Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Vocasept 8.75 mg Lozenges

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each lozenge contains 8.75 mg of flurbiprofen.

Excipients with known effect:
Isomalt (E953): 2047.60 mg / lozenge
Maltitol, liquid: 511.75 mg / lozenge
Honey flavour (contains citronellol): 2.40 mg/lozenge.
Lemon flavour (contains citral, citronellol, geraniol, limonene and linalool): 9.00 mg/lozenge

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Lozenge

White to pale yellow coloured, round, flat bevelled lozenge with honey and lemon flavour and with a thickness of 7 to 8 mm and a diameter of 18 to 19 mm.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Vocasept 8.75 mg lozenges are indicated for the local short-term symptomatic relief of sore throat in adults and adolescents over the age of 12 years.

4.2 Posology and method of administration

Posology

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

Adults and adolescents over the age of 12 years:
One lozenge sucked/dissolved slowly in the mouth every 3 to 6 hours as needed. Maximum 5 lozenges in a 24-hour period.
This product should be used for a maximum of three days.

Paediatric population:
The use of Vocasept in children under 12 years of age is not recommended because safety and efficacy in this age group have not been established.

Elderly population
Due to the limited clinical trials, available, a general dose cannot be recommended. Elderly patients are at higher risk of suffering serious consequences of adverse reactions.

Impaired renal function
In patients with mild to moderate impairment of renal function no dose reduction is required. In patients with severe renal insufficiency flurbiprofen is contraindicated (see section 4.3).

Impaired hepatic function
In patients with mild to moderate impairment of hepatic function no dose reduction is required. In patients with severe hepatic insufficiency (see section 5.2.) flurbiprofen is contraindicated (see section 4.3).

Method of administration

For oromucosal administration and short-term use only.

Lozenge should be freely dissolved in the mouth.

As with all lozenges, Vocasept 8.75 mg lozenges should be moved around inside the mouth to avoid local irritation. Treatment should be withdrawn in case of mouth irritation.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Patients who have previously shown hypersensitivity reactions (e.g. asthma, bronchospasm, rhinitis, angioedema or urticaria) in response to acetylsalicylic acid or other non-steroidal anti-inflammatory drugs (NSAIDs).
- Active or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration) and intestinal ulceration.
- History of gastrointestinal bleeding or perforation, severe colitis, haemorrhagic, or haematopoietic disorders related to previous treatment with NSAIDs.
- Last trimester of pregnancy (see section 4.6).
- Severe heart failure, severe renal failure, or severe hepatic failure (see section 4.4)

4.4 Special warnings and precautions for use

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

The treatment should be reevaluated if symptoms get worse or if new symptoms occur.

Other NSAIDs
Concomitant use of flurbiprofen and other NSAIDs, including selective cyclooxygenase-2 inhibitors, should be avoided (see section 4.5).

Elderly population
Elderly patients have an increased frequency of adverse reactions to NSAIDs, particularly gastrointestinal bleeding and perforation, which may be fatal (see 4.2).

Gastrointestinal
NSAIDs should be given with care in patients with a history of gastrointestinal diseases (ulcerative colitis, Crohn's disease), as these conditions could be exacerbated (see section 4.8).
Gastrointestinal bleeding, ulceration or perforation, which can be fatal has been reported, with all NSAIDs at any time during treatment, with or without warning symptoms or a previous history of serious gastrointestinal events.
The risk of gastrointestinal bleeding, ulceration or perforation is higher with increasing NSAIDs doses, in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation (see section 4.3), and in the elderly, however this effect is not usually seen with short term limited use products such as Vocasept 8.75 mg lozenges.
Patients with a history of gastrointestinal toxicity, particularly the elderly, should report any unusual abdominal symptoms (especially gastrointestinal bleeding), to their treating physician .
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 acetylsalicylic acid (see section 4.5).
In patients taking flurbiprofen, the treatment should be withdrawn if gastrointestinal bleeding or ulceration occurs.

Cardiovascular, renal and hepatic impairment
NSAIDs have been reported to cause nephrotoxicity in various forms including interstitial nephritis, nephrotic syndrome and renal failure. The administration of an NSAID may cause a dose-dependent reduction in prostaglandin formation and precipitate renal failure. Patients at greatest risk of this reaction are those with impaired renal function, cardiac impairment,

liver dysfunction, those taking diuretics and the elderly. However, this effect is not usually seen with short term, limited use products such as flurbiprofen lozenges.

Cardiovascular and cerebrovascular effects
Caution (discussion with doctor or pharmacist) is required before initiating treatment in patients with a history of hypertension and/or heart failure, as fluid retention, hypertension and oedema have been reported in association with NSAID therapy (see sections 4.3 and 4.8).

Clinical trial and epidemiological data suggest that the administration of some NSAIDs (particularly at high doses and long-term treatment) may be associated with a small increased risk of arterial thrombotic events (for example, myocardial infarction or stroke). There is not enough data to exclude this risk for flurbiprofen when administered at a maximum daily dose of 5 lozenges.

Nervous System effects
Analgesic-induced headache: with prolonged use of analgesics or when analgesics are not used as directed, headache may occur, which must not be treated with increased doses of the medicinal product.

Hepatic impairment
In patients with mild to moderate hepatic impairment this medicinal product should be used with caution (see section 4.8). This medicinal product is contraindicated in patients with severe hepatic impairment (see section 4.3).

Dermatological
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). Flurbiprofen should be discontinued at the first appearance of skin rash, mucosal lesions or any other sign of hypersensitivity.

SLE (Systemic Lupus Erythematosus) and mixed connective tissue disease
Patients with SLE and mixed connective tissue disease may have an increased risk of aseptic meningitis (see section 4.8). However, this effect is not usually seen with short term limited use products such as flurbiprofen lozenges.

Respiratory disorders
Bronchospasm can be triggered in patients suffering from, or with history of bronchial asthma or allergic diseases. Flurbiprofen must be used with caution in these patients.

Infections
The patient should immediately see a doctor if symptoms of bacterial infection occur or get worse during the treatment with flurbiprofen as in isolated cases, exacerbation of infectious inflammations was described (e.g. development of necrotizing fasciitis) in connection with the time when the systemic NSAIDs were used. The need to start antibiotic treatment with an anti-infective agent should be evaluated.

Masking of symptoms of underlying infections
Epidemiological studies suggest that systemic non-steroidal anti-inflammatory drugs (NSAIDs) 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 Vocasept is administered while the patient suffers from fever or pain in relation to infection, monitoring of infection is advised.

Excipients with known effect
This medicinal product contains isomalt and liquid maltitol which may have a mild laxative effect. Patients with rare hereditary problems of fructose intolerance should not take this medicinal product. Calorific value 2.3 kcal/g maltitol and isomalt.

This medicinal product contains fragrances with citral, citronellol, geraniol, limonene and linalool which may cause allergic reactions.

4.5 Interaction with other medicinal products and other forms of interaction

Flurbiprofen should be avoided in combination with:	
Other NSAIDs, including cycloxygenase-2 selective inhibitors:	Avoid concomitant use of two or more NSAIDs, since this may increase the risk of adverse effects (particularly, gastrointestinal adverse events such as ulcers and bleeding) (see section 4.4).

Acetylsalicylic acid (low dose)	Unless low-dose acetylsalicylic acid has been recommended by the doctor (not above 75 mg/day), as it may increase the risk of adverse reactions (see section 4.4).

Flurbiprofen should be taken with caution in combination with:	
Anticoagulants:	NSAIDs may increase the effects of anticoagulants, such as warfarin (see section 4.4).
Antiplatelet agents:	Increased risk of gastrointestinal ulceration or bleeding (see section 4.4).
Antihypertensive drugs (diuretics, ACE- inhibitors, angiotensin II receptor blockers):	NSAIDs may reduce the effect of diuretics and other antihypertensive drugs; they may increase the nephrotoxicity caused by inhibition of cyclooxygenase, particularly in patients with compromised renal function (patients should be adequately hydrated and monitoring of renal function should be considered when initiating concomitant therapy, and periodically thereafter).
Alcohol	May increase the risk of adverse reactions, particularly gastrointestinal tract bleeding.
Cardiac glycosides:	NSAIDs may exacerbate cardiac failure, reduce the glomerular filtration (GFR) rate and increase plasma glycosides levels - appropriate monitoring is recommended and, if necessary, dose adjustment
Cyclosporine:	Increased risk of nephrotoxicity.
Corticosteroids:	May increase the risk of adverse reactions, particularly in the gastrointestinal tract (see section 4.3).
Lithium:	May increase serum levels of lithium-appropriate monitoring is recommended and, if necessary, dose adjustment.
Methotrexate:	The administration of NSAIDs within 24 hours before or after administration of methotrexate may lead to elevated concentrations of methotrexate and an increase in its toxic effect.
Mifepristone:	NSAIDs should not be used 8-12 days after the administration of mifepristone, as NSAIDs can reduce the effect of mifepristone.
Oral antidiabetics	Alteration of blood glucose levels have been reported (increased check rate is recommended).
Phenytoin	May increase serum levels of phenytoin - appropriate monitoring and, if necessary, dose adjustment is recommended
Potassium-sparing diuretics	Concomitant use may cause hyperkalaemia (serum potassium level testing is recommended).
Probenecid, sulfinpyrazone	Medicinal products containing probenecid or sulfinpyrazone may delay the excretion of flurbiprofen.
Quinolone antibiotics:	Animal and human data suggest that NSAIDs may increase the risk of seizures associated with quinolones. Patients taking NSAIDs and quinolones may have a higher risk of developing convulsions.
Selective serotonin reuptake inhibitors (SSRIs)	Increased risk of gastrointestinal ulceration or bleeding (see section 4.4).
Tacrolimus:	Possible increase of the nephrotoxicity risk when NSAIDs are administered with tacrolimus.
Zidovudine:	Increased risk of hematological toxicity when NSAIDs are administered with zidovudine.

So far, studies have not revealed any interaction between flurbiprofen and tolbutamide or antacids.

4.6 Fertility, pregnancy and lactation

Pregnancy

The inhibition of prostaglandin synthesis may adversely affect pregnancy and/or embryo/fetal development. Epidemiological study results suggest an increased risk of miscarriage and cardiac malformation and gastroschisis after the use of a prostaglandin synthesis inhibitor in early pregnancy. The absolute risk of cardiovascular malformation increased from less than 1% to approximately 1.5%. It is believed that the risk increases with treatment dose and duration. In animals, administration of a prostaglandin synthesis inhibitor had been shown to result in increased pre- and post-implantation loss and embryo-foetal lethality. In addition, increase incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period.

There are no clinical data from the use of flurbiprofen lozenges during pregnancy. Even if systemic exposure is lower compared with oral administration, it is not known if the systemic flurbiprofen exposure reached after topical administration can be harmful to an embryo/foetus.

During the first and second trimesters of pregnancy, flurbiprofen should not be administered unless strictly necessary. If flurbiprofen is used by women who are trying to conceive, or in the first and second trimesters of pregnancy, the lowest possible dose and the shortest possible treatment should be used.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose
the fetus to:

- cardiopulmonary toxicity (premature closure of the ductus arteriosus and pulmonary hypertension);
- renal dysfunction, which may progress to renal failure with oligohydramnios;

the mother and newborn, at the end of pregnancy, to:

- Possible prolongation of bleeding time, an anti-aggregating effect that may occur even at very low doses.
- Inhibition of uterine contractions resulting in delayed or prolonged labor.

Consequently, flurbiprofen is contraindicated during the third trimester of pregnancy (see section 4.3).

Breast-feeding

In limited studies, flurbiprofen appears in the breast milk in very low concentrations and is unlikely to affect breast-fed infant adversely. However, because of possible adverse effects of NSAIDs on breast-fed infants, flurbiprofen lozenges are not recommended for use in nursing mothers.

Fertility

There is some evidence that medicinal products which inhibit cyclo-oxygenase/ prostaglandin synthesis may cause impairment of female fertility by an effect on ovulation. This is reversible on withdrawal of treatment.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. However, dizziness and visual disturbances are possible side effects after taking NSAIDs.

4.8 Undesirable effects

Hypersensitivity reactions to NSAIDs have been reported and these may consist of:

- non-specific allergic reactions and anaphylaxis
- respiratory tract reactivity such as asthma, aggravated asthma worsening, bronchospasm and dyspnoea
- several skin reactions, such as pruritus, urticaria, angioedema and more rarely exfoliative and bullous dermatoses (including epidermal necrolysis and *erythema multiforme*)

Oedema, hypertension, and cardiac failure have been reported in association with NSAID treatment.
Clinical trial and epidemiological data suggest that use of some NSAIDs, (particularly at high doses and in long term treatment) may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke), (see section 4.4). There is insufficient data to exclude such a risk for flurbiprofen 8.75 mg lozenges

The following list of adverse effects refers to those reported with flurbiprofen at OTC doses, for short-term use:
(Very common (≥ 1/10, common (≥ 1/100, < 1/10), uncommon (≥ 1/1,000 < 1/100), rare (≥ 1/10,000 < 1/1,000), very rare (< 1/10,000), not known (cannot be estimated from the available data)).

System Organ Class	Frequency	Undesirable effects
Blood and lymphatic system disorders	Not known	Thrombocytopenia, anaemia
Immune System disorders	Rare	anaphylactic reaction
Psychiatric disorders	Uncommon	insomnia
Cardiovascular and cerebrovascular disorders	Not known	oedema, hypertension and cardiac failure
Nervous System disorders	Common	dizziness, headache, paraesthesia
	Uncommon	somnolence,
Respiratory, thoracic and mediastinal disorders:	Common	throat irritation
	Uncommon	exacerbation of asthma and bronchospasm, dyspnoea, wheezing, oropharyngeal blistering, pharyngeal hypoaesthesia.
Gastrointestinal disorders	Common	diarrhoea, mouth ulceration, nausea, oral pain, paraesthesia oral, oropharyngeal pain, oral discomfort (warm or burning feeling or tingling of the mouth).
	Uncommon	abdominal pain, abdominal distension, constipation, dry mouth, dyspepsia, flatulence, glossodynia, dysgeusia, oral dysaesthesia, vomiting
Hepatobiliary disorders	Not known:	hepatitis
Skin and subcutaneous tissue disorders	Uncommon:	various skin rashes, pruritus.
	Not known:	severe forms of skin reaction such as bullous reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis
General disorders and administration site conditions	Uncommon	fever, pain

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization 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
Website: www.hpra.ie.

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. Tinnitus, headache and gastrointestinal bleeding are also possible. In more serious poisoning with NSAIDs, toxicity is seen in the central nervous system, manifesting as drowsiness, occasionally excitation, blurred vision and disorientation or coma. Occasionally, patients develop convulsions. In serious poisoning with NSAIDs, metabolic acidosis may occur and prothrombin time may be prolonged/INR increased, probably due to interference with the actions of circulating clotting factors. Acute renal failure and liver damage may occur. In asthmatic patients, exacerbation of asthma is possible.

Management
There is no specific antidote for flurbiprofen. Management should be symptomatic and supportive and include the maintenance of a clear airway and monitoring of cardiac and vital signs until they become stable.
Consider the use of activated charcoal and if needed serum electrolyte correction, especially if less than one hour has elapsed since ingestion of a potentially toxic amount.Frequent or prolonged convulsions should be treated with intravenous diazepam or lorazepam. Administer bronchodilators for asthma.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Throat preparations, other throat preparations, ATC Code: R02AX01

Mechanism of action
Flurbiprofen is a propionic acid derivative NSAID which acts through inhibition of prostaglandin synthesis.

Pharmacodynamic effects
In humans, flurbiprofen has potent analgesic, antipyretic and anti-inflammatory properties and the 8.75 mg dose dissolved in artificial saliva has been shown to reduce prostaglandin synthesis in cultured human respiratory cells. According to studies using the whole blood assay, flurbiprofen is a mixed COX- 1/COX-2 inhibitor with some selectivity towards COX- 1.

Preclinical studies suggest that the R (-) enantiomer of flurbiprofen and related NSAIDs may act on the central nervous system; the suggested mechanism is by inhibition of induced COX-2- at the level of the spinal cord.

Clinical efficacy and safety
Flurbiprofen from the 8.75 mg lozenge has been shown to penetrate into the layers of the whole human pharynx tissue including the deeper layer in an *ex vivo* model.

A single dose of flurbiprofen 8.75 mg delivered locally to the throat in a lozenge has also been demonstrated to relieve sore throat, including swollen and inflamed sore throats through a significant reduction (LS Mean Difference) in sore throat pain intensity from 22 minutes (- 5.5mm), reaching a maximum at 70 minutes (-13.7mm) and remaining significant for up to 240 minutes (-3.5mm) including patients with streptococcal and non-streptococcal infections, reduction in difficulty swallowing from 20 minutes (-6.7mm), reaching a maximum at 110 minutes (-13.9mm) and for up to 240 minutes (-3.5mm) and reduction in the feeling of a swollen throat at 60 minutes (-9.9mm), reaching a maximum at 120 minutes (-11.4mm) and for up to 210 minutes (-5.1mm).

Multiple dose efficacy measured using Sum of Pain Intensity Differences (SPID) over 24 hours has demonstrated significant reduction in sore throat pain intensity (-473.7mm*h to - 529.1mm*h), difficulty swallowing (-458.4mm*h to -575.0mm*h) and swollen throat (- 482.4mm*h to -549.9mm*h) with statistically significant greater summed reduction in pain at each hourly interval over 23 hours for all three measures and statistically significantly greater sore throat relief each hour over the 6 hour assessment time. Efficacy of multiple doses after 24 hours and over 3 days has also been demonstrated.

For those patients taking antibiotics for streptococcal infection, there was statistically significant greater relief of sore throat pain intensity for flurbiprofen 8.75mg from 7 hours and onwards after antibiotics were taken. The analgesic effect of flurbiprofen 8.75 mg was not reduced by the administration of antibiotics to treat patients with streptococcal sore throat.

At 2 hours post first dose, flurbiprofen 8.75mg lozenges provided significant resolution of some of the associated symptoms of sore throat present at baseline including coughing (50% vs 4%), loss of appetite (84% vs 57%) and feverishness (68% vs 29%). The lozenge format dissolves in the mouth over 5 - 12 minutes and provides a measurable soothing and coating effect at 2 minutes.

Paediatric population
No specific studies in children have been undertaken. Efficacy and safety studies on flurbiprofen 8.75mg lozenges have included adolescents aged 12 – 17 years, although small sample size means that no statistical conclusions can be drawn.

5.2 Pharmacokinetic properties

Absorption
Flurbiprofen 8.75 mg lozenges dissolve over 5 – 12 minutes and the flurbiprofen is readily absorbed, with detection in the blood at 5 minutes and plasma concentrations peaking at 40 – 45 minutes after administration but remaining at a mean low level of 1.4 µg/mL which is approximately 4.4 times lower than a 50 mg tablet dose. Absorption of flurbiprofen can occur from the buccal cavity by passive diffusion. Rate of absorption is dependent on pharmaceutical form with peak concentrations achieved more rapidly than, but of similar magnitude to, those achieved after an equivalent swallowed dose.

Distribution
Flurbiprofen is rapidly distributed throughout the body and is extensively bound to plasma proteins.

Biotransformation/Elimination

Flurbiprofen is mainly metabolised by hydroxylation and excreted via the kidneys. It has an elimination half-life of 3 to 6 hours. Flurbiprofen is excreted in very small amounts in human milk (less than 0.05 µg/ml). Approximately 20-25% of a flurbiprofen oral dose is excreted unchanged.

Special populations
No difference in pharmacokinetic parameters between elderly and young adult volunteers has been reported following oral administration of flurbiprofen tablets. No pharmacokinetic data have been generated in children below 12 years of age following administration of Flurbiprofen 8.75 mg however administration of both flurbiprofen syrup and suppository formulations indicate no significant differences in pharmacokinetic parameters compared with adults.

5.3 Preclinical safety data

There is no preclinical data of relevance additional to information already included in other relevant sections.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Isomalt (E953)
Maltitol, liquid
Acesulfame potassium (E950)
Macrogol
Levomenthol
Honey flavour (contains ethyl phenyl acetate, phenyl ethyl acetate, citronellol, aldehyde C-16 and propylene glycol (E 1520))
Lemon flavour (contains citral, citronellol, geraniol, limonene and linalool)

May contain trace amounts of light liquid paraffin used as processing aid.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

PVC/PVDC//Aluminium blister. Package sizes: 8, 16, 24 and 32 lozenges.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER

PA25361/001/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 31st July 2026

10 DATE OF REVISION OF THE TEXT