

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Ibuprofen Azevedos 20 mg/ml Oral Suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml of oral suspension contains 20 mg of Ibuprofen, as active substance.

Excipients with known effect:

Glycerol - 50 mg/ml

Azorrubine (E 122) - 0.015 mg/ml

Maltitol - 500 mg/ml

Sodium – 3.590 mg/ml (as sodium chloride, sodium benzoate, sodium citrate, sodium saccharin.)

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral Suspension.

Viscous suspension, pink coloured with a characteristic strawberry flavour.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

- symptomatology associated with flu states and colds (fever and pain);
- odynophagia and pharyngitis;
- mild to moderate headaches;
- mild to moderate muscle aches;
- bruises;
- fever (not more than 3 days);
- primary dysmenorrhoea

4.2 Posology and method of administration

Posology

▪ *Children*

The recommended daily dose is 20-30 mg per Kg of body weight, spread over several doses throughout the day:

Age	Dose	Number of doses in 24 hours
6 months – 1 year	2.5 ml (50 mg)	3 to 4
1 year – 6 years	5 ml (100 mg)	3 to 4
6 years – 12 years	10 ml (200 mg)	3 to 4

The administration in children less than 6 months should only be made by medical prescription.

▪ *Adults*

Although it usually resorts to other pharmaceutical forms of Ibuprofen for adults, in case of difficulty in swallowing, Ibuprofen Azevedos can be administered in a dose of 3 measuring spoons (300 mg), 4 times per day.

▪ *Renal failure patients*

Cautions should be taken when a NSAID is administrated in patients with renal failure. In patients with mild to moderate renal dysfunction the initial dose should be reduced. Ibuprofen should not be administered in patients with severe renal failure (see section 4.3 contraindications).

▪ *Hepatic failure patients*

Ibuprofen should not be taken by patients with severe liver failure (see section 4.3 contraindications).

▪ *Elderly*

Ibuprofen should be administered with caution in elderly patients, since they are particularly susceptible to NSAIDs adverse reactions.

Undesirable effects may be minimized by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.4).

Method of administration

Oral use

Ibuprofen Azevedos should be administered after meals.

Do not take for more than 3 days without consulting a doctor.

4.3 Contraindications

- Hypersensitivity to the active substance or any of the excipients listed in section 6.1.
- Patients who have antecedents of asthma, rhinitis, urticaria, neurotic angioedema, bronchospasm associated with the use of acetylsalicylic acid or other nonsteroidal anti-inflammatory drugs (NSAIDs).
- Patients with active or recurrent peptic ulcer, gastrointestinal bleeding or other active bleeding as cerebrovascular or ulcerous colitis.

- History of gastrointestinal bleeding or perforation, related to previous NSAID therapy.
- Peptic ulcer/active bleeding or history of peptic ulcer/recurrent bleeding (two or more distinct episodes of proven ulceration or bleeding).
- Patients with severe renal or hepatic failure.
- Patients with alterations in coagulation.
- During the last trimester of pregnancy.
- Severe heart failure (NYHA IV).

4.4 Special warnings and precautions for use

Undesirable effects may be minimised by using the lower effective dose for the shortest duration necessary to control symptoms.

In the initiation of the treatment, ibuprofen, as other NSAIDs should be administered with caution in patient with considerable dehydration.

Masking of symptoms of underlying infections

Ibuprofen Azevedos can mask symptoms of infection, which may lead to delayed initiation of appropriate treatment and thereby worsening the outcome of the infection. This has been observed in bacterial community acquired pneumonia and bacterial complications to varicella. When Ibuprofen Azevedos 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.

The administration of Ibuprofen Azevedos may reduce the female fertility and it is recommended to women that are planning to have a baby. In women that have difficulty in becoming pregnant or in which the possibility of infertility is being investigated the interruption of Ibuprofen Azevedos shall be considered.

Severe cutaneous adverse reactions (SCARs)

Severe cutaneous adverse reactions (SCARs), including exfoliative dermatitis, erythema multiforme, Stevens-Johnson syndrome (SJS), Toxic Epidermal Necrolysis (TEN), Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS syndrome), and acute generalized exanthematous pustulosis (AGEP), which can be life-threatening or fatal, have been reported in association with the use of ibuprofen (see section 4.8). Most of these reactions occurred within the first month. If signs and symptoms suggestive of these reactions appear ibuprofen should be withdrawn immediately and an alternative treatment considered (as appropriate)

Gastrointestinal effects

Ibuprofen should be used with caution in patients with a history of gastrointestinal disease.

For all NSAIDs have been reported cases of bleeding, ulceration and gastrointestinal perforation potentially fatal, in several phases of treatment, associated or not with warning symptoms or history of serious gastrointestinal events. The risk of bleeding, ulceration or perforation is higher with increased doses of NSAID, in patients with history of peptic ulcer, especially if associated with bleeding or perforation and in elderly patients. In these conditions patients should be instructed to inform their assistant doctor about the occurrence of abdominal symptoms and digestive bleeding, especially in the initial phases of treatment. In these patients the treatment should be initiated with a minimum effective dose. Co-administration of protective agents (e.g. misoprostol or proton pump inhibitors) shall be considered in these patients, as well as those who need to take simultaneously acetylsalicylic acid in lower doses, or other medicines susceptible to increase the risk of ulcer or bleeding, as corticosteroids, anticoagulants (as warfarin), selective serotonin reuptake inhibitors or platelet aggregation inhibitors such as acetylsalicylic acid.

In case of gastrointestinal bleeding or ulceration in patients taking ibuprofen the treatment should be discontinued. NSAID should be administered with caution in patients with history of inflammatory bowel disease (ulcerative colitis, Crohn's disease), since these situations can be exacerbated.

Concomitant use of Ibuprofen with corticosteroids or other NSAIDs may increase the risk of ulceration and gastrointestinal bleeding.

As with the other products containing NSAIDs, concomitant administration of ibuprofen with acetylsalicylic acid is not recommended due to a potential increase of adverse effects.

The concomitant administration of Ibuprofen Azevedos with other NSAIDs, including selective cyclooxygenase-2 inhibitors, should be avoided.

The elderly have a higher frequency of adverse reactions with NSAID, especially of gastrointestinal bleedings and perforation that may be fatal.

Renal and urinary effects

As with other NSAIDs, the long-term administration of ibuprofen has resulted in renal papillary necrosis and other pathologic renal reactions. Cases of renal toxicity have also been seen in patients in whom prostaglandins have a compensatory role in the maintenance of renal perfusion. In these patients, the administration of NSAIDs may cause a decrease in dose-dependent prostaglandins formation and, secondarily, in renal blood flow, who may precipitate an evident renal decompensation. Patients at greatest risk for this reaction are those with renal dysfunction, heart failure, hepatic dysfunction those who take diuretics and ACE inhibitors and the elderly patients. Discontinuation of therapy with NSAIDs is generally followed by a recovery to a pre-treatment state.

In patients with renal, hepatic or cardiac failure predisposed to hydrosaline retention, caution should be exercised since the use of NSAIDs may result in deterioration of renal

function. In these patients the dose should be as low as possible and renal function should be monitored.

Effects on respiratory system

In asthmatic patients or with a previous history of bronchial asthma, special caution should be exercised since Ibuprofen may trigger a clinical picture of bronchospasm in those patients.

Hepatic effects

Hepatic function should be carefully monitored in patients treated with Ibuprofen which referred presenting symptoms compatible with hepatic lesion (anorexia, nausea, vomiting, jaundice) and/or developing hepatic function changes alterations of hepatic function (transaminases, bilirubin, alkaline phosphatase, gamma-GT). In the presence of values higher than 2 times the upper normal value, the medicine should be suspended immediately and an investigation should be initiated in order to clarify the situation. The re-exposure to Ibuprofen should be avoided.

Ibuprofen, as other NSAIDs, may inhibit platelet aggregation and extend the bleeding time. Caution is recommended when administering Ibuprofen concomitantly with oral anticoagulants.

Immune system effects

Ibuprofen should be used with caution in patients with systemic lupus erythematosus or other autoimmune diseases, due to the risk of aseptic meningitis and/or renal failure.

Eye effects

Patients presenting vision disorders during the treatment with Ibuprofen should suspend the therapy and should be submitted to an ophthalmological examination.

Cardiovascular and cerebrovascular effects

Ibuprofen should be administered with caution in patients with a history of heart failure or hypertension, since there have been reports of oedemas associated to Ibuprofen administration.

Cases of Kounis syndrome have been reported in patients treated with Ibuprofen Azevedos.

Kounis syndrome has been defined as cardiovascular symptoms secondary to an allergic or hypersensitive reaction associated with constriction of coronary arteries and potentially leading to myocardial infarction.

Clinical studies suggest that use of ibuprofen, particularly at a high dose (2400 mg/day) 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-III), established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with ibuprofen after careful consideration and high doses (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.

Special advices:

This medicine contains glycerol. It may cause headaches, stomach pains and diarrhoea. It also contains azorubine (E 122) as colorant. It may cause allergic reactions, It also contains maltitol liquid; this fact should be taken into account in patients with rare hereditary problems of fructose intolerance.

This medicinal product contains 0.156 mmol (or 3.590 mg) sodium per dose. To be taken into consideration by patients on a controlled sodium diet

4.5 Interaction with other medicinal products and other forms of interaction

Ibuprofen inhibits the synthesis of prostaglandins at a renal level.

Prostaglandins, especially the A and E, are potent vasodilators agents. Their blood level decrease may lead to vasoconstriction with a consequent reduction in renal blood flow. Thus, the removal of fluids and electrolytes is reduced, resulting in not only an increase in blood pressure as the probable plasma accumulation of certain drugs, preferably renally eliminated.

Concomitant use not recommended with Ibuprofen and:

▪ Other NSAIDs:

Simultaneous administration of Ibuprofen should be avoided with other drugs of this group because it may increase the risk of gastrointestinal ulcer and bleeding.

▪ Methotrexate administered in doses of 15 mg / week or more:

Concomitant administration of an NSAID and methotrexate in a 24 hours interval may result in increased plasma methotrexate level, with the consequent increase of its toxicity.

▪ Hydantoins and sulphonamides:

Toxic effects of these substances may increase with concomitant administration of Ibuprofen.

▪ Ticlopidine:

NSAIDs should not be combined with ticlopidine due to increased risk of additive effect in the inhibition of platelet function.

▪ Lithium (Lithium carbonate):

Concomitant administration of lithium carbonate and Ibuprofen can lead to increased toxicity of the first, by reducing its renal clearance (see above) and consequent increase in plasma concentration.

▪ Oral anticoagulants (warfarin):

Concomitant administration of oral anticoagulants and Ibuprofen may potentiate the anticoagulant action, with increased prothrombin time, due to a possible decrease in plasma proteins binding.

▪ Diuretics, Angiotensin Converting Enzyme (ACE) inhibitors and Angiotensin II Antagonists (AII):

Nonsteroidal anti-inflammatory drugs may reduce the efficacy of diuretics as other antihypertensive drugs. In some patients with impaired renal function (dehydrated or elderly patients with compromised renal function) the co-administration of an ACE inhibitor or an angiotensin II antagonist (AII) and cyclooxygenase inhibitors may result in further deterioration of renal function, including the possibility of acute renal failure, which is usually reversible. The occurrence of these interactions should be taken into account in patients taking ibuprofen in association with ACE inhibitors or AII. Consequently, this drug association should be administered with caution, especially in elderly patients. Patients should be adequately hydrated and the need of monitoring renal function should be considered after starting concomitant therapy, and periodically since then.

▪ Anti-platelet agents and selective serotonin reuptake inhibitors:

Increased risk of gastrointestinal bleeding (see section 4.4).

Acetylsalicylic acid

Concomitant administration of ibuprofen and acetylsalicylic 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 acetylsalicylic 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).

▪ Mifepristone:

NSAIDs should not be administered in the subsequent 8-12 days after the administration of mifepristone as they may cause a reduction in its effect.

Special precautions are recommended in simultaneous administration of Ibuprofen and:

▪ Digoxin:

Increased plasma levels of digoxin (62%), with possible potentiation of their action and increased toxicity, due to their decreased active renal excretion.

▪ Methotrexate administered in low doses, less than 15 mg/week:

Ibuprofen increases plasma levels of methotrexate. In case of combination with methotrexate in low doses, plasma levels of the patient should be supervised, especially during the first weeks of simultaneous administration. It will also be necessary to monitor renal function in order to prevent a possible decrease in methotrexate excretion.

▪ Pentoxifylline:

In patients who receive treatment with Ibuprofen in combination with pentoxifylline, an increased risk of bleeding may occur, a monitorisation of prothrombin time is recommended.

▪ Phenytoin:

During simultaneous treatment with Ibuprofen, may increase plasma levels of phenytoin.

▪ Quinolones:

Convulsions have been reported for concomitant use with NSAIDs.

▪ Thiazides and related substances:

Increase of potassium concentrations with medical supervision needed.

▪ Other diuretics:

Reduction of diuretic effect by Ibuprofen action, through the antagonism of prostaglandins and increase in potassium levels, with the need for medical supervision.

▪ Sulfonylureas:

NSAIDs may enhance the hypoglycaemic effect of sulfonylureas, by decreasing their binding to plasma proteins.

▪ Cyclosporin:

Potentiation of cyclosporine toxicity, with manifested oliguria and anuria, due to decreased synthesis of prostaglandins (see above).

▪ Corticosteroids:

Simultaneous administration of NSAIDs and corticosteroids may increase the risk of gastrointestinal ulceration or bleeding (see section 4.4).

▪ β – blockers (metoprolol, pindolol):

Decreasing of beta-blocking effect by antagonism of prostaglandins (see above).

4.6 Fertility, pregnancy and lactation

Pregnancy:

Studies in animals at doses higher than those recommended in humans did not registered teratogenic effects. However, Ibuprofen Azevedos should not be administered during pregnancy, being absolutely contraindicated during the last trimester of gestation.

Inhibition of prostaglandins synthesis may negatively affect pregnancy and/or the embryo-fetal development. Data from the epidemiological studies suggest an increased risk of spontaneous abortion, heart defects and of gastroschisis as a result of the use of an inhibitor of the prostaglandin synthesis in early pregnancy. The risk of abortion of cardiovascular malformations has increased from less than 1% to about 1.5%. It is assumed that the risk increases with the dose and duration of treatment.

In animals, it has been demonstrated that administration of prostaglandin synthesis inhibitors results in the increase of abortions peri and post-implantation and embryo-foetal mortality. Additionally, there was a higher incidence of multiple malformations, including cardiovascular malformations in animals exposed to prostaglandin synthesis inhibitors during the organogenetic period.

From the 20th week of pregnancy onward, Ibuprofen Azevedos 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, Ibuprofen Azevedos should not be administered unless strictly necessary. If Ibuprofen Azevedos is used by a women 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 Ibuprofen Azevedos for several days from gestational week 20 onward. Ibuprofen Azevedos 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 *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, the administration of Ibuprofen Azevedos is contraindicated during the third trimester of pregnancy (see sections 4.3 and 5.3)

Lactation:

Due to the absence of clinical studies, the use of Ibuprofen Azevedos in women breast-feeding it is not recommended.

4.7 Effects on ability to drive and use machines

In the event of dizziness, confusion, vision disturbances or other Central Nervous System Disorders, during the administration of Ibuprofen Azevedos, patients should not drive or operate machines.

In the case of administration of a single dose of Ibuprofen Azevedos, during a short period, it is not necessary to take special precautions.

4.8 Undesirable effects

The frequencies of adverse events are ranked according to the following: Very common ($\geq 1/10$); Common ($\geq 1/100$, $< 1/10$); Uncommon ($\geq 1/1.000$, $< 1/100$); Rare ($\geq 1/10.000$, $< 1/1.000$); Very rare ($< 1/10.000$), not known (cannot be estimated from the available data).

Gastrointestinal disorders:

Very common: dyspnoea, diarrhoea.

Common: nausea, vomiting and abdominal pain.

Uncommon: gastrointestinal bleeding and ulcer, ulcerous stomatitis.

Rare: gastrointestinal perforation, flatulence, esophagitis, esophageal stenosis, exacerbation of diverticular disease, nonspecific haemorrhagic colitis, ulcerative colitis or Crohn's disease.

Very rare: haematemesis, melaenas, gastritis, constipation, pancreatitis.

Skin and subcutaneous tissue disorders:

Common: cutaneous eruption.

Very common: urticaria, pruritus, purpura, angioedema, rinitis e bronchospasm.

Rare: anaphylactic reaction.

Very rare: systemic lupus erythematosus, alopecia, severe cutaneous adverse reactions (SCARs) (including Erythema multiforme, exfoliative dermatitis, Stevens-Johnson's syndrome, and toxic epidermal necrolysis), Lyell's Syndrome and allergic vasculitis, exanthema, angioneurotic oedema, bullous dermatitis (vesiculo-bullous eruptions), rash maculo-papular (cutaneous rash maculo-papular type), erythema nodosum, Henoch-Schonlein purpura (vasculitis).

Frequency "Not known": Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome), acute generalised exanthematous pustulosis (AGEP), photosensitivity reaction

Infections and infestations:

Very rare: aseptic meningitis (fever or coma), rhinitis

Blood and lymphatic system disorders:

Very rare: eosinophilia, aplastic anaemia, neutropenia, thrombocytopenia, leukopenia, granulocytopenia, agranulocytosis, haemolytic anaemia.

Immune system disorders:

Very rare: anaphylactic reactions (anaphylaxis), serum sickness (serum syndrome)

Metabolism and nutrition disorders:

Very rare: acidosis, fluid retention, hypoglycaemia, hyponatremia, decreased appetite.

Psychiatric disorders:

Very rare: hallucinations, confusional state, depression, insomnia, nervousness, influence on the lability (emotional lability).

Nervous system disorders

Common: fatigue and drowsiness, headaches, nausea and vertigo.

Uncommon: Anxiety and vision disturbances.

Rare: psychotic reaction, irritability, confusion and disorientation, toxic amblyopia reversible.

Very rare: dizziness, paraesthesia, benign intracranial hypertension (pseudotumor cerebri).

Eye disorders

Very rare: visual disturbance, conjunctivitis, diplopia, chromatopsia (chromatic vision changes), amblyopia, cataracts, optic neuritis, scotomas.

Ear and labyrinth disorders

Very rare: tinnitus, vertigo, hypoacusis (hearing impairment).

Cardiac disorders

Very rare: palpitations, arrhythmias, congestive heart failure (patients with marginal cardiac function), sinus bradycardia, sinus tachycardia.

Kounis syndrome (frequency: *Not Known*)

Respiratory, thoracic and mediastinal disorders

Very rare: asthma, dyspnoea, bronchospasm, epistaxis, eosinophilic pneumonia (pneumopathy to eosinophils).

Hepatobiliary disorders

Very rare: hepatitis, jaundice, cholestatic hepatitis (severe and sometimes fatal), cytolytic hepatitis.

Renal and urinary disorders

Very rare: acute renal failure, renal failure, nephrotic syndrome, haematuria, dysuria, renal papillary necrosis, interstitial nephritis, tubulointerstitial nephritis (acute tubulointerstitial nephropathy), azotaemia, polyuria, chronic renal failure.

Reproductive system and breast disorders

Very rare: gynaecomastia and menorrhagia.

General disorders and administration site conditions

Very rare: pyrexia (fever) and oedema.

Side effects seen in NSAIDs:

Gastrointestinal: The most frequently observed adverse events are from gastrointestinal nature. It may occur, particularly in the elderly, peptic ulcers, gastrointestinal perforation or bleeding potentially fatal (see section 4.4). Nausea, dyspepsia, vomiting, haematemesis, flatulence, abdominal pain, diarrhoea, constipation, melaena, aphthous stomatitis, exacerbation of colitis and Crohn's disease (see section 4.4.) have been reported following administration of these drugs. Cases of gastritis have been observed less often.

Cardiovascular e cerebrovascular:

Oedema, hypertension and heart failure in association with NSAID treatment have been reported.

Clinical studies suggest that use of ibuprofen, particularly at a 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).

Dermatological

Bullous reactions including Stevens-Johnson's syndrome and toxic epidermal necrolysis (very rare).

Others:

In very rare cases inflammations associated with infections can be exacerbated.

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 ADR Reporting Website: www.medicinesauthority.gov.mt/adrportal.

4.9 Overdose

Prolonged use at higher than recommended doses or overdose may result in renal tubular acidosis and hypokalaemia.

The symptoms of overdose are: CNS disorders, headache, dizziness, loss of consciousness, as well as abdominal pain, nausea and vomiting. Hypotension, respiratory depression, cyanosis, metabolic acidosis and renal failure may occur later.

In case of overdose, general common measures to other poisonings should be proceeded, such as gastric lavage and activated charcoal administration and special measures, such as administration of antacids (and/or H₂ antagonists), proper hydration and correction of the acidosis (if any) with sodium bicarbonate.

In severe cases of poisoning, metabolic acidosis may occur.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anti-inflammatory and antirheumatic products, non-steroids; propionic acid derivatives

Code ATC: M01A E01

Ibuprofen has significant anti-inflammatory, analgesic and antipyretic properties. These actions hold fundamentally with the ability of this substance to inhibit cyclooxygenase and consequently prostaglandins, important mediators of inflammation and fever.

Ibuprofen also appears to have an inhibitory effect on platelet aggregation.

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 hours 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 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 4.5).

5.2 Pharmacokinetic properties

Approximately 80% of the orally administered dose of Ibuprofen is absorbed in the gastrointestinal tract. Plasma concentration is reached about 1 hour after the administration of Ibuprofen Azevedos. Concomitant intake with food or antacids does not change significantly the absorption.

Protein binding percentage is about 90 to 99%.

The drug is quickly metabolized at hepatic level and eliminated through urine, with a plasma half-life of about 2-4 hours.

Pharmacokinetics of Ibuprofen in children does not seem to differ from that of the adult.

5.3 Preclinical safety data

Ibuprofen toxicity in animal experiments was observed in the form of lesions and ulcerations of the gastrointestinal tract. In vitro and in vivo experiments have not revealed any mutagenic potential of Ibuprofen. Carcinogenicity studies in rats and mice have not revealed any carcinogenic activity. Experimental studies have shown that Ibuprofen crosses the placenta, however, there isn't any evidence of teratogenic activity.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium benzoate (E 211), citric acid anhydrous, sodium citrate, sodium saccharin, sodium chloride, hypromellose, xanthan gum, maltitol liquid, strawberry flavour, colorant azorubine (E 122), glycerol and purified water.

6.2 Incompatibilities

The process of absorption of the active ingredient, Ibuprofen, is treated in the presence of alkalizing substances, namely antacids.

6.3 Shelf life

3 years

The stability of the product does not change after opening the package, as long as remained under normal storage conditions.

6.4 Special precautions for storage

This medicine does not require any special storage conditions.

6.5 Nature and contents of container

Polyethylene terephthalate (PET) amber bottle provided with a safety cap for children (pilfer) of high-density polyethylene (HDPE). The bottle is accompanied with a double spoon of polypropylene or polystyrene (2.5 and 5 ml) and/or one syringe of polyethylene of 5 ml.

Package with 200 ml of oral suspension.

It is possible that not all presentations may be marketed.

6.6 Special precautions for disposal

Shake before use.

The syringe or double spoon must be removed, cleaned and dried after each use.

7. MARKETING AUTHORIZATION HOLDER

Laboratórios Azevedos - Indústria Farmacêutica S.A.
Rua Bernardim Ribeiro, N°10-B, R/C Esquerdo
2700-111 Amadora
Portugal

8. MARKETING AUTHORIZATION NUMBERS

MA865/01001

9. DATE OF THE FIRST MARKETING AUTHORIZATION

Date of first authorization: 23rd November 2022

10. DATE OF REVISION OF THE TEXT

02/2026