

## VI.2 Elements for a Public Summary

### VI.2.1 *Overview of disease epidemiology*

Seractil (Dexibuprofen) for prescription use is indicated to relieve pain and inflammation caused by osteoarthritis (when your joints become worn), to relieve period (menstrual) pain and to relieve mild to moderate pain, such as pains in the muscles and joints and toothaches.

#### Osteoarthritis (when your joints become worn)

Osteoarthritis (OA) is a group of mechanical abnormalities involving degradation of joints, including articular cartilage and the bone under the cartilage. OA is the most common form of arthritis and the leading cause of chronic disability.

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Symptoms may include joint pain, tenderness, stiffness, locking, and sometimes an effusion. A variety of causes (hereditary, developmental, metabolic, and mechanical deficits) may initiate processes leading to loss of cartilage. When bone surfaces become less well protected by cartilage, bone may be exposed and damaged. As a result of decreased movement secondary to pain, regional muscles may atrophy, and ligaments may become more lax.

The main symptom is pain, causing loss of ability and often stiffness. Pain is generally described as a sharp ache, or a burning sensation in the associate muscles and tendons. OA can cause a crackling noise when the affected joint is moved or touched, and patients may experience muscle cramps and contractions in the tendons. Occasionally, the joints may also be filled with fluid. Humid and cold weather increases the pain in many patients.

OA commonly affects the hands, feet, spine, and the large weight bearing joints, such as the hips and knees, although in theory, any joint in the body can be affected. As OA progresses, the affected joints appear larger, are stiff and painful, and usually feel better with gentle use but worse with excessive or prolonged use, thus distinguishing it from rheumatoid arthritis.

### Menstrual pain or painful periods

Menstrual pain or painful periods is often used synonymously with menstrual cramps, but the latter may also refer to menstrual uterine contractions, which are generally of higher strength, duration and frequency than in the rest of the menstrual cycle.

Menstrual pain can feature different kinds of pain, including sharp, throbbing, dull, nauseating, burning, or shooting pain. It may precede menstruation by several days or may accompany it, and it usually subsides as menstruation tapers off. Menstrual pain may coexist with excessively heavy blood loss, known as menorrhagia.

The main symptom is pain concentrated in the lower abdomen, in the umbilical region or above the pubic region of the abdomen. It is also commonly felt in the right or left abdomen. It may radiate to the thighs and lower back.

Symptoms often co-occurring with menstrual pain include nausea and vomiting, diarrhea or constipation, headache, dizziness, disorientation, hypersensitivity to sound, light, smell and touch, fainting, and fatigue. The symptoms often begin immediately following ovulation and can last until the end of menstruation. This is because menstrual pain is often associated with changes in hormonal levels in the body that occur with ovulation.

The frequency of menstrual pain is estimated to be approximately 25% of women. Reports of menstrual pain are greatest among individuals in their late teens and 20s, with reports usually declining with age. The occurrence in adolescent females has been reported to be 67.2% by one study and 90% by another.

### Mild to moderate pain

Pain is an unpleasant feeling often caused by intense or damaging stimuli, such as stubbing a toe, burning a finger, putting alcohol on a cut, and bumping the "funny bone". The International Association for the Study of Pain's widely used definition states: "Pain is an unpleasant sensory

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and emotional experience associated with actual or potential tissue damage, or described in terms of such damage."

Pain motivates the individual to withdraw from damaging situations, to protect a damaged body part while it heals, and to avoid similar experiences in the future. Most pain resolves promptly once the painful stimulus is removed and the body has healed, but sometimes pain persists despite removal of the stimulus and apparent healing of the body; and sometimes pain arises in the absence of any detectable stimulus, damage or disease.

### OTC Use

#### Cold and flu symptoms

Symptoms of cold include coughing, sore throat, runny nose, sneezing, fever and are mostly due to the body's immune response to the infection rather than to tissue destruction by the viruses themselves. The primary method of prevention is by hand washing with some evidence to support the effectiveness of wearing face masks. No cure for the common cold exists, but the symptoms can be treated.

Common cold is the most frequent infectious disease in humans and all peoples globally are affected with the average adult contracting two to three colds a year and the average child contracting between six and twelve. A number of the viruses that cause the common cold may also result in asymptomatic infections.

Rates of symptomatic infections increase in the elderly due to a worsening immune system.

#### **VI.2.2 Summary of treatment benefits**

Pain is the most common reason for physician consultation. It is a major symptom in many medical conditions, and can significantly interfere with a person's quality of life and general functioning. Psychological factors such as social support, hypnotic suggestion, excitement, or distraction can significantly modulate pain's intensity or unpleasantness.

Dexibuprofen, the active ingredient in Monactil, belongs to a family of medicines called non-steroidal anti-inflammatory drugs (NSAIDs). It is the active dextrorotatory enantiomer of ibuprofen. NSAIDs such as dexibuprofen are used as a painkiller and to control inflammation. They work by reducing the amount of prostaglandins (substances that control inflammation and pain) your body produces.

The antipyretic effect can be effective at lowering the temperature, which may improve the affected person's comfort.

#### **VI.2.3 Unknowns relating to treatment benefits**

There is no evidence that the efficacy (beneficial effect of the medicinal product) is expected to be different in people regarding their age, sex, race and organ impairment.

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**VI.2.4 Summary of safety concerns**

**Important identified risks**

Risk	What is known	Preventability
<p>Severe reactions in the digestive system (Severe gastrointestinal reactions)</p>	<p>It is known that Seractil must not be used in patients with previous bleedings or perforations in the gastrointestinal system caused by NSAIDs due to direct irritation of the gastric mucosa and the reduction of protective prostaglandin level Seractil must not be used in patients with or previously have had recurrent stomach or duodenal (the first section of the small intestine) ulcers (vomiting blood or having black bowel motions or bloody diarrhoea could be a sign that the stomach or intestines are bleeding). Ulcer / bleedings can occur due to direct irritation of the gastric mucosa and the reduction of protective prostaglandin level by NSAIDs. Furthermore Seractil must not be used in patients who currently have a flare up of an inflammatory disease of the intestines.</p> <p>It is known that precautions should be taken if patients have had bowel ulcers, ulcerative colitis or Crohn´s disease (both are forms of inflammatory bowel disease). due to the products tendency</p>	<p>The risk can be minimised by</p> <ul style="list-style-type: none"> <li>- Considering these co-existing factors</li> <li>- Not exceeding the recommended dose or duration of treatment, especially in elderly patients</li> <li>- Prescribing protective agents together with Seractil by the doctor</li> </ul>

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Risk	What is known	Preventability
	<p>to cause gastric bleeding and form ulceration in the gastric mucosa.</p> <p>Special care should be taken if patients had stomach or duodenal ulcers, particularly with bleeding and perforation and in the elderly.</p> <p>The side effect is serious and uncommon or rare (affects 1 to 10 users in 1,000 or 1 to 10 users in 10,000).</p>	
<p>Bleedings in the brain (Cerebrovascular bleeding)</p>	<p>Seractil must not be used in patients who have bleedings in the brain or other active bleedings as the bleeding time could be prolonged and increased. Special care should be taken in patients who have previous stroke or a risk of this condition (e.g. high blood pressure, diabetes, high cholesterol or smoker). High doses and long term treatment may be associated with a small increased risk of bleedings in the brain. The side effect is classified as serious.</p>	<p>The risk can be minimised by</p> <ul style="list-style-type: none"> <li>- Considering these co-existing factors</li> <li>- Not exceeding the recommended dose or duration of treatment as any risk is more likely with high doses and prolonged treatment.</li> </ul> <p>Patients should discuss the treatment with the doctor or pharmacist.</p>
<p>Serious heart failure (Congestive heart failure)</p>	<p>It is known that Seractil must not be used in patients with serious heart failure as the risk of heart attack ("myocardial infarction") may be increased.</p> <p>Patients who have heart problems including heart failure, angina (chest pain), or have had a heart attack, bypass surgery, peripheral</p>	<p>The risk can be minimised by</p> <ul style="list-style-type: none"> <li>- Considering these co-existing factors</li> <li>- Not exceeding the recommended dose or duration of treatment</li> </ul> <p>Patients with serious heart failure must not use the medicinal product.</p>

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Risk	What is known	Preventability
	<p>artery disease (poor circulation in the legs or feet due to narrow or blocked arteries), or any kind of stroke (including "mini stroke" or transient ischaemic attack "TIA") or a risk of these conditions (e.g. high blood pressure, diabetes, high cholesterol, have a family history of heart disease or stroke or smoker) should discuss the treatment with the doctor or pharmacist. Anti-inflammatory/pain-killer medicines like Seractil may be associated with a small increased risk of heart attack or stroke, particularly when used at high doses.</p> <p>The side effect can be fatal but the probable incidence is small.</p>	
<p>Allergic reaction including serious reactions which causes difficulty in breathing or dizziness                      (Hypersensitivity / anaphylactic reactions)</p>	<p>The medicinal product must not be used for patients who are allergic to the active substance dexibuprofen or any for the other ingredients of the product. The side effect can be serious and is classified as rare (affects 1 to 10 users in 10,000).</p>	<p>Such patients must not use the medicinal product.</p>
<p>Kidney disease                      (Renal dysfunction)</p>	<p>Seractil must not be used in patients who are suffering from serious kidney disease. NSAIDs can cause serious kidney diseases in very rare</p>	<p>The risk can be minimised by</p> <ul style="list-style-type: none"> <li>- Considering these co-existing factors</li> <li>- Not exceeding the recommended dose or</li> </ul>

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Risk	What is known	Preventability
	<p>cases (affects less than 1 user in 10,000). The mechanism is due to changes in kidney blood flow, ordinarily mediated by prostaglandins. This productgroup (NSAIDs) blocks the prostaglandin-mediated effect and causes constriction of the vessels and decreases renal perfusion pressure leading to damage of the kidneys.</p> <p>Special care should be taken in patients with known kidney problems.</p>	<p>duration of treatment</p> <ul style="list-style-type: none"> <li>- Regular check-ups by the doctor</li> </ul>
<p>Liver damage (Hepatic impairment)</p>	<p>Seractil must not be used in patients who are suffering from serious liver damage as it may increase problems with the liver in rare cases (affects 1 to 10 users in 10,000). Special care should be taken in patients with other liver problems or addicted to alcohol.</p>	<p>The risk can be minimised by</p> <ul style="list-style-type: none"> <li>- Considering these co-existing factors</li> <li>- Not exceeding the recommended dose or duration of treatment</li> <li>- Regular check-ups by the doctor</li> </ul>
<p>Disorders to the development of blood (Disorders of haematogenesis)</p>	<p>It is known that Seractil may have effects to blood disorders, including disorders that reduce the number of white or red blood cells or platelets in rare cases (affects 1 to 10 users in 10,000)</p>	<p>The risk can be minimised by</p> <ul style="list-style-type: none"> <li>- Not exceeding the recommended dose or duration of treatment</li> <li>- Regular check-ups by the doctor</li> </ul>

**Important potential risks**

Risk	What is known
<p>Serious skin reactions (Serious skin reactions)</p>	<p>Seractil has to be stopped if patients have a severe skin rash, severe blistering or peeling of the skin, mucosal lesions or any</p>

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Risk	What is known
	signs of hypersensitivity. The possible side effect can occur in very rare cases (affects less than 1 user in 10,000).
High blood pressure and decreased effect of concomitant use of medicines for high blood pressure (Hypertension and decreased effect of co-administered anti-hypertensive medicines)	Special care has to be taken with Seractil in patients with high blood pressure. Patients who have heart problems including heart failure, angina (chest pain), or have had a heart attack, bypass surgery, peripheral artery disease (poor circulation in the legs or feet due to narrow or blocked arteries), or any kind of stroke (including "mini stroke" or transient ischaemic attack "TIA") or a risk of these conditions (e.g. high blood pressure, diabetes, high cholesterol, have a family history of heart disease or stroke or smoker) should discuss the treatment with the doctor or pharmacist.  Patients should tell their doctor if Seractil is taken with medicines used to treat high blood pressure. The effect of these medicines may be reduced.
Stroke or heart attack (Thromboembolic events)	Anti-inflammatory/pain-killer medicines like Seractil may be associated with a small increased risk of heart attack or stroke, particularly when used at high doses. Patients do not exceed the recommended dose or duration of treatment.
Use in patients with systemic lupus erythematosus (a disease which affects joints, muscles and skin) (Use in patients with systemic lupus erythematosus)	Patients with this allergic condition which causes joint pain, skin rashes and fever should not take Seractil as these patients are predisposed to serious side effects such as aseptic meningitis (symptoms are headache, fever, stiff neck, and generally feeling ill). The possible side effect is classified as very rare (affects less than 1 user in 10,000).
Concomitant use with other drugs (Drug interactions)	Seractil may affect or be affected by some other medicines that are anti-coagulants (i.e. thin blood/prevent clotting e.g. aspirin/acetylsalicylic acid, warfarin, ticlopidine). NSAIDs such as Seractil reduce renal blood flow and thereby increase the blood level and so the risk of side effects of drugs used to treat certain mood disorders (lithium) and methotrexate (a medicine for cancer and rheumatism). Patients should therefore always seek the advice of their doctor or pharmacist before using Seractil with other medicines.
Long term use / Misuse	Although Seractil is available without medical prescription,



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Risk	What is known
(Long term use / Misuse)	certain diseases or conditions during the treatment or co-administration of certain medicinal products might increase the risk of potentially serious adverse effects. The medicinal product may be used in a wrong administration. In the information leaflet for the patient the correct use of the medicinal product is exactly described. Taking Seractil without medical control for a longer period or in higher dose than set out in the patient information leaflet may increase the risk of potentially serious adverse effects.
Blood clotting disorders (Coagulation disorders)	Seractil should not be taken in patients who are suffering from blood cell production or clotting disorders. The product causes blood thinning effects which may be serious when combined with other drugs that also decrease blood clotting. It could prolong the bleeding time and bleeding can be increased.
Use in pregnancy (Use in pregnancy)	Patients must not take Seractil from the beginning of the 6 <sup>th</sup> month of pregnancy as this may seriously harm (heart and renal adverse effects) the unborn baby, even at very low doses. In the first five months patients should only use Seractil after consulting a doctor. If patients are pregnant, think they may be pregnant or are planning to have a baby, ask the doctor for advice before taking this medicine. The frequency of this risk is not classified.

**Missing information**

Risk	What is known
Use in patients with chickenpox (Use in patients with varicella infection)	Patients should avoid taking NSAIDs during a chickenpox infection as it might be worsening these infections. The possible side effect is classified as very rare (affects less than 1 user in 10,000).
Fertility (Fertility)	Seractil belongs to a group of medicines which may impair fertility in women in rare cases. This is reversible on stopping the medicine and fertility will return to normal. Patients should talk to their doctor if they have problems becoming pregnant.

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**VI.2.5 Summary of additional risk minimisation measures by safety concern**

Not applicable

**VI.2.6 Planned post authorisation development plan**

Not applicable

**VI.2.7 Summary of changes to the Risk Management Plan over time**

**Table 4.** Major changes to the Risk Management Plan over time

Version	Date	Safety Concerns	Comment
00	08 May 2008	Cardiovascular risk Gastrointestinal risk Serious skin reactions Pregnancy	version 00 referred to powder for oral suspension only
01	23 December 2009	No changes	version 01 referred to powder for oral suspension only; Update due to marketing condition clinical study IV/48.4
02	25 June 2014	Update and adaption to SmPC	Version 02 refers to all Dexibuprofen forms including OTC use;
03	30 December 2015	Update regarding Outcome of Referral EMEA/H/A-31/1401	Version 03 refers to all Dexibuprofen forms including OTC use;