Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

Ibucot tablets

2. Qualitative and quantitative composition

Each tablet contains Ibuprofen BP 200 mg

3. Pharmaceutical form

Film coated tablet

Purple, round, biconvex film coated tablets of diameter 9.10mm.

4. Clinical particulars

4.1 Therapeutic indications

Indications:
Ibuprofen is indicated in the management of mild to moderate pain in conditions such as dysmenorrhoea, migraine, postoperative pain, ankylosing spondylitis, osteoarthritis and rheumatoid arthritis including juvenile rheumatoid arthritis and in other musculoskeletal and joint disorders such as sprains and strains.

Ibuprofen relieves pain and reduces inflammation and temperature as well as relieving headaches and other types of pain. It also relieves cold and flu symptoms.

4.2 Posology and method of administration

Posology

Adults:
The usual dose is 1.2 to 1.8 g daily in divided doses although maintenance doses of 0.6 to 1.2 g daily may be effective in some patients. If necessary the dose may be increased to 2.4 g daily.

Children:
20 mg per kg body weight daily in divided doses with upto 40 mg per kg daily being given in juvenile rheumatoid arthritis if necessary.

Method of Administration
Ibuprofen should preferably be administered after meals.

4.3 Contraindications

Ibuprofen should not be given to patients with active peptic ulceration.
Patients who are sensitive to aspirin or other non-steroidal, anti-inflammatory drugs should generally not be given ibuprofen.

It should be given with care to the elderly, to patients with asthma or bronchospasm, bleeding disorders, cardiovascular disease, a history of peptic ulceration and in liver or renal failure. Care is required in those who are also receiving coumarin anticoagulants.

Ibuprofen should be discontinued in patients who experience blurred or diminished vision or changes in colour vision**.**

Last trimester of pregnancy.

4.4 Special warnings and precautions for use

The use of Ibuprofen with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided due to the increased risk of ulceration or bleeding.
Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms. Patients treated with NSAIDs long term should undergo regular medical supervision to monitor for adverse events.

Ibuprofen should only be administered under strict consideration of the benefit-risk ratio in the following conditions:
- Systemic Lupus Erythematosus (SLE) or mixed connective tissue diseases.
- Congenital disturbance of porphyrin metabolism (e.g. acute intermittent porphyria)
- The first and second trimester of pregnancy
- Lactation

Special care has to be taken in the following cases:
- Gastrointestinal diseases including chronic inflammatory intestinal disease (ulcerative colitis, Crohn's disease)
- Cardiac insufficiency and hypertension
- Reduced renal function
- Hepatic dysfunction
- Disturbed haematopoiesis
- Blood coagulation defects
- Allergies, hay fever, chronic swelling of nasal mucosa, adenoids, chronic obstructive airway disease or bronchial asthma
- Immediately after major surgical interventions
- 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 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 (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 acetylsalicylic acid, or other medicinal products likely to increase gastrointestinal risk.

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 or heparin, selective serotonin reuptake inhibitors or anti-platelet agents such as acetylsalicylic acid.
When GI bleeding or ulceration occurs in patients receiving Ibuprofen, 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.

Elderly
The elderly have an increased frequency of adverse reactions to NSAIDs, especially gastrointestinal bleeding and perforation which may be fatal.

Cardiovascular and cerebrovascular effects
Appropriate monitoring and advice are required for patients with a history of hypertension and/or mild to moderate congestive heart failure as fluid retention, hypertension and oedema have been reported in association with NSAID therapy.
Clinical studies suggest that use of ibuprofen, particularly at a high doses (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 daily) 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.

Severe 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. 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. Ibuprofen should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.
Exceptionally, varicella can be at the origin of serious cutaneous and soft tissues 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 Ibuprofen in case of varicella.

Masking of symptoms of underlying infections
Ibuprofen 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 is administered for fever or pain relief in relation to infection, monitoring of infection is advised. In nonhospital settings, the patient should consult a doctor if symptoms persist or worsen.

Renal effect
Ibuprofen may cause the retention of sodium, potassium and fluid in patients who have not previously suffered from renal disorders because of its effect on renal perfusion. This may cause oedema or even lead to cardiac insufficiency or hypertension in predisposed patients.

As with other NSAIDs, the prolonged administration of ibuprofen to animals has resulted in renal papillary necrosis and other pathological renal changes. In humans, there have been reports of acute interstitial nephritis with haematuria, proteinuria and occasionally nephrotic syndrome. Cases of renal toxicity have also been observed in patients in whom prostaglandins play a compensatory role in the maintenance of renal perfusion. In these patients, administration of NSAIDs may cause a dose-dependent reduction in prostaglandin formation and, secondarily, in renal blood flow, which may precipitate overt renal decompensation. Patients at greatest risk of suffering this reaction are those with renal dysfunction, heart failure, hepatic dysfunction, those taking diuretics and ACE inhibitors and the elderly. Discontinuation of NSAID treatment is generally followed by recovery to the pre-treatment state.

Renal tubular acidosis and hypokalaemia may occur following acute overdose and in patients taking ibuprofen products over long periods at high doses (typically greater than 4 weeks), including doses exceeding the recommended daily dose.

Hepatic:
Hepatic dysfunction
SLE and mixed connective tissue disease
In patients with systemic lupus erythematosus (SLE) and mixed connective tissue diseases there may be an increased risk of aseptic meningitis.

Aseptic meningitis
Symptoms of aseptic meningitis, such as stiff neck, headache, nausea, vomiting, fever or disorientation have been observed.
Aseptic meningitis has been observed on rare occasions in patients on ibuprofen therapy. Although it is probably more likely to occur in patients with systemic lupus erythematosus and related connective tissue diseases, it has been reported in patients who do not have an underlying chronic disease.

Other precautions
Severe acute hypersensitivity reactions (for example anaphylactic shock) are observed very rarely. At the first signs of hypersensitivity reaction after taking/administering ibuprofen therapy must be stopped. Medically required measures, in line with the symptoms, must be initiated by specialist personnel.
Bronchospasm, urticaria or angioedema may be precipitated in patients suffering from or with a previous history of bronchial asthma, chronic rhinitis, sinusitis, nasal polyps, adenoids or allergic diseases.
Ibuprofen may mask the signs or symptoms of an infection (fever, pain and swelling).
Prolonged use of any type of painkiller for headaches can make them worse. If this situation is experienced or suspected, medical advice should be obtained and treatment should be discontinued. The diagnosis of medication overuse headache (MOH) should be suspected in patients who have frequent or daily headaches despite (or because of) the regular use of headache medications.
In general the habitual intake of analgesics, particularly the combination use of different analgesic substances, may cause permanent renal damage and a risk of renal failure (analgesics nephropathy).
Ibuprofen may temporarily inhibit platelet aggregation and prolong the bleeding time. Therefore, patients with coagulation defects or on anticoagulant therapy should be observed carefully.
In case of long-term treatment with ibuprofen a periodical monitoring of hepatic and renal function as well as the blood count is necessary, especially in high risk patients.

Consumption of alcohol should be avoided since it may intensify side effects of NSAIDs, especially if affecting the gastrointestinal tract or the central nervous system.
Patients on ibuprofen should report to their doctor signs or symptoms of gastro-intestinal ulceration or bleeding, blurred vision or other eye symptoms, skin rash, weight gain or oedema.

4.5 Interaction with other medicinal products and other forms of interaction

Ibuprofen (like other NSAIDs) should be avoided in combination with:
Aspirin (Acetylsalicylic Acid):
Concomitant administration of ibuprofen and acetylsalicylic acid is not generally recommended because of the potential of increased adverse effects unless low-dose aspirin (not above 75mg daily) has been advised by a doctor

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

Other NSAIDs including cyclooxygenase-2 selective inhibitors:
Avoid concomitant use of two or more NSAIDs as this may increase the risk of adverse effects.

Ibuprofen should be used with caution in combination with:
Corticosteroids:
As these may increase the risk of gastrointestinal ulceration or bleeding .
Antihypertensives and diuretics:
Since NSAIDs may diminish the effect of these 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.
Anticoagulants:
NSAIDS may enhance the effects of anti-coagulants, such as warfarin (see section 4.4).
Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs):
Increased risk of gastrointestinal bleeding (see section 4.4).
Cardiac glycosides:
NSAIDs may exacerbate cardiac failure, reduce GFR and increase plasma glycoside levels.
Lithium:
There is evidence for potential increase in plasma levels of lithium.

Methotrexate:
There is evidence for the potential increase in plasma methotrexate.
Ciclosporin:
Increased risk of nephrotoxicity.
Mifepristone:
NSAIDs should not be used for 8-12 days after mifepristone administration as NSAIDs can reduce the effect of mifepristone.
Tacrolimus:
Possible increased risk of nephrotoxicity when NSAIDs are given with tacrolimus.
Zidovudine:
Increased risk of haematological toxicity when NSAIDs are given with zidovudine. There is evidence of an increased risk of haemarthroses and haematoma in HIV (+) haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen.
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.

4.6 Pregnancy and Lactation

Pregnancy
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. From the 20th week of pregnancy onward, ibuprofen 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 should not be given unless clearly necessary. If Ibuprofen 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 ibuprofen for several days from gestational week 20 onward. Ibuprofen 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 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, Ibuprofen is contraindicated during the last trimester of pregnancy

Breastfeeding
Ibuprofen is excreted in breast milk, but with therapeutic doses during short term treatment the risk for influence on infant seems unlikely. If, however, longer treatment is prescribed, early weaning should be considered.

Fertility
The use of ibuprofen may impair fertility and is not recommended in women attempting to conceive. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of ibuprofen should be considered.

4.7 Effects on ability to drive and use machines

Ibuprofen generally has no adverse effects on the ability to drive and use machinery. However, since at high dosage side effects such as fatigue, somnolence, vertigo (reported as common) and visual disturbances (reported as uncommon) may be experienced, the ability to take part actively in road traffic or operate machinery may be impaired in individual cases. This effect is potentiated by simultaneous consumption of alcohol.

4.8 Undesirable effects

The most commonly observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation or GI bleeding, sometimes fatal, particularly in the elderly, may. Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, heamatemesis, ulcerative stomatits, exacerbation of colitis and Crohn's disease have been reported following administration. Less frequently, gastritis has been observed.

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) .

Oedema, hypertension, and cardiac failure, have been reported in association with NSAID treatment.In children the use of aspirin has been implicated in some cases of Reye's syndrome, which is characterised by acute encephalopathy and fatty degeneration of the liver typically occuring after a viral infection such as Chicken pox or Influenza. Adverse effects associated with Caffeine include headache, fatigue, drowsiness. High doses of caffeine may cause tremors and palpitations.

4.9 Overdose

Symptoms
Most patients who have ingested clinically important amounts of NSAIDs will develop no more than nausea, vomiting, epigastric pain, or more rarely, diarrhoea. Nystagmus, blurred vision, tinnitus, headache and gastrointestinal bleeding may also occur. In more serious poisoning, toxicity is seen in the central nervous system, manifesting as vertigo, dizziness, drowsiness, occasionally excitation and disorientation, loss of consciousness or coma. Occasionally patients develop convulsions. Children may also develop myoclonic cramps. In serious poisoning metabolic acidosis may occur, hypothermia and hyperkalaemia may also occur and the prothrombin time/INR may be prolonged, probably due to interference with the actions of circulating clotting factors. Acute renal failure, liver damage, hypotension, respiratory depression and cyanosis may occur. Exacerbation of asthma is possible in asthmatic

Treatment
Treatment should be symptomatic and supportive and include the maintenance of a clear airway and monitoring of cardiac and vital signs until stable. Gastric emptying or oral administration of activated charcoal is indicated if the patient presents within one hour of ingestion of more than 400 mg per kg of body weight. If ibuprofen has already been absorbed, alkaline substances should be administered to promote the excretion of the acid ibuprofen in the urine. If frequent or prolonged, convulsions should be treated with intravenous diazepam or lorazepam. Bronchodilators should be given for asthma. No specific antidote is available.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: M01A Anti-inflammatory and Antirheumatic Products, Non-Steroids; M01AE Propionic acid derivatives;
ATC Code: M01AE01

Ibuprofen is a NSAID that possesses anti-inflammatory, analgesic and antipyretic activity. Animal models for pain and inflammation indicate that

ibuprofen effectively inhibits the synthesis of prostaglandins. In humans, ibuprofen reduces pain possibly caused by inflammation or connected with it, swelling and fever. Ibuprofen exerts an inhibitory effect on prostaglandin synthesis by inhibiting the activity of cyclo-oxygenase. In addition ibuprofen has an inhibitory effect on ADP (adenosine diphosphate) or collagen stimulated 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 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 cardioprotective effect of low-dose acetylsalicylic acid cannot be excluded.

No clinically relevant effect is considered to be likely for occasional ibuprofen use.

Ibuprofen inhibits prostaglandin synthesis in the uterus, thereby reducing intrauterine rest and active pressure, the periodic uterine contractions and the amount of prostaglandins released into the circulation. These changes are assumed to explain the alleviation of menstrual pain. Ibuprofen inhibits renal prostaglandin synthesis which can lead to renal insufficiency, fluid retention and heart failure in risk patients.

5.2 Pharmacokinetic properties

Absorption
Ibuprofen is rapidly absorbed from the gastrointestinal tract, peak serum concentrations occurring 1-2 hours after administration.

Distribution
Ibuprofen is rapidly distributed throughout the whole body. The plasma protein binding is approximately 99%.

Biotransformation
Ibuprofen is metabolised in the liver (hydroxylation, carboxylation).

Elimination
The elimination half-life is approximately 2.5 hours in healthy individuals. Pharmacologically inactive metabolites are mainly excreted (90%) by the kidneys but also in bile.

5.3 Preclinical safety data

As a well-established and widely used product, the pre-clinical safety of ibuprofen is well documented.
Ibuprofen's sub chronic and chronic toxicity was mainly shown by animal tests as gastric tract damage and ulcers.
The vitro and in vivo tests have not shown any clinically significant signs about ibuprofen's mutagenicity. Furthermore, no carcinogenic effects have been observed in mice and rats.
Ibuprofen inhibits ovulation in rabbits and impairs implantation in various animal species (rabbit, rat, and mouse). In reproduction tests undertaken with rats and rabbits, ibuprofen passed across the placenta. When using doses toxic to the mother, malformations occur more frequently (i.e. ventricular septum defects).

6. Pharmaceutical Particulars

6.1 List of Excipients

- Maize Starch
- Potassium Sorbate
- Aerosil
- Titanium Dioxide
- Carnauba Wax,
- Rectified Spirit
- Castor Oil
- Propylparaben Sodium
- Povidone
- Erythrosine Color and Lake Dye
- Blue Lake Dye
- Talc
- Gum Acacia
- Sucrose
- Calcium Carbonate
- Methyl Paraben Sodium

6.2 Incompatibilities

None known

6.3 Shelf-Life

36 months

6.4 Special Precautions for storage

Store below 30^0C. Protect from light. Keep out of reach of children.

6.5 Nature and Content of container

Purple film-coated tablets of diameter 9.10mm packed in Alu/PVC laminate blister pack of 10 tablets per blister packed in boxes of 10 blisters per box with a patient leaflet in each box.

6.6 Special precautions for disposal and other handling

No special requirements. Any expired or unused drug should be disposed of as per local regulatory requirements.

7. Marketing Authorization Holder

ELYS CHEMICAL INDUSTRIES LTD

8. Marketing Authorization Number

CTD8884

9. Date of first authorization/renewal of the authorization

1st December 2023

10. Date of revision of the text

11th May 2025