe intoxication. 10-25 g to 14-15 year olds gave after gastric lavage mild-moderate intoxication. Severe hypersensitivity reactions may occur especially in children during the first six months of life. Poisoning can also appear by absorption through the skin following repeated administration (psoriasis and ichthyosis patients).

Symptoms
Possibly a few hours of latency. Vertigo, tinnitus, loss of hearing, anxiety, irritability, hallucinations, tremor, asterixis. Hyperventilation, thirst, flushing, sweating. In severe cases, loss of consciousness, seizures, hyperthermia. Nausea, vomiting, abdominal pain. Respiratory alkalosis initially in adults. Metabolic acidosis in young children and always with heavy exposure in both adults and children (pronounced acidosis indicates serious poisoning). Hyperglycemia or hypoglycemia (especially in toddlers). Hypokalemia, dehydration, ammonia elevation. Oliguria. Coagulopathies. Hepatic effects. In severe cases, risk of pulmonary oedema of non-cardiac nature and rhabdomyolysis and kidney failure, possibly ARDS as well as arrhythmias and heart failure.

Treatment
Following an overdose, patients should be given symptomatic and supportive treatment. There are no specific antidotes.

If necessary gastric lavage. Repeated doses of activated charcoal (shortens the half-life considerably). S- salicylate should be determined. Rehydration, correction of metabolic acidosis and any electrolyte disturbances. Omeprazole to protect the stomach lining. Antiemetic e.g. ondansetron when needed. (to provide activated charcoal repeatedly with frequent vomiting.) Alkalinisation of the urine with sodium bicarbonate (sodium hydrogen carbonate) i.v. to accelerate elimination. Add glucose. Follow the coagulation status. Vitamin K is given in case of massive poisoning or coagulation disorder. For bleeding complications, platelet concentrate and / or fresh frozen plasma is given. In case of insufficient efficacy, fibrinolysis inhibitor is given in consultation with a coagulation expert. Respiratory therapy of unconsciousness or severe constitutional symptoms. In case of severe poisoning (high salicylate value or moderate value in combination with pronounced acidosis and CNS disorder), as well as events of renal failure, hemodialysis should be considered. Symptomatic therapy (for e.g. hyperthermia, cerebral edema, pulmonary edema).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Platelet aggregation inhibitors
ATC code: B01AC06

Acetylsalicylic acid has an inhibitory effect on platelet aggregation. Although the mechanism is not fully understood, the effect appears primarily to be exerted through acetylation and therefore irreversible inactivation of the enzyme cyclooxygenase, which is involved in the formation of thromboxane A2 in platelets and of prostacyclin in the endothelium. These are basically antagonists of platelet aggregation and vascular effects. The effect on platelets is permanent since they lack the ability to regenerate cyclooxygenase. Therefore, the effect persists throughout the platelet life cycle, which is 7-10 days. The prophylactic and therapeutic use in arterial thromboembolism is based on this effect. Acetylsalicylic acid inhibits the renal prostacyclin synthesis. In patients with normal renal function, this effect is not significant. In patients with chronic renal insufficiency, cardiac or hepatic impairment or condition with reduced plasma volume, inhibition of the prostacyclin synthesis may lead to acute renal insufficiency, fluid retention and heart failure. See section 4.3.

Experimental data suggest that ibuprofen may inhibit the effect low dose acetylsalicylic acid has on platelet aggregation when given simultaneously. In one study, when a single dose of ibuprofen 400 mg was taken either within 8 hours before or within 30 minutes after intake of acetylsalicylic acid (81 mg), a decreased effect of acetylsalicylic acid was shown on the formation of thromboxane or platelet aggregation.
Limitations of these data and the uncertainties regarding extrapolation of *ex vivo* data to the clinical situation imply that no firm conclusion can be made for regular use of ibuprofen, and no effect of clinical significance is considered likely for occasional use of ibuprofen.

5.2 Pharmacokinetic properties

Absorption
After oral administration, acetylsalicylic acid is rapidly absorbed from the gastrointestinal tract. However, a significant portion of the dosage is already hydrolysed to salicylic acid in the intestinal wall during the absorption process.

Distribution
Acetylsalicylic acid as well as the main metabolite salicylic acid, are extensively bound to plasma proteins, primarily albumin, and distributed rapidly into all parts of the body. Maximum plasma concentration is reached after 0.3 - 2 hours (total salicylate). The volume of distribution of acetylsalicylic acid is ca. 0.16 l/kg of body weight.

Biotransformation
Acetylsalicylic acid is rapidly metabolised to salicylic acid, with a half-life of 15-30 minutes. Salicylic acid is subsequently predominantly converted into glycine and glucuronic acid conjugates. Elimination kinetics of salicylic acid is dose-dependent, because the metabolism is limited by liver enzyme capacity. Thus, elimination half-time varies and is 2-3 hours after low doses (75 mg – 160 mg).

Excretion
Salicylic acid and its metabolites are predominantly excreted via the kidneys.

5.3 Preclinical safety data

No data available

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Magnesium oxide (E 530)
Cellulose microcrystalline (E 460)
Maize starch
Gelatin
Silica, colloidal anhydrous (E 551)
Talc (E 553b)
Stearic acid (E 570)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Do not store above 25°C.
Store in the original package in order to protect from moisture.

6.5 Nature and contents of container

The 75 mg and 160 mg tablets are packed in HDPE bottles with a polypropylene (PP) screw cap and silica gel desiccant.

75 mg: 100, 105 and 500 tablets
160 mg: 100 and 105 tablets

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

[To be completed nationally]

8. MARKETING AUTHORISATION NUMBERS

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

[To be completed nationally]

10. DATE OF REVISION OF THE TEXT

2025-08-14