

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Anadin Extra Film-coated Tablets Aspirin 300mg Paracetamol 200mg Caffeine 45mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredients mg/tablet

Acetylsalicylic acid	300.0 mg
Paracetamol	200.0 mg
Caffeine	45.0 mg

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film coated tablet (tablet)

A capsule-shaped white tablet with a break bar on one side and with "A" and "E" debossed on the other side.

The scoreline is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the relief of pain of:

- Headache
- Neuralgia
- Myalgia
- Rheumatism
- Toothache
- Dysmenorrhoea
- Symptoms of the common cold or influenza

4.2 Posology and method of administration

Posology

Adults and adolescents over 16 years:

1-2 tablets every 4 hours with a maximum of 6 in any 24 hour period.

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

The Elderly

Dosage is as above.

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

Treatment should be reviewed at regular intervals and discontinued if no benefit is seen or intolerance occurs.

Method of Administration: Oral.

4.3 Contraindications

- Hypersensitivity to the active ingredients or any of the excipients listed in section 6.1. Patients with a history of hypersensitivity reactions (e.g. bronchospasm, rhinitis, urticaria) in response to Anadin Extra, aspirin or other non-steroidal anti-inflammatory drugs or any of the other constituents.
- Bleeding disorders, concurrent anti-coagulant therapy.
- Children, adolescents under 16 years
- Breast feeding because of a possible risk of Reye's syndrome (see section 4.6).
- 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)
- Severe heart failure
- Severe renal failure
- Severe hepatic failure
- The last trimester of pregnancy

4.4 Special warnings and precautions for use

- The use of Anadin Extra Tablets with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided.
- In patients suffering from severe glucose-6-phosphate dehydrogenase (G6PD) deficiency, aspirin is known to rarely cause haemolytic anaemia.
- This product should not be taken with any other paracetamol containing products.
- Immediate medical advice should be sought in the event of overdose, even if the patient feels well because of the risk of irreversible liver damage.
- The hazards of overdose are greater in those with non-cirrhotic liver disease.
- Undesirable effects may be minimized by using the minimum effective dose for the shortest duration necessary to control symptoms.
- This product should be used only when clearly necessary.
- The stated dose should not be exceeded.
- 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).Gastrointestinal bleeding, ulceration and perforation: GI bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAIDs at anytime during treatment, with or without warning symptoms or a previous history of serious GI events.
- The risk if 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.
- 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 aspirin (see section 4.5).
- When GI bleeding or ulceration occurs in patients receiving Anadin Extra Tablets, the treatment should be withdrawn.
- NSAIDs should be given with care to patients with a history of gastrointestinal disease (ulcerative colitis, Crohn's disease) as their condition may be exacerbated (see sections 4.8 – undesirable effects).
- Patients with a history of, inflammatory bowel disease, coagulation disorders, asthma or allergic disease should consult a doctor before using this product.
- Aspirin may induce asthmatic attacks in hypersensitive 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 and adolescents aged under 16 years unless specifically indicated.
- Prolonged use except under medical supervision can be harmful. If symptoms persist the physician should be consulted.

- If the patient is taking any other medications or is under the care of a doctor he/she should consult the doctor before using.
- In patients with renal, cardiac or hepatic impairment, caution is required since the use of NSAIDs may result in deterioration of renal function. Assessment of renal function should occur prior to the initiation of therapy and regularly thereafter.
- As NSAIDs can interfere with platelet function, they should be used with caution in patients with intracranial haemorrhage and bleeding diathesis.
- 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.
- 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 NSAID therapy.
- 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. Anadin Extra Tablets should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Patients should be advised that Paracetamol may cause severe skin reactions. If a skin reaction such as skin reddening, blisters, or rash occurs, they should stop use and seek medical assistance right away.

4.5 Interaction with other medicinal products and other forms of interactions

ASPIRIN

Care should be taken in patients treated with any of the following drugs as interactions have been reported:

Anti-coagulants: It is considered unsafe to take NSAIDs in combination with warfarin or heparin unless under direct medical supervision as NSAIDs may enhance the effects of anti-coagulants.

Experimental data suggest that ibuprofen may inhibit the effect of low dose aspirin 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).

Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs): increased risk of gastrointestinal bleeding (see section 4.4).

Anti-hypertensives: Reduced anti-hypertensive effect.

Diuretics: Reduced diuretic effect. Diuretics can increase the risk of nephrotoxicity of NSAIDs.

Cardiac Glycosides: NSAIDs may exacerbate cardiac failure, reduce GFR and increase plasma cardiac glycoside levels.

Lithium: Decreased elimination of lithium.

Methotrexate: In animal experiments non-steroidal anti-inflammatory drugs (NSAIDs) including salicylic acid caused reduction of tubular methotrexate secretion and consequently increased its toxic effects. However, in clinical studies, where NSAIDs and salicylic acid were given as concomitant medicinal products to patients with rheumatoid arthritis, no increase of adverse reactions was observed. Treatment of rheumatoid arthritis with such drugs can be continued during low-dose methotrexate therapy but only under close medical supervision.

Cyclosporin: Increased risk of nephrotoxicity with NSAIDs.

Other NSAIDs: Avoid concomitant use of two or more NSAIDs.

Corticosteroids: Increased risk of gastrointestinal bleeding and ulceration.

Aminoglycosides: Reduction in renal function in susceptible individuals. Decreased elimination of aminoglycoside and increased plasma concentrations.

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

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

Metoclopramide: Metoclopramide increases the rate of absorption of aspirin. However, concurrent use need not be avoided.

Phenytoin: The effect of phenytoin may be enhanced by aspirin. However, no special precautions are needed.

Valproate: The effect of valproate may be enhanced by aspirin.

PARACETAMOL

Cholestyramine: The absorption of paracetamol is reduced by cholestyramine. Therefore cholestyramine should not be taken within one hour if maximal analgesia is required.

Metoclopramide and Domperidone: The absorption of paracetamol is increased by metoclopramide and domperidone. However, concurrent use need not be avoided.

Warfarin: Potentiation of warfarin with continual high dosage of paracetamol.

Chloramphenicol: Increased plasma concentration of chloramphenicol.

4.6 Fertility, pregnancy and lactation

Pregnancy

As with all other drugs, aspirin and paracetamol should only be used during pregnancy after strict risk-benefit evaluation.

Paracetamol

A large amount of data on pregnant women indicate neither malformative, nor feto/neonatal toxicity. Epidemiological studies on neurodevelopment in children exposed to paracetamol in utero show inconclusive results. If clinically needed, paracetamol can be used during pregnancy however it should be used at the lowest effective dose for the shortest possible time and at the lowest possible frequency.

Acetylsalicylic acid

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 have the following effects:
On the foetus:

- cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension);
- renal dysfunction, which may progress to renal failure with oligo-hydroamniosis;

On the mother and the neonate,

- at the end of pregnancy, 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 is contraindicated during the third trimester of pregnancy.

Caffeine

Pregnant women are advised to limit caffeine intake to no more than 200 mg per day. Lowering daily caffeine intake during pregnancy is recommended to reduce the risk of pregnancy loss and low birth weight neonates.

Breast-feeding

Aspirin appears in breast milk and regular high doses may affect neonatal clotting. Not recommended while breast feeding due to possible risk of Reye's Syndrome as well as neonatal bleeding due to hypoprothrombinaemia.

Caffeine appears in breast milk. Irritability and poor sleeping pattern in the infant have been reported.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

Adverse reactions are listed below as MedDRA preferred term by system organ class and frequency. Frequencies are defined as: very common (>1/10), common ($\geq 1/100$ and <1/10), uncommon ($\geq 1/1000$ and <1/100) Rare ($\geq 1/10,000$ to <1/1,000), Very rare (<1/10,000) and not known (cannot be estimated from the available data).

System organ class	Frequency	Adverse reactions
Gastrointestinal disorders	Common ($\geq 1/100$ to <1/10)	Peptic ulcers, perforation or GI bleeding, sometimes fatal in the elderly, may occur (see section 4.4). Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease (see section 4.4 – Special warnings and precautions for use) have been reported following administration. Less frequently, gastritis has been observed.
	Not known	
Skin and subcutaneous tissue disorders	Very rare (<1/10,000)	Skin reactions in hypersensitive patients Serious skin reactions (including severe cutaneous reactions such as Stevens-Johnson Syndrome, Toxic Epidermal Necrolysis, and Acute Generalised Exanthematous Pustulosis) have been reported.
Respiratory, thoracic and mediastinal disorders	Not known	Bronchospasm, rhinitis particularly in patients hypersensitive to NSAIDs.
Blood and lymphatic system disorders	Not known	Isolated reports of thrombocytopenia purpura, methaemoglobinaemia and agranulocytosis have occurred after paracetamol use Anaemia, Aplastic Anaemia, Pancytopenia.
	Very rare (<1/10,000)	
Immune system disorders	Not known	Hypersensitivity reactions. Acetylsalicylic acid may precipitate gout in susceptible individuals.

Cardiac disorders	Not known	Cardiac failure and oedema have been reported in association with NSAID treatment. High doses of caffeine can cause palpitations.
Vascular disorders	Not known	Hypertension
Hepatobiliary disorders	Not known	There is a possible risk of Reye's Syndrome in children under 16 years.
Musculoskeletal and connective tissue disorders	Not known	High doses of caffeine can cause tremor
Renal and Urinary disorders	Not known	The following have been reported with prolonged use or overdosage, hepatic necrosis, acute pancreatitis, nephrotoxicity. These side effects are not expected when the product is used as intended.

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 HPRC Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

This product contains both paracetamol and aspirin, and as such, any overdose events should be assessed using information available on both active substances.

Paracetamol:

Paracetamol overdose can result in liver damage which may be fatal.

Symptoms generally appear within the first 24 hours and may comprise: nausea, vomiting, anorexia, pallor, and abdominal pain, or patients may be asymptomatic.

Overdose of paracetamol can cause liver cell necrosis likely to induce complete and irreversible necrosis, resulting in hepatocellular insufficiency, metabolic acidosis and encephalopathy which may lead to coma and death. Simultaneously, increased levels of hepatic transaminases (AST, ALT), lactate dehydrogenase and bilirubin are observed together with increased prothrombin levels that may appear 12 to 48 hours after administration.

Liver damage is likely in patients who have taken more than the recommended amounts of paracetamol. It is considered that excess quantities of toxic metabolite become irreversibly bound to liver tissue.

Liver damage may become apparent 12 to 48 hours after ingestion and this may be manifested in increasing pro-thrombin time, which is a reliable indicator of deteriorating liver function. Abnormalities of glucose metabolism and metabolic acidosis may occur. In severe poisoning, hepatic failure may progress to encephalopathy, coma and death. Acute renal failure with acute tubular necrosis may develop even in the absence of severe liver damage.

Cardiac arrhythmias and pancreatitis have been reported.

Liver damage is likely in adults who have taken 10g or more of paracetamol but has also occurred at doses lower than this. It is considered that excess quantities of toxic metabolite (usually adequately detoxified by glutathione when normal doses of paracetamol are ingested) become irreversibly bound to liver tissue.

Some patients may be at increased risk of liver damage from paracetamol toxicity:
Risk factors include;

- Patients with liver disease

- Elderly patients
- Young children
- Patients receiving long-term treatment with carbamazepine, phenobarbitone, phenytoin, primidone, rifampicin, St John's Wort or other drugs that induce liver enzymes.
- Patients who regularly consume ethanol in excess of recommended amounts
- Patients with glutathione depletion e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia
- Acute renal failure with acute tubular necrosis may also develop.
- Cardiac arrhythmias and pancreatitis have also been reported.

Emergency Procedure:

Immediate transfer to hospital.

Blood sampling to determine initial paracetamol plasma concentration. In the case of a single acute overdose, paracetamol plasma concentration should be measured 4 hours post ingestion. Administration of activated charcoal should be considered if the overdose of paracetamol has been ingested within the previous hour.

The antidote N-acetylcysteine, should be administered as soon as possible in accordance with national treatment guidelines.

Symptomatic treatment should be implemented.

Aspirin (Salicylates):

Treatment with activated charcoal should be considered if salicylate plasma concentration is greater than 250mg/kg.

Plasma salicylate concentrations 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 of aspirin is increased by urinary alkalinisation, which is achieved by the administration of 1.26% sodium bicarbonate. The urine pH should be monitored.

Metabolic acidosis should be corrected 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 10 years or over 70 years of age may be at an increased risk of salicylate toxicity and may require dialysis at an earlier stage.

Severe intoxication from heavy overdosage is shown by hyperventilation, fever, restlessness, ketosis, respiratory alkalosis, metabolic acidosis and convulsions. Gastrointestinal haemorrhage is frequent in overdose.

Emergency Procedure:

Immediate transfer to hospital.

A worthwhile recovery of salicylates can be achieved up to 24 hours after ingestion. Treatment must be in hospital where plasma salicylate pH and electrolytes can be measured. Fluid losses are replaced and forced alkaline diuresis is considered when the plasma salicylate concentration is greater than 500mg/litre (3.6 mmol/litre) in adults or 300mg/litre (2.2mmol/litre) in children.

Caffeine:

Treatment of caffeine overdose is primarily symptomatic and supportive. Diuresis should be treated by maintaining fluid and electrolyte balance and CNS symptoms can be controlled by intravenous administration of diazepam.

5 PHARMACOLOGICAL PROPERTIES

ATC code: N02BA51

Pharmacotherapeutic group: Other analgesics and antipyretics.

5.1 Pharmacodynamic properties

ASPIRIN

Mechanisms of action effect

Salicylates inhibit the activity of the enzyme cyclo-oxygenase to decrease the formation of precursors of prostaglandins and thromboxanes from arachidonic acid. Although many of the therapeutic effects may result from inhibition of prostaglandin synthesis (and consequent reduction of prostaglandin activity) in various tissues, other actions may also contribute significantly to the therapeutic effects.

Analgesic

Produces analgesia through a peripheral action by blocking pain impulse generation and via a central action, possibly in the hypothalamus.

Anti-inflammatory (Nonsteroidal)

Exact mechanisms have not been determined. Salicylates may act peripherally in inflamed tissue probably by inhibiting the synthesis of prostaglandins and possibly by inhibiting the synthesis and/or actions of other mediators of the inflammatory response.

Antipyretic

May produce antipyresis by acting centrally on the hypothalamic heat regulating centre to produce peripheral vasodilation resulting in increased cutaneous blood flow, sweating and heat loss.

PARACETAMOL

Mechanism of action/effect

Analgesic

The mechanism of analgesic action has not been fully determined. Paracetamol may act predominately by inhibiting prostaglandin synthesis in the central nervous system (CNS) and, to a lesser extent, through a peripheral action by blocking pain impulse generation.

The peripheral action may also be due to inhibition of prostaglandin synthesis or inhibition of the synthesis or actions of other substances that sensitise pain receptors to mechanical or chemical stimulations.

Antipyretic

Paracetamol probably produces antipyresis by acting centrally on the hypothalamic heat-regulation centre to produce peripheral vasodilation resulting in increased blood flow through the skin, sweating and heat loss. The central action probably involves inhibition of prostaglandin synthesis in the hypothalamus.

CAFFEINE

Mechanisms of action / effect

Central nervous system stimulant

Caffeine stimulates all levels of the CNS, although its cortical effects are milder and of shorter duration than those of amphetamines.

Analgesia adjunct

Caffeine constricts cerebral vasculature with an accompanying decrease in the cerebral blood flow and in the oxygen tension of the brain. It is believed that caffeine helps to relieve headache by providing more rapid onset of action and/or enhanced pain relief with lower doses of analgesic. Recent studies with ergotamine indicate that the enhancement of effect by the addition of caffeine may also be due to improved gastrointestinal absorption of ergotamine when administered with caffeine.

Experimental data suggest 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****Absorption and Fate**

Absorption is generally rapid and complete following administration. It is largely hydrolysed in the gastrointestinal tract, liver and blood to salicylate which is further metabolised primarily in the liver.

PARACETAMOL**Absorption and Fate**

Paracetamol is readily absorbed from the gastro-intestinal tract with peak plasma concentrations occurring about 30 minutes to 2 hours after ingestion. It is metabolised in the liver and excreted in the urine mainly as the glucuronide and sulfate conjugates. Less than 5% is excreted as unchanged paracetamol. The elimination half-life varies from about 1 to 4 hours. Plasma-protein binding is negligible at usual therapeutic concentrations but increases with increasing concentrations.

A minor hydroxylated metabolite which is usually produced in very small amounts by mixed-function oxidases in the liver and which is usually detoxified by conjugation with liver glutathione may accumulate following paracetamol overdosage and cause liver damage.

CAFFEINE**Absorption and Fate**

Caffeine is completely and rapidly absorbed after oral administration with peak concentrations occurring between 5 and 90 minutes after dose in fasted subjects. There is no evidence of presystemic metabolism. Elimination is almost entirely by hepatic metabolism in adults.

In adults, marked individual variability in the rate of elimination occurs. The mean plasma elimination half life is 4.9 hours with a range of 1.9 - 12.2 hours. Caffeine distributes into all body fluids. The mean plasma protein binding of caffeine is 35%.

Caffeine is metabolised almost completely via oxidation, demethylation, and acetylation and is excreted in the urine. The major metabolites are 1-methylxanthine, 7-methylxanthine, 1,7-dimethylxanthine (paraxanthine). Minor metabolites include 1-methyluric acid and 5-acetylamino-6-formylamion, 3-methyluracil (AMFU).

5.3 Preclinical safety data

Conventional studies using the currently accepted standards for the evaluation of toxicity to reproduction and development are not available.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:

Maize starch
Microcrystalline cellulose
Hydrogenated vegetable oil (Sterotex)
Pregelatinised starch
Povidone

Tablet coat:

Hypromellose (Methocel E5)
Hypromellose (Methocel E15)
Macrogol (Carbowax 3350)

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 (to protect from moisture).

6.5 Nature and contents of container

Cartons containing uPVC/Aluminium blister strip - 6, 8, 12 and 24 tablets.

Not all pack sizes may be marketed.

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

Pfizer Healthcare Ireland
9 Riverwalk
National Digital Park
Citywest Business Campus
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0822/166/001

10 February 2020

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9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 28 February 1984

Date of last renewal: 28 February 2009

10 DATE OF REVISION OF THE TEXT

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