Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Disprin Direct 300 mg Orodispersible Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 300 mg acetylsalicylic acid.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Orodispersible tablet
A white circular flat tablet with odour and taste of lemon. On one surface indented with 'sword' motif, the other plain.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the relief of mild to moderate pain such as is associated with headache, toothache and neuralgia. Reduction of temperature. Reduction of inflammation such as in lumbago.

4.2 Posology and method of administration

The lowest effective dose should be used for the shortest duration necessary to relieve symptoms.

Posology
Adults and children 16 years and over: One to two tablets every 4-6 hours to a maximum of twelve tablets in 24 hours.

Do not give to children and adolescents aged under 16 years, except on medical advice, where the benefit outweighs the risk.

Aspirin must not be taken for longer than 3 days without consulting your doctor.

Hepatic Impairment: Patients with hepatic impairment should seek the advice of a doctor before taking this product (see sections 4.3 and 4.4).

Renal Impairment: Patients with renal impairment should seek the advice of a doctor before taking this product (see sections 4.3 and 4.4).

Elderly: There is no indication that dosage need be modified in the elderly. Non-steroidal anti-inflammatory drugs should be used with particular caution in elderly patients who are more prone to adverse events. The lowest dose compatible with adequate safe clinical control should be employed. See also Section 4.4.

Method of administration
For oral administration.
Disperses on the tongue without water.

4.3 Contraindications

Hypersensitivity to acetylsalicylic acid or to any of the excipients listed in section 6.1.

Hypersensitivity to other non-steroidal anti-inflammatory drugs.

History of gastrointestinal bleeding or perforation related to previous NSAIDs therapy.

Active, or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding).

Bleeding disorders including haemophilia.

Severe hepatic impairment.

Severe renal impairment.

Severe heart failure.

In patients under the age of 16 years owing to an association with Reye's Syndrome, unless specifically indicated.

Doses > 100mg/day during the third trimester of pregnancy (see section 4.6).

Breast-feeding (see section 4.6).

4.4 Special warnings and precautions for use

This product should be taken only when necessary.

Prolonged use except under medical advice can be harmful.

If the patient is on any medication consult the doctor or pharmacist before using.

Undesirable effects may be minimised by using the minimum effective dose for the shortest duration necessary to control symptoms (See section 4.2, and GI and cardiovascular risks below).

Gastrointestinal effects: NSAIDs should be given with care to patients with a history of gastrointestinal disease (ulcerative colitis, Crohn's disease, inflammatory bowel disease), peptic ulcers and gastro-oesophageal reflux disease (GORD) as their condition may be exacerbated (see section 4.8).

Gastrointestinal bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAIDs at any time during treatment, with or without any warning symptoms or a previous history of serious GI events.

The risk of GI bleeding, ulceration or perforation is higher with increasing NSAID doses, in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation (see section 4.3), and in the elderly. These patients should commence treatment on the lowest dose available. Combination therapy with protective agents (e.g. misoprostol or proton pump inhibitors) should be considered for these patients, and also for patients requiring concomitant low dose aspirin, or other drugs likely to increase gastrointestinal risk (see below and 4.5).

Patients with a history of GI toxicity, particularly when elderly, should report any unusual abdominal symptoms (especially GI bleeding) particularly in the initial stages of treatment.

When GI bleeding or ulceration occurs in patients receiving Disprin Direct, the treatment should be withdrawn.
Acetylsalicylic acid decreases platelet adhesiveness and increases bleeding time.

Caution should be advised in patients receiving concomitant medications which could increase the risk of ulceration or bleeding, such as oral corticosteroids, anticoagulants such as warfarin, selective serotonin reuptake inhibitors or anti-platelet agents such as clopidogrel and ticlopidine (see section 4.5).

Cardiovascular and cerebrovascular effects: Clinical trial and epidemiological data suggest that use of some NSAIDs (particularly at high doses and in long term treatment) may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke). There are insufficient data to exclude such a risk for aspirin when given at a daily dose of ≤3600mg. Caution (discussion with doctor or pharmacist) is required prior to starting treatment in patients with a history of hypertension and/or heart failure as fluid retention, hypertension, and oedema have been reported in association with NSAID therapy. Intracranial haemorrhage has been reported with acetylsalicylic acid use, caution should be implemented in patients with a history of other bleeding events (see section 4.8).

In patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency, aspirin may induce haemolysis or haemolytic anaemia. Factors that may increase the risk of haemolysis are high dosage, fever, or acute infections.

Patients with SLE and mixed connective tissue disease: may have an increased risk of developing aseptic meningitis when treated with NSAID's (see section 4.8).

Dermatological effects: Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, have been reported very rarely in association with the use of NSAIDs (see 4.8). Patients appear to be at highest risk of these reactions early in the course of therapy, the onset of the reaction occurring in the majority of cases within the first month of treatment. Disprin Direct should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Paediatric use: There is a possible association between acetylsalicylic acid 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 acetylsalicylic acid should not be given to children aged under 16 years unless specifically indicated.

Respiratory effects: 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.

Renal: Caution is advised in patients with renal impairment (see sections 4.3 and 4.8).

Hepatic: Caution is advised in patients with hepatic impairment (see sections 4.3 and 4.8).

Elderly: The elderly have an increased frequency of adverse reactions to NSAIDs especially gastrointestinal bleeding and perforation which may be fatal (see section 4.2) Unsupervised prolonged use of non-steroidal anti-inflammatory drugs in the elderly is not recommended.

Other NSAIDs: The use with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided (see section 4.5).

Impaired female fertility: There is some evidence that drugs which inhibit cyclooxygenase/ prostaglandin synthesis may cause impairment of female fertility by an effect on ovulation. This is reversible on withdrawal of treatment. (See section 4.6)

Patients with gout: The product should not be given to patients with gout, as serum urate may be increased, unless recommended by a healthcare professional.

Surgical procedures: Acetylsalicylic acid should generally be stopped several days before scheduled surgical procedures due to increased bleeding time.

If the patient suffers from asthma, has renal or hepatic impairment, or a history of peptic ulceration or inflammatory bowel disease, then a doctor should be consulted before taking the product.

4.5 Interaction with other medicinal products and other forms of interaction

None of the Disprin range of products should be taken in combination with other products containing aspirin.

Other NSAIDs or other salicylates including cyclooxygenase-2 selective inhibitors: Avoid concomitant use of two or more NSAIDs as this may increase the risk of adverse effects (see section 4.4).

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).

Corticosteroids: Increased risk of gastrointestinal ulceration or bleeding (see section 4.4).

Anti-platelet agents: increased risk of gastrointestinal bleeding (see section 4.4).

Selective serotonin reuptake inhibitors (SSRIs): increased risk of gastrointestinal bleeding (see section 4.4).

Calcium channel blockers: Reduced hypotensive effects, increased anti-platelet effects rarely resulting in prolonged bleeding time.

Cardiac glycosides: Non-steroidal anti-inflammatory drugs may exacerbate cardiac failure, reduce GFR and increase plasma cardiac glycoside levels.

Varicella vaccine: Avoid use of acetylsalicylic acid in varicella vaccine recipients due to a possible association with Reye's syndrome.

Antihypertensives (ACE inhibitors and Angiotensin II Antagonists) and diuretics: NSAIDs may reduce the effect of diuretics and other antihypertensive drugs. In some patients with compromised renal function (e.g. dehydrated patients or elderly patients with compromised renal function) the co-administration of an ACE inhibitor or Angiotensin II antagonist and agents that inhibit cyclo-oxygenase may result in further deterioration of renal function, including possible acute renal failure, which is usually reversible. These interactions should be considered in patients taking a coxib concomitantly with ACE inhibitors or angiotensin II antagonists. Therefore, the combination should be administered with caution, especially in the elderly. Patients should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy, and periodically thereafter. Diuretics can increase the risk of nephrotoxicity of NSAIDs.

Oral hypoglycaemic agents: Inhibition of metabolism of sulfonylurea drugs, prolonged half-life and increased risk of hypoglycaemia.

Anti-coagulants: NSAIDs may enhance the effects of anti-coagulants, such as warfarin (see section 4.4). It is considered unsafe to take non-steroidal anti-inflammatory drugs in combination with warfarin or heparin unless under direct medical supervision.

Cyclosporin: Increased risk of nephrotoxicity with NSAIDs

Tacrolimus: Possible increased risk of nephrotoxicity when NSAIDs are given with tacrolimus.

Zidovudine: Increased risk of haematological toxicity when NSAIDs are given with zidovudine.

Metoclopramide & domperidone: May increase the rate of absorption of acetylsalicylic acid.

Valproate: Acetylsalicylic acid may increase valproate levels resulting in valproate toxicity.

Quinolone antibiotics: Animal data indicate that NSAIDs can increase the risk of convulsions associated with quinolone antibiotics. Patients taking NSAIDs and quinolones may have an increased risk of developing convulsions.

Uricosurics: Acetylsalicylic acid may inhibit the effects of uricosurics.

Mifepristone: NSAIDs can reduce the effect of mifepristone.

Methotrexate: Decreased elimination of methotrexate.

Laboratory investigations: Acetylsalicylic acid may interfere with some laboratory tests used to measure urine glucose. Acetylsalicylic acid and other salicylates can interfere with thyroid function tests.

Lithium: Decreased elimination of lithium.

Aminoglycosides: Reduction in renal function in susceptible individuals, decreased elimination of aminoglycosides and increased plasma concentration.

Probenecid: Reduction in metabolism and elimination of NSAID and metabolites.

Carbonic anhydrase inhibitors e.g. Acetazolamide: May result in severe acidosis and increased central nervous system toxicity.

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 aspirin for cardioprotection.

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 specialised 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 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.

From the 20th week of pregnancy onward, acetylsalicylic acid 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 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. Antenatal monitoring for oligohydramnios and ductus arteriosus constriction should be considered after exposure to acetylsalicylic acid for several days from gestational week 20 onward. Acetylsalicylic acid 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-aggregating effect which may occur even at very low doses
- inhibition of uterine contractions resulting in delayed onset and prolonged labour

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

Breast-feeding

Use of the product is contraindicated in breast-feeding. Acetylsalicylic acid given in breast-feeding mothers may pose a risk of Reye's syndrome in nursing infants (see section 4.3).

Fertility

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

4.7 Effects on ability to drive and use machines

None stated.

4.8 Undesirable effects

Adverse events which have been associated with acetylsalicylic acid are given below, tabulated by system organ class and frequency. Frequencies are defined as: Very common (≥1/10); Common (≥1/100 and <1/10); Uncommon (≥1/1000 and <1/100); Rare (≥1/10,000 and <1/1000); Very rare (< 1/10,000); Not known (cannot be estimated from the available data). Within each frequency grouping, adverse events are presented in order of decreasing seriousness**.**

Adverse Events table

System Organ Class	Frequency	Adverse Events
Blood and Lymphatic System Disorders	Not known	Hypoprothrombinaemia, thrombocytopenia, aplastic anaemia, agranulocytosis, pancytopenia
Immune System Disorders	Not known	Hypersensitivity, pyrexia, urticaria, pruritus, angioedema[1], skin reaction
Metabolism and Nutrition Disorders	Not known	Sodium retention, fluid retention
Nervous System Disorders	Not known	Aseptic meningitis, headache, blurred vision, Haemorrhage intracranial
Cardiac Disorders	Not known	Cardiac failure, oedema
Vascular Disorders	Not known	Hypertension
Respiratory, Thoracic and Mediastinal Disorders	Not known	Bronchospasm, asthma, dyspnoea, rhinitis[1]
	Not known	Aspirin-exacerbated respiratory disease (AERD)
Gastrointestinal Disorders	Not known	Gastrointestinal disturbances[2], peptic ulcer, melaena, haematemesis, mouth ulceration, gastrointestinal perforation, abdominal pain, colitis[3], gastritis, gastrointestinal haemorrhage[4], flatulence
Hepatobiliary Disorders	Not known	Hepatotoxicity
Skin and Subcutaneous Tissue Disorders	Very Rare	Stevens-Johnson syndrome, toxic epidermal necrolysis,
	Not Known	rash[1]
Renal and Urinary Disorders	Not known	Blood uric acid increased, renal impairment
Investigations	Not known	Bleeding time prolonged, platelet adhesiveness decreased, hepatic enzyme increased

Description of Selected Adverse Reactions

[1]Hypersensitivity reactions may consist of (a) respiratory tract reactivity, including asthma, bronchospasm (potentially severe, even fatal) and dyspnoea; (b) various skin reactions, including urticaria, angioedema, pruritus, other skin eruptions, and more rarely bullous reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis.

[2]Gastrointestinal effects may include nausea, vomiting, dyspepsia, gastritis, diarrhoea, and constipation.

[3]exacerbation of colitis and Crohn's disease have been reported.

[4]Gastrointestinal blood losses leading to anaemia have been reported with non-steroidal anti-inflammatory drugs such as aspirin.

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
HPRA Pharmacovigilance. Website: www.hpra.ie.

4.9 Overdose

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

Features

Common features of overdose include restlessness, nausea, vomiting, dehydration, tinnitus, vertigo, deafness, sweating, warm extremities with bounding pulses, increased respiratory rate, fever, dizziness, 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 4 years. In children aged 4 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.

Gastrointestinal haemorrhage is frequent.

Uncommon features include haematemesis, 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. The symptoms can mimic those resulting from illness for which the drug was given. Irritability, lethargy, delayed unresponsiveness and encephalopathy may be seen one to three days following withdrawal of aspirin. At the same time, the concentration of salicylate in the CNS may be high, with non-toxic values in the serum.

In severe cases, respiratory failure is also possible.

Management
Give activated charcoal if an adult presents within 1 hour of ingestion of more than 125 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 salicylic excretion and may cause pulmonary oedema. Fluid and electrolyte management should be used to correct hypokalaemia, dehydration, acidosis and hyperpyrexia.
Haemodialysis is the treatment of choice for severe poisoning and should be considered in patients with plasma salicylate concentrations >700mg/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: Analgesics; **ATC Code:** N02BA01

Aspirin inhibits the cyclo-oxygenase enzyme involved in conversion of phospholipids to prostaglandins and its effects on the body are believed to result primarily from prevention of prostaglandin production. These effects include peripheral analgesia, fever reduction, reduction in inflammation and inhibition of platelet aggregation.

Experimental data suggests that ibuprofen may inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly. In one study, when a single dose of ibuprofen 400mg was taken within 8 h before or within 30 min after immediate release aspirin dosing 81mg, a decreased effect of ASA on the formation of thromboxane or platelet aggregation occurred. 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.

5.2 Pharmacokinetic properties

Aspirin is rapidly absorbed from the stomach and upper gastrointestinal tract with peak levels after around 20-30 minutes following dissolution. It is subject to first-pass metabolism with an overall bioavailability of around 70%. Metabolism is by conversion to salicylic acid and then by further conversion to other metabolites. These are excreted by the kidneys in both free and conjugated form. The plasma half-life of aspirin is around 15-20 minutes and that of salicylic acid is 2-3 hours.

5.3 Preclinical safety data

No preclinical findings of relevance have been reported.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glycine
Maize starch
Microcrystalline cellulose
Purified talc
Saccharin
Lemon flavour 51124

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

Vinyl coated heat sealed aluminium foils, 24 tablets to a carton.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Reckitt Benckiser Ireland Ltd
7 Riverwalk
Citywest Business Campus
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0979/007/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last renewal: 26th July 2008

10 DATE OF REVISION OF THE TEXT

June 2025