

VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Pain is one of the common reasons for a patient to take medicine.¹ Moderate or severe pain can remain for short or long duration, sometimes, for weeks, months or even years. Long term pain can be due to some accidental injury or there may be an ongoing pain due to swelling of joints (arthritis), but some people suffer with long term pain in the absence of any past injury or body damage. It has been judged that one in five adults suffers from pain and that another one in 10 adults is diagnosed with long term pain each year. A recent market research report states that more than 1.5 billion people worldwide suffer from long term pain. In European Union, 49.7 million people reported pain by both its severity and occurrence which included 11.2 million with severe, 29.4 million with moderate and 9.0 million with mild pain.²⁻⁴

More than 650,000 people in the UK have painful osteoarthritis in one or both hips, three fourth people of whom are aged over 65. More than one third of the population aged over 50 have pain at any site that interferes with their normal activities. More than 10 million adults (6 million women and 4 million men) consult their treating doctors each year with arthritis and related conditions. Number of people visiting doctor for musculoskeletal problem is rising each year with age, which is 1 in 10 people aged 15–24 has increased to 1 in 3 people over 75 years of age.⁵

VI.2.2 Summary of treatment benefits

The successful management of pain depends on selecting the proper drug at the correct dosage and balancing effectiveness against side effects. For this reason, the World Health Organization introduced the concept of the analgesic ladder. Oral painkillers are usually used as first-line treatment for pain. Initially, painful conditions are treated with painkillers such as paracetamol, aspirin, or NSAIDs. Thereafter, if the pain continues to remain, mild painkillers, such as codeine, and strong painkillers, such as morphine, pethidine, methadone, etc are used in a stepwise manner. Also, new formulations of medicines such as nasal sprays and under the tongue (sublingual) tablets have increased the options available for pain management.⁶

Ibuprofen works by blocking the action of a substance in the body called cyclo-oxygenase (COX) which is involved in the production of various chemicals in the body, some of which are known as prostaglandins. Prostaglandins are produced in response to injury and certain diseases and conditions,

Ibuprofen Bril 200 mg, 400 mg and 600 mg Film-coated Tablets.

and cause pain, swelling and inflammation. NSAIDs block the production of these prostaglandins and thereby reduce inflammation and pain. By reducing prostaglandins in the brain, ibuprofen lowers body temperature and hence reduces fever. It can also be used to relieve other painful conditions such as headaches, migraine, toothache, nerve pain (neuralgia), period pain muscular pain and pain with stiffness in the joints or muscles.

VI.2.3 Unknowns relating to treatment benefits

Not Applicable

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
<p>Side effects related to stomach or gut (gastrointestinal adverse effects)</p>	<p>Ulcers, perforation and bleeding in the stomach or gut have been reported with all NSAIDs (medicines used to treat pain and inflammation) which may lead to death (fatal).</p> <p>The risk of ulcers, perforation or bleeding in the stomach or intestines generally increases with higher doses of ibuprofen, in patients who had ulcers in past or in older patients.</p> <p>The risk also increases if certain other medicines such as NSAIDs (medicines used for pain and inflammation), corticosteroids (medicines used against inflammations), anti-coagulants (blood thinning medicines), selective serotonin reuptake inhibitors (medicines to treat low mood), alcohol, bisphosphonates (used in softening of bones [osteoporosis] and to reduce high blood calcium levels) and oxpentifylline (used in the treatment of circulatory problems of the arteries of the legs or arms).</p> <p>There are more chances of occurrence of side effects in older people especially bleeding and perforation in the digestive tract, which may be life threatening.</p> <p>Ulcers in stomach and gut, sometimes with bleeding and perforation (holes or abnormal opening), microscopic bleeding from the intestine which may lead to anaemia, passage of dark, clotted blood in the stool (melaena), gut inflammation and worsening of inflammation of the large gut (colitis) and digestive tract (Crohn's disease) and worsening of abnormal pouch opening from gut (perforation or abnormal opening between two organs in the body or between an organ and the exterior of the body {fistula}) are the common side effects which may affect up to 1 in 10 treated people.</p>	<p>The medicinal products should not be used by patients suffering from an ulcer or bleeding in the stomach or small intestine related to past use of drugs for pain and inflammation (NSAIDs) or has had two or more of these episodes in the past.</p> <p>Simultaneous use of the drug product with NSAIDs should be avoided.</p> <p>Patients who had ulcers in past, should start the treatment on the lowest dose available.</p> <p>Patients should avoid alcohol since it may enhance the side effects of ibuprofen, especially those affecting the stomach and intestines.</p> <p>The protective agents (e.g. misoprostol or proton pump inhibitors) should be given along with ibuprofen to these patients who have high risk of ulcers or bleeding in stomach or intestine.</p> <p>NSAIDs should be used with care in older patients who are more likely to get side effects and are at increased risk of life-threatening bleeding and ulcers in stomach and gut.</p> <p>If treatment is considered necessary, the lowest dose for the shortest duration necessary to control symptoms should be used.</p> <p>Treatment should be reviewed at regular intervals and stopped if no benefit is seen.</p> <p>Special care should be taken while using NSAIDs in patients</p>

Risk	What is known	Preventability
	<p>Nausea, vomiting, flatulence, diarrhoea, heartburn, abdominal pain, indigestion and constipation are the very common side effects which may affect more than 1 in 10 treated people. Digestive tract ulcer with or without perforation is a common side effect which may affect up to 1 in 10 treated people. Inflammation of stomach (gastritis) is an uncommon side effect which may affect up to 1 in 100 treated people. Inflammation of the food pipe (oesophagitis), Inflammation of the pancreas, an organ that is important for digestion and narrowing of gut (intestinal strictures) are very rare side effects which may affect up to 1 in 10,000 treated people.</p>	<p>who have stomach or gut problems like inflammation of the large gut with ulcers and inflammation affecting the digestive tract as their condition may get worsen.</p>
<p>Heart and blood vessels related side effects (Cardiovascular adverse effects)</p>	<p>Medicines such as ibuprofen may be associated with a small increased risk of heart attack (myocardial infarction) or sudden cut off of blood supply to the part of the brain (stroke). The risk is more likely with high doses and long-term treatment.</p> <p>Fluid retention, high blood pressure and heart failure have been reported with NSAIDs treatment.</p> <p>Unpleasant awareness of heart beat, heart failure, heart attack or high blood pressure are the side effect reported with very rare frequency which may affect up to 1 in 10,000 treated people.</p>	<p>The medicinal products should not be given to the patients with heart problems.</p> <p>Patients should discuss treatment with doctor or pharmacist if have heart problems, previous stroke or might be at risk of these conditions (for example if has high blood pressure, high blood sugar [diabetes], or high fat [cholesterol] or is a smoker).</p> <p>Side effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms.</p>
<p>Allergic reactions (hypersensitivity and allergic reactions)</p>	<p>Use of ibuprofen tablets can lead to allergic reactions in the following patients:</p> <p>Patients with a history of allergy such as of lung problem associated with tightening of air passages, making breathing difficult (asthma), runny nose, itchy skin rash or swelling of the lips, face, tongue, or throat after taking medicines containing acetylsalicylic acid, such as aspirin or other medicines for pain and inflammation (called NSAIDs) and in patients allergic to ibuprofen or any other contents of the</p>	<p>The medicinal products should not be taken by the patients those are allergic to ibuprofen or any of the other contents or have had allergic reactions after taking medicines containing acetylsalicylic acid such as aspirin or other medicines for pain and inflammation (called NSAIDs).</p> <p>The medicinal products should be stopped at the first appearance of skin rash, mucosal lesions, or any other</p>

Risk	What is known	Preventability
	<p>tablets. The risk for developing narrowing of the airways with difficulty in breathing (bronchospasm), hives (urticaria) or swelling of the face, tongue or throat which can cause great difficulty in breathing (angioedema) may be seen in patients suffering from or with a past history of allergies, allergic cold (hay fever), asthma, long term swelling of nasal mucosa, sinuses, adenoids, or long term blockage in respiratory tract.</p> <p>The highest risk of these reactions is in the first month of treatment.</p> <p>Allergic reactions such as skin rash, itching, asthma attacks (sometimes with low blood pressure) are reported with uncommon frequency which may affect up to 1 in 100 treated persons.</p> <p>Swelling of the face, tongue or throat (larynx) which can cause great difficulty in breathing, rapid heartbeat, severe fall in blood pressure or life threatening shock are reported with very rare frequency which may affect up to 1 in 10,000 treated people. Severe forms of skin reactions such as severe rash with blisters on the skin especially on the legs, arms, hands and feet which can also involve the face and lips (erythema multiforme, Stevens-Johnson's syndrome), severe infection with destruction (necrosis) of skin tissue and muscle, hair loss is reported with very rare frequency which may affect up to 1 in 10,000 treated people.</p>	<p>sign of allergy.</p> <p>Special care should be taken in the cases of allergic conditions.</p>
Impaired kidney function (impaired renal function)	<p>In general the habitual use of painkillers can lead to lasting severe kidney problems. This risk may be increased under physical strain associated with loss of salt and water. Therefore, it should be avoided.</p> <p>Ibuprofen may cause problems with kidney function even in patients who have not had kidney problems before. This may result in swelling of the legs and may even lead to heart failure or high blood pressure in susceptible</p>	<p>Before taking ibuprofen, patient should contact doctor if suffering from reduced kidney function.</p> <p>The medicinal products should not be used in patients with serious kidney problem.</p> <p>The dose should be kept as low as possible for the shortest duration in the patient with serious kidney problem.</p>

Risk	What is known	Preventability
	<p>individuals.</p> <p>Ibuprofen may cause kidney damage especially in patients who already have kidney, heart or liver problems, or are taking methotrexate (used to treat cancer), water pills (diuretics) or ACE inhibitors (used for treating high blood pressure), as well as in the older people. Stopping ibuprofen however generally leads to recovery.</p> <p>There is a risk of kidney problem in dehydrated (loss of water in the body) children.</p> <p>Kidney problems including development of swelling caused by fluid in body's tissues (oedema), inflammation of the kidneys and kidney failure are uncommon side effects reported, which may affect up to 1 in 100 treated people.</p>	<p>In case of long term treatment, patients taking the medicinal product, especially high risk patients should be monitored periodically for kidney function.</p>
Increased risk of bleeding	<p>Ibuprofen may temporarily block the action of blood clotting cells (platelet aggregation) and increase the bleeding time.</p> <p>NSAIDs should not be combined with ticlopidine (a blood thinning medicines) due to increased risk of bleeding.</p> <p>NSAIDs may increase the effects of anticoagulants, such as warfarin or heparin.</p>	<p>The medicinal products should not be given to the patients having active bleeding (including in the brain).</p> <p>Patients with bleeding problem or on medicines to prevent clotting of blood should be observed carefully.</p> <p>Patients with brain dysfunction should only be treated with ibuprofen after careful consideration.</p> <p>In case of simultaneous treatment with warfarin or heparin or ticlopidine bleeding time should be monitored.</p>
Use during last 3 months of pregnancy use during late pregnancy	<p>Ibuprofen must not be taken during the last 3 months of pregnancy since it may cause major heart, lung and kidney problems in the unborn child.</p> <p>If used at the end of pregnancy, it may cause bleeding tendencies in both mother and child and weaken the strength of uterine contractions thus delaying the onset of delivery.</p>	<p>The medicinal products should not be given during last 3 months of pregnancy.</p>
Headache because of	Long term use of any type of	If this situation is experienced

Risk	What is known	Preventability
long term use of medicine (medication overuse headache)	<p>painkillers for headaches can make them worse (medication overuse headache).</p> <p>Headache is the common (may affect up to 1 in 10 treated people) side effect reported with use of ibuprofen.</p>	<p>or suspected, advice of doctor should be obtained and treatment should be stopped.</p> <p>Medication overuse headache (MOH) is suspected in patients who have frequent or daily headaches despite (or because of) the regular use of medicines used to treat headache.</p>

Important potential risks

Risk	What is known
Female fertility	<p>This medicine belongs to class of NSAIDs which can affect fertility in women. The effect on fertility is reversible on stopping the medicine. In situation where pregnancy is planned or there is problem in becoming pregnant, this medicine may not be taken.</p>
Use during first 6 months of pregnancy (use during early pregnancy)	<p>The drug product should be used in the first 6 months of pregnancy after consulting doctor and only when clearly necessary.</p> <p>If the drug product is used by women during first six months of her pregnancy, the dose should be kept low and duration of treatment as short as possible.</p>
Off-label use of simultaneous NSAIDs (Off-label use of concomitant NSAIDs)	<p>Off-label use is the unapproved use of a medicine other than the specified use.</p> <p>Simultaneous use of various NSAIDs can increase the risk of ulcers and bleeding in the stomach and gut.</p> <p>Patients should not use ibuprofen simultaneously with other NSAIDs.</p>

Missing information

Risk	What is known
None	

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the

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risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

The Summary of Product Characteristics and the Package leaflet for Ibuprofen can be found in the Ibuprofen's EPAR page.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

Not applicable

VI.2.7 Summary of changes to the risk management plan over time

This is the first risk management plan for Ibuprofen 200 mg, 400 mg and 600 mg film-coated tablets.