SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Alka-Seltzer Original

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Acetylsalicylic acid  324 mg
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Effervescent tablets for oral administration.
White, round tablet, embossed ‘Alka Seltzer’ on one side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
For rapid relief of pain including migraine, headache, period pains, neuralgia, toothache, sore throat.
Symptomatic relief of rheumatic pain, sciatica, lumbago, fibrositis, muscular aches and pains.
Symptomatic relief of influenza, feverishness, feverish colds.

4.2 Posology and method of administration
Alka-Seltzer Original tablets may always be dissolved in a glass of water prior to oral administration. The tablets dissolve more quickly in warm water.
The dose in adults, elderly and children aged 16 years and over, is two tablets in water. The dose may be repeated every four hours, as required, with a maximum of four dosages in 24 hours. These dosages should not be continued for more than three days without consulting a physician. The stated dose must not be exceeded.
Do not give to children under 16 years, unless specifically indicated (e.g. for Kawasaki’s disease).

4.3 Contraindications

Acetylsalicylic acid must not be used in the following cases:

- hypersensitivity to acetylsalicylic acid or other salicylates, or to any other components of the product,
- a history of hypersensitivity reactions (e.g. asthma, rhinitis, urticaria) induced by the administration of salicylates or substances with a similar action, notably non-steroidal anti-inflammatory drugs,
- active or a history of peptic ulcers,
- haemorrhagic diathesis,
- severe renal failure,
- severe hepatic failure,
- severe cardiac failure,
- in combination with methotrexate at doses of 15 mg/week or more (see interactions with other medicinal products and other forms of interaction),
- third trimester of pregnancy.

4.4 Special warnings and precautions for use

Acetylsalicylic acid should be used with particular caution in the following cases:

- hypersensitivity to analgesics / anti-inflammatory agents / anti-rheumatics and in the presence of other allergies,
- with a history of gastrointestinal disorders,
- with concomitant treatment with anticoagulants (see interactions with other medicinal products and other forms of interaction),
- 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 haemorrhagic events), since acetylsalicylic acid may further increase the risk of renal impairment,
- impaired hepatic function.

Acetylsalicylic acid 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.

Due to its inhibitory effect on platelet aggregation which persists for several days after administration, 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 possibly trigger gout attacks in predisposed patients.

There is a possible association between aspirin and Reye’s syndrome when given to children. Reye’s syndrome is a very rare disease, which affects the brain, and
liver, and can be fatal. For this reason aspirin should not be given to children aged under 16 unless specifically indicated (e.g. Kawasaki’s disease).

In patients suffering from severe glucose-6-phosphate dehydrogenase (G6PD) deficiency, acetylsalicylic acid may induce haemolysis or haemolytic anaemia. Factors that may increase the risk of haemolysis are high dosage, fever, or acute infections, for example.

This medicinal product contains 477mg sodium per tablet. To be taken into consideration by patients on a controlled sodium diet.

4.5 Interactions with other medicaments and other forms of interactions

Contraindicated 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 Contraindications).

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.

Other non-steroidal anti-inflammatory drugs with salicylates at higher doses:
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 possibly synergistic effect

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

Antidiabetics, e.g. insulin, sulphonylureas:
Increased hypoglycaemic effect by high doses of acetylsalicylic acid via hypoglycaemic action of acetylsalicylic acid and displacement of sulphonylurea from its plasma protein binding.

Diuretics in combination with acetylsalicylic acid at higher doses:
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.
Corticosteroids:
Potentiate the risk of gastro-intestinal bleeding during concomitant therapy with corticosteroids.

Angiotensin converting enzyme inhibitors (ACE) in combination with acetylsalicylic acid at higher doses:
Decreased glomerular filtration via inhibition of vasodilatory prostaglandins. Furthermore, decreased antihypertensive effect.

Valproic acid and Phenytoin:
Increased toxicity of valproic acid due to displacement from protein binding sites. Phenytoin is also extensively bound to plasma proteins therefore it can be displaced by acetylsalicylic acid from plasma binding.

Alcohol:
Increased damage to gastro-intestinal mucosa and prolonged bleeding time due to additive effects of acetylsalicylic acid and alcohol.

Uricosurics such as benzbromarone, probenecid:
Decreased uricosuric effect (competition of renal tubular uric acid elimination).

4.6 Fertility, pregnancy and lactation

Pregnancy

Doses of 500 mg/day and above:
Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/foetal development. Data from epidemiological studies suggest an increased risk of miscarriage and of cardiac malformation and gastroschisis after use of a prostaglandin synthesis inhibitor in early pregnancy. The absolute risk for cardiovascular malformation was increased from less than 1%, up to approximately 1.5%. The risk is believed to increase with dose and duration of therapy. In animals, administration of a prostaglandin synthesis inhibitor has been shown to result in increased pre- and post-implantation loss and embryo-foetal lethality. In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period. During the first and second trimester of pregnancy, acetylsalicylic acid should not be given unless clearly necessary. If acetylsalicylic 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-hydroamnios;

the mother and the neonate, at the end of pregnancy, to:
- possible prolongation of bleeding time, an anti-aggregating effect which may occur even at very low doses.
- inhibition of uterine contractions resulting in delayed or prolonged labour.
Consequently, acetylsalicylic acid at doses of 100 mg/day and higher is contraindicated during the third trimester of pregnancy.

**Lactation**

Breast feeding is contraindicated at high doses because of the theoretical risk of affecting clotting mechanisms.

### 4.7 Effects on ability to drive and use machines

None known.

### 4.8 Undesirable effects

The listed adverse drug reactions are based on spontaneous reports, thus an organization according to CIOMS III categories of frequency is not possible.

**Blood and lymphatic system disorders**

Increased risk of bleeding (due to effect on platelet aggregation). In the context of bleeding: haemorrhagic anaemia, iron deficiency anaemia with the respective laboratory and clinical signs and symptoms. In the context of glucose-6-phosphate dehydrogenase (G6PD) deficiency: haemolysis, haemolytic anaemia

**Immune system disorders**

Hypersensitivity, drug hypersensitivity, allergic edema and angioedema, anaphylactic reaction, anaphylactic shock with respective laboratory and clinical manifestations

**Nervous system disorders**

Cerebral and intracranial haemorrhage, dizziness

**Ear and labyrinth disorders**

Tinnitus

**Cardiac disorders**

In the context of severe allergic reactions: cardio-respiratory distress

**Vascular disorders**

Haemorrhage, operative haemorrhage, haematoma, muscle haemorrhage

**Respiratory, thoracic and mediastinal disorders**

Epistaxis, analgesic asthma syndrome, rhinitis, nasal congestion, bronchospasm

**Gastrointestinal disorders**

Dyspepsia, gastrointestinal pain, abdominal pain, gingival bleeding, gastrointestinal inflammation, gastrointestinal ulcer, gastrointestinal haemorrhage, gastrointestinal ulcer perforation with the respective laboratory and clinical signs and symptoms, nausea, diarrhoea, vomiting
**Hepatobiliary disorders**
Liver disorder, transaminases increased

**Skin and subcutaneous tissue disorders**
Rash, urticaria, pruritus, severe skin reactions

**Renal and urinary disorders**
Impaired renal function

**Injury, poisoning and procedural complications**
See overdose section

**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 Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

### 4.9 Overdose

Salicylate poisoning is usually associated with plasma concentrations >350 mg/L (2.5 mmol/L). Most adult deaths occur in patients whose concentrations exceed 700 mg/L (5.1 mmol/L). Single doses less than 100 mg/kg are unlikely to cause serious poisoning.

**Symptoms**

*Common features* include vomiting, dehydration, tinnitus, vertigo, deafness, sweating, warm extremities with bounding pulses, increased respiratory rate and hyperventilation. Some degree of acid-base disturbance is present in most cases.

A mixed respiratory alkalosis and metabolic acidosis with normal or high arterial pH (normal or reduced hydrogen ion concentration) is usual in adults and children over the age of four years. In children aged four years or less, a dominant metabolic acidosis with low arterial pH (raised hydrogen ion concentration) is common. Acidosis may increase salicylate transfer across the blood brain barrier.

*Uncommon features* include haematemeses, hyperpyrexia, hypoglycaemia, hypokalaemia, thrombocytopenia, increased INR/PTR, intravascular coagulation, renal failure and non-cardiac pulmonary oedema.

Central nervous system features including confusion, disorientation, coma and convulsions are less common in adults than in children.

**Management**

Give activated charcoal if an adult presents within one hour of ingestion of more than 250 mg/kg. The plasma salicylate concentration should be measured, although the severity of poisoning cannot be determined from this
alone and the clinical and biochemical features must be taken into account. Elimination is increased by urinary alkalinisation, which is achieved by the administration of 1.26% sodium bicarbonate. The urine pH should be monitored. Correct metabolic acidosis with intravenous 8.4% sodium bicarbonate (first check serum potassium). Forced diuresis should not be used since it does not enhance salicylate excretion and may cause pulmonary oedema. Haemodialysis is the treatment of choice for severe poisoning and should be considered in patients with plasma salicylate concentrations >700 mg/L (5.1 mmol/L), or lower concentrations associated with severe clinical or metabolic features. Patients under ten years or over 70 have increased risk of salicylate toxicity and may require dialysis at an earlier stage.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Nervous system, other analgesics and antipyretics – acetylsalicylic acid, ATC code: N02BA01

The therapeutic uses of Alka-Seltzer Original are based on the following pharmacological properties of the active ingredients. Acetylsalicylate has analgesic, anti-pyretic and anti-inflammatory properties. The buffer converts acetylsalicylic acid to sodium acetylsalicylate and promotes gastric emptying.

5.2 Pharmacokinetic properties

Acetylsalicylate is rapidly absorbed from the small intestine after oral ingestion of Alka-Seltzer Original and rapidly distributed to all body tissues. Peak plasma levels occur at approximately 20 minutes.

Excretion is mainly renal.

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 foetotoxic effects and impairment of learning ability in the offspring after prenatal exposure have been described.

6  PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Citric Acid
Sodium Hydrogen Carbonate

6.2 Incompatibilities

None known.

6.3 Shelf life

Shelf-life of the product as packaged for sale: 36 months.

6.4 Special precautions for storage

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

6.5 Nature and contents of container

Primary packaging consists of laminated paper/polyethylene/aluminium foil with surlyn heat foil or a direct printed lamination of aluminium and surlyn heat seal.

Aluminium foil pouches, each containing two tablets. Available in pack sizes of 2, 8, 10, 12, 20 or 30 tablets.
6.6 Special precautions for disposal

The tablets should not be removed from the foil pouches until immediately before use. If only one tablet from the foil pouch is used, the remaining one should be disposed of.

If a foil pouch is damaged and/or the tablets are powdery or discoloured, they should not be used. However, in the event that tablets are used, they are not harmful.

Alka-Seltzer Original must not be used after the expiry date.

Keep out of the reach of children.

7 MARKETING AUTHORISATION HOLDER
Bayer PLC
Bayer House
Strawberry Hill
Newbury, Berkshire
RG14 1JA

8 MARKETING AUTHORISATION NUMBER(S)
PL 00010/0511

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORITY
Original date of grant: 10 June 1988
Date of last renewal: 10 June 1993

10 DATE OF REVISION OF THE TEXT
15/12/2016