Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Actiprofen 200 mg tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Ibuprofen 200 mg

Excipient: Contains 50mg lactose. Printing ink contains carmoisine (E122).

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Film-Coated Tablet

White, capsule-shaped film coated tablet with flat edges printed with the name 'Actiprofen' in red on one face.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the short term management of mild to moderate pain such as is associated with rheumatic and muscular pain, backache, neuralgia, migraine, headache, dental pain, dysmenorrhoea, feverishness, symptoms of cold and influenza.

4.2 Posology and method of administration

Do not exceed the stated dose
Tablets should be swallowed with water. Preferably with or after food.

Adults, elderly and children aged 12 years and over:
Dosage: The usual initial dose is 400mg and subsequently, if necessary, 200- 400mg every 4 – 6 hours. Maximum dose is 1200mg in divided doses in a 24 hour period. Do not take more often than every 4 - 6 hours.

Undesirable effects may be minimized by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.4).
Patients should consult a doctor if symptoms persist or worsen or if the product is required for more than 3 days for fever and 10 days for pain.
Treatment should be reviewed at regular intervals and discontinued if no benefit is seen or intolerance occurs.

Children 12 - 18 years: If this medicinal product is required for more than 3 days, or if symptoms worsen a doctor should be consulted.

This product is not suitable for use in children under 12 years of age.

Elderly
NSAIDS 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.

Renal Impairment:
Patients with renal impairment (GFR >15 mL/min/1.73m2) must seek medical advice before taking this medication (see section 4.3, 4.4)

Hepatic Impairment:
Patients with hepatic impairment must seek medical advice before taking this medication. (see section 4.3, 4.4).

Established cardiovascular disease or significant cardiovascular risk factors:
Patients with established cardiovascular disease (congestive heart failure, established ischemic heart disease, peripheral arterial disease), uncontrolled hypertension or significant risk factors for cardiovascular disease (e.g. hypertension, hyperlipidemia, diabetes mellitus, and smoking) should be treated with ibuprofen only after careful consideration.

4.3 Contraindications

History of gastrointestinal bleeding or perforation, related to previous NSAID therapy.
Active or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding).

Patients with severe hepatic, renal (GFR <15mL/mi/1.73m2) or severe heart failure (NYHA Class IV).

Patients with a history of hypersensitivity reactions (e.g. bronchospasm, rhinitis, urticaria) in response to ibuprofen, aspirin or non-steroidal anti-inflammatory drugs.

Use in children under 12 years of age.

Use with concomitant NSAIDs including cyclo-oxygenase-2 selective inhibitors.

Third trimester of pregnancy.

4.4 Special warnings and precautions for use

Do not exceed the stated dose.

If symptoms persist or worsen, medical advice must be sought.

Undesirable effects may be minimized by using the minimum effective dose for the shortest possible duration necessary to control symptoms.

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). Prolonged use of NSAIDs in the elderly is not recommended. Where prolonged therapy is required, patients should be reviewed regularly.

Masking of symptoms of underlying infections:
Like other NSAIDs, Actiprofen can mask the signs and symptoms of infection due to its anti-inflammatory, analgesic and anti-pyretic properties. This may lead to delayed initiation of appropriate treatment and thereby worsening the outcome of the infection. This has been observed in bacterial community acquitted pneumonia and bacterial complications to varicella. When Actiprofen is administered for fever or pain relief in relation to infection, monitoring of infection is advised. In non-hospital settings, the patient should consult a doctor if symptoms persist or worsen.

Gastrointestinal effects: 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 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. As with all NSAIDs, including ibuprofen, prescribers should exercise caution and ensure regular follow-ups when prescribing ibuprofen in patients with symptoms indicative of gastrointestinal (GI) disorders. 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 section 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 Actiprofen 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 section 4.8 – undesirable effects).

Hepatic effect:
Caution and regular follow-up by prescriber is recommended in case of use of ibuprofen in patients with impaired hepatic function, as their condition may be exacerbated (see section 4.3).

Renal effects:
In patients with renal, cardiac or hepatic impairment, caution is required since the use of NSAIDs may result in deterioration of renal function. As fluid retention and oedema have been reported in association with NSAIDs, including ibuprofen, caution is required in patients with impaired cardiac or renal function, history of hypertension, the elderly, patients receiving concomitant treatment with diuretics or medicinal products that can significantly impact renal function, and in those patients with substantial extracellular volume depletion from any cause, e.g. before or after major surgery (see section 4.3). Monitoring of renal function is recommended as a precautionary measure when using ibuprofen in such cases. Discontinuation of NSAID therapy is usually followed by recovery to the pre-treatment state.

Pre-existing asthma:
Bronchospasm may be precipitated in patients suffering from or with a previous history of asthma or allergic disease or nasal polyps.

SLE and mixed connective tissue disease:
Use with caution in patients with Systemic Lupus Erthematosus and mixed connective tissue disease due to increased risk of aseptic meningitis.

As NSAIDs can interfere with platelet function, they should be used with caution in patients with intracranial haemorrhage and bleeding diathesis.

Undesirable effects may be minimised using the lowest effective dose for the shortest duration necessary to control symptoms (see GI cardiovascular risks below).

Cardiovascular and cerebrovascular effects:

Clinical studies suggest that use of ibuprofen, particularly at a high dose (2400 mg/day) and in long term treatment may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke). Overall, epidemiological studies do not suggest that low dose ibuprofen (e.g. ≤ 1200 mg/day) is associated with an increased risk of arterial thrombotic events.

Patients with uncontrolled hypertension, congestive heart failure (NYHA II-IV), established ischaemic heart diseases, peripheral arterial disease, and/or cerebrovascular disease should only be treated with Ibuprofen after careful consideration and high doses of ibuprofen (2400 mg/day) should be avoided.
Careful consideration should also be exercised before initiating long-term treatment of patients with risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking), particularly if high doses of ibuprofen (2400 mg/day) are required.

Serious skin reactions:
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 section 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. Acute generalised exanthematous pustulosis (AGEP) has been reported in relation to ibuprofen-containing products. Actiprofen tablets should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose- galactose malabsorption should not take this medicine.

Exceptionally, varicella can be at the origin of serious cutaneous and soft tissue infectious complications. To date, the contributing role of NSAIDs in the worsening of these infections cannot be ruled out thus it is advisable to avoid use of Actiprofen 200mg Tablets in case of varicella.

Keep out of sight and reach of children.

There is a risk of renal impairment in dehydrated adolescents.

4.5 Interaction with other medicinal products and other forms of interaction

Acetylsalicyclic acid
Concomitant administration of ibuprofen and acetylsalicyclic acid is not generally recommended because of the potential of increased adverse effects.

Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose acetylsalicyclic acid on platelet aggregation when they are dosed concomitantly. Although there are uncertainties regarding extrapolation of these data to the clinical situation, the possibility that regular, long-term use of ibuprofen may reduce the cardioprotective effect of low dose acetylsalicylic acid cannot be excluded. No clinically relevant effect is considered to be likely for occasional ibuprofen use (see section 5.1).

Ibuprofen should not be used in combination with other non-steroidal anti-inflammatory drugs (NSAIDs) including aspirin and cyclo-oxygenase-2 specific inhibitors as these may increase the risk of adverse effects.

Ibuprofen may inhibit the anti-platelet effect of aspirin. Patients under anti-platelet treatment with aspirin should be instructed to consult their doctor or pharmacist before taking ibuprofen.

Ibuprofen should be used with caution in combination with the following drugs as interactions have been reported:

Concomitant medication	**Drug interaction**
Anticoagulants	NSAIDs may enhance the effects of anti-coagulants, such as warfarin or heparin (see section 4.4).
Aminoglycosides	Reduction in renal function in susceptible individuals, decreased elimination of aminoglycoside and increased plasma concentrations.
Diuretics and antihypertensive agents	Like other NSAIDs, concomitant use of ibuprofen with diuretics or antihypertensive agents (e.g. beta-blockers, angiotensin converting enzyme (ACE) inhibitors) may cause a decrease in their antihypertensive effect. Therefore, the combination should be administered with caution and patients, especially the elderly, should have their blood pressure periodically monitored. Patients should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy and periodically thereafter, particularly for diuretics and ACE inhibitors due to the increased risk of nephrotoxicity. Concomitant treatment with potassium-sparing drugs may be associated with increased serum potassium levels, which should therefore be monitored frequently.
Anti-platelet agents	Increased risk of gastrointestinal bleeding (see section 4.4).
Digoxin	May exacerbate cardiac failure, reduce GFR and increase plasma cardiac glycoside levels. Monitoring of the serum glycoside levels is recommended.
Corticosteroids	May increase risk of adverse reactions in the gastrointestinal tract.
Cyclosporin	Increased risk of nephrotoxicity
CYP2C9 Inhibitors	Concomitant administration of ibuprofen with CYP2C9 inhibitors may increase the exposure to ibuprofen (CYP2C9 substrate). In a study with voriconazole and fluconazole (CYP2C9 inhibitors), an increased S(+)-ibuprofen exposure by approximately 80 to 100% has been shown. Reduction of the ibuprofen dose should be considered when potent CYP2C9 inhibitors are administered concomitantly, particularly when high-dose ibuprofen is administered with either voriconazole or fluconazole.
Hypoglycemic agents	Inhibition of metabolism of sulfonylurea drugs, (oral) prolonged half-life and increased risk of hypoglycaemia. In case of concomitant use with ibuprofen, monitoring of the blood glucose level is recommended.
Lithium	There is evidence for potential increases in plasma levels if lithium. Monitoring of the serum lithium level is recommended.

Methotrexate	There is evidence of increases in plasma levels of methotrexate and increase in its toxic effect. In case of concomitant use with ibuprofen, renal function should be monitored.
Other NSAIDs	Avoid concomitant use of two or more NSAIDs.
Probenecid	Reduction in metabolism and elimination of NSAID and metabolites.
Quinolones	NSAIDs can increase the risk of convulsion associated with quinolone antibiotics.
Selective serotonin	Increased risk of gastrointestinal bleeding (see section 4.4) (SSRIs).
Zidovudine	Increased risk of haemerthroses and haematoma in HIV (+) haemophiliacs.

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).

4.6 Fertility, pregnancy and lactation

Fertility

There are no adequate data from the use of ibuprofen in women of childbearing potential. 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 upon withdrawal of treatment *(see section 4.4)*. Caution should be exercised when used by women of childbearing potential.

Pregnancy

From the 20th week of pregnancy onward, Actiprofen 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, Actiprofen should not be given unless clearly necessary. If Actiprofen 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 Actiprofen for several days from gestational week 20 onward. Actiprofen 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 (with 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 or prolonged labour.
Consequently, Actiprofen is contraindicated during the third trimester of pregnancy (see sections 4.3 and 5.3).

Lactation

Ibuprofen is excreted in breast milk in very low concentrations and is considered unlikely to affect the breast-fed infant adversely.

4.7 Effects on ability to drive and use machines

Patients should be advised not to drive or operate machinery if affected by drowsiness or dizziness.

4.8 Undesirable effects

Adverse reactions reported from extensive post-marketing experience are tabulated below by System Organ Class and frequency. The following convention has been utilised for the classification of undesirable effects: very common (≥1/10), common (≥1/100, <1/10), uncommon (≥1/1,000, <1/100), rare (≥1/10,000, <1/1000), very rare (<1/10,000), not known (cannot be estimated from available data).

The following list of adverse effects relates to those experienced with ibuprofen at OTC doses, for short-term use. In treatment of chronic conditions, under long-term treatment, additional adverse effects may occur.

Body System	Undesirable Effect	Frequency
Gastrointestinal disorders	Abdominal pain, nausea and dyspepsia.	Uncommon
	Diarrhoea, flatulence, constipation and vomiting.	Rare
	Peptic ulcer, perforation or gastrointestinal haemorrhage, sometimes fatal, particularly in the elderly. Exacerbation of ulcerative colitis and Crohn's disease.	Very rare
	Intestinal diaphragm disease	Not known
Nervous system disorders	Headache, drowsiness, dizziness, hearing disturbance (tinnitus).	Common
Renal and urinary disorders	Acute renal failure, papillary necrosis, especially in long-term use, associated with increased serum urea and oedema.	Very rare
Hepatobiliary disorders	Liver disorders, hepatic failure, hepatitis.	Very rare
Blood and lymphatic system disorders	Haematopoietic disorders (anaemia, leucopenia, thrombocytopenia, pancytopenia, agranulocytosis). First signs are: fever, sore throat, superficial mouth ulcers, flu-like symptoms, severe exhaustion, unexplained bleeding and bruising).	Very rare
Skin and subcutaneous tissue disorders	Skin rashes.	Uncommon
	Severe forms of skin reactions, exfoliative and bullous dermatoses, such as erythema multiforme and epidermal necrolysis can occur (Stevens-Johnson Syndrome).	Very rare
	Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome)	Not known
	Acute generalised exanthematous pustulosis (AGEP)	Not known
	Photosensitivity reactions	Not known
Immune system disorders	Hypersensitivity reactions including: • Urticaria and pruritus. • Severe hypersensitivity reactions. Symptoms could be: facial, tongue and laryngeal swelling, dyspnoea, tachycardia, hypotension (anaphylaxis, angioedema or severe shock). • Exacerbation of asthma and bronchospasm.	Very rare
Others with unknown frequency	Oedema, hypertension, and cardiac failure, have been reported in association with NSAID treatment. In patients with existing auto-immune disorders (such as systemic lupus erythematosus, mixed connective tissue disease) during treatment with ibuprofen, single cases of symptoms of aseptic meningitis, such as stiff neck, headache, nausea, vomiting, fever or disorientation have been observed.	Not known
Eye disorder	Visual disturbances	Rare
Cardiac disorder	Myocardial infarction	Not known

Melaena, haematemesis, ulcerative stomatitis and gastritis also have been reported.

Clinical studies suggest that use of ibuprofen, particularly at high dose (2400 mg/day) may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke) (see section 4.4)

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, 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

In children ingestion of more than 400 mg/kg may cause symptoms. In adults the dose response effect is less clear cut. The half-life in overdose is 1.5 - 3 hours.

Signs and Symptoms
Most patients who have ingested clinically important amounts of NSAIDs will develop no more than nausea, vomiting, epigastric pain, or more rarely diarrhoea. Tinnitus, headache and gastrointestinal bleeding are also possible. In more serious poisoning, toxicity is seen in the central nervous system, manifesting as drowsiness, occasionally excitation and disorientation or coma. Occasionally patients develop convulsions. In serious poisoning metabolic acidosis may occur and the prothrombin time/INR may be prolonged, probably due to interference with the actions of circulating clotting factors. Acute renal failure and liver damage may occur. Exacerbation of asthma is possible in asthmatics.

Treatment
Further management should be as clinically indicated or as recommended by the national poisons centre, where available. Treatment should be symptomatic and supportive and include the maintenance of a clear airway and monitoring of cardiac and vital signs until stable. If frequent or prolonged, convulsions should be treated with intravenous diazepam or lorazepam. Give bronchodilators for asthma.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Ibuprofen has analgesic, antipyretic and anti-inflammatory properties. Ibuprofen inhibits prostaglandin synthesis.

Experimental data suggest that ibuprofen may competitively inhibit the effect of low dose acetylsalicylic acid on platelet aggregation when they are dosed concomitantly. Some pharmacodynamic studies show that when single doses of ibuprofen 400 mg were taken within 8 h before or within 30 min after immediate release acetylsalicylic acid dosing (81 mg), a decreased effect of acetylsalicylic acid on the formation of thromboxane or platelet aggregation occurred. Although there are uncertainties regarding extrapolation of these data to the clinical situation, the possibility that regular, long-term use of ibuprofen may reduce the cardio protective effect of low-dose acetylsalicylic acid cannot be excluded. No clinically relevant effect is considered to be likely for occasional ibuprofen use (see section 4.5).

5.2 Pharmacokinetic properties

Ibuprofen is rapidly absorbed following administration and is rapidly distributed throughout the whole body. The excretion is both rapid and complete via the kidneys.

Maximum plasma concentrations are reached approximately 1.5 hours after ingestion if taken on an empty stomach.

The half life of ibuprofen is about two hours.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet Core
Lactose monohydrate
Microcrystalline cellulose
Maize starch
Croscarmellose sodium
Magnesium stearate
Silicon dioxide

Film-Coat
Hypromellose
Triacetin

Printing Ink
Carmoisine (E122)
Hypromellose

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

PVC/Aluminium blisters in cardboard cartons containing 4, 6, 12, 24, 48, 96 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

Haleon Ireland Limited
12 Riverwalk
Citywest Business Campus
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8 MARKETING AUTHORISATION NUMBER

PA0678/061/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

May 2023