

SUMMARY OF PRODUCT CHARACTERISTIC

1. NAME OF THE MEDICINAL PRODUCT

FLUREND[®] % 0,25 oral spray

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:

30 ml spray solution contains 0.075 g flurbiprofen

Excipients:

Sodium benzoate (E211)	0.06 g
Glycerin	3.0 g
Ethyl alcohol (96%)	3.0 g
Sorbitol (E420)	2.1 g
Sodium saccharin	0.045 g
Sodium hydroxide	0.026 g

See 6.1 for the list of excipients.

3. PHARMACEUTICAL FORM

Spray, solution for oral mucosa
Colorless, clear solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

It is used as an anti-inflammatory treatment for the relief of pain in conditions of the oropharynx (e.g. gingivitis, oral inflammation, pharyngeal inflammation). Also, it is used as a preventive treatment after dental procedures.

4.2. Posology and method of administration

Posology/duration and frequency of administration:

It is directly sprayed onto the affected area 3 times daily with two sprays in each administration. Each spray provides 0.2 ml of solution containing 0.50 mg of flurbiprofen.

Method of administration:

FLUREND[®] oral spray is used on the affected area in the mouth and should not be swallowed.

Additional information for special populations

Renal failure:

Care should be taken in treating patients with renal failure.

Liver failure:

Care should be taken in treating patients with liver failure.

Pediatric populations:

Should not be used in children under 12 years of age

Geriatric populations:

No data exists regarding its use in geriatric individuals.

4.3. Contraindications

- Hypersensitivity to flurbiprofen or to any of the excipients in the formulation.
- Hypersensitivity to acetylsalicylic acid or other non-steroidal anti-inflammatory drugs.
- A history of bronchospasm, or rhinitis or urticaria due to use of acetylsalicylic acid or non-steroidal anti-inflammatory drugs.
- Past or current history of peptic ulceration.

4.4. Special warnings and precautions for use

To be used externally.

FLUREND[®] oral spray is sprayed on the affected part of the oral cavity and should not be swollen.

Care should be exercised in patients with renal, cardiac, or hepatic failure.

FLUREND[®] contains sorbitol (E420). If you have been previously told by your doctor that you have intolerance to certain types of sugar, please consult with your doctor before using this medicine.

FLUREND[®] contains less than 10 g of glycerine in each dose. No effects due to glycerine is expected at this dose level.

FLUREND[®] contains less than 1 mmol (23 mg) of sodium in each dose; no side effects are likely at this dose level.

This medicinal product contains small amount of ethanol (alcohol) (less than 100 mg in each dose).

FLUREND[®] contains 0.6 g of sodium benzoate in each 30 ml. This agent may cause mild irritation in the skin, eyes, or mucous membranes.

4.5. Interaction with other medicinal products and other forms of interaction

Flurbiprofen may rarely reduce the diuretic activity of furosemide. Also, it may rarely interact with anticoagulant medications. No interaction between flurbiprofen and digoxin, tolbutamide, or antacids occur.

4.6 Pregnancy and lactation**General recommendation**

Pregnancy category: C (**D in the third trimester**).

Women of childbearing potential/Contraception

No data exists regarding the use of flurbiprofen a in women of childbearing potential.

Pregnancy

Although animal studies have shown no teratogenic potential for flurbiprofen, it should not be used in pregnant women if potential risks on the fetus outweigh the benefit in pregnant women, since there are no adequate studies on humans.

Breastfeeding

Due to potential effects of prostaglandin inhibitors on newborns, use of flurbiprofen during lactation is not recommended.

Ability to reproduce/Fertility

There are no known effects on the ability to reproduce.

4.7. Effects on the ability to drive and use machines

No studies have been carried out to test the effect of flurbiprofen on the ability to drive or use machinery. However, based on its pharmacodynamic properties and overall safety profile, no effects are likely.

4.8. Undesirable effects

The adverse effects were classified as follows based on their frequency of occurrence:

Very common ($\geq 1/10$), common ($\geq 1/100$ to $< 1/10$), uncommon ($\geq 1/1000$ to $< 1/100$), rare ($\geq 1/10000$ to $< 1/1000$), very rare ($< 1/10000$), unknown (existing data does not allow frequency estimates).

General disorders and conditions of the site of administration

Unknown:

Symptoms of sensitivity.

Local irritation.

4.9. Overdose and its treatment

When the low concentration of the active ingredient as well as the intended local use are considered, overdose is unlikely. In cases of overdose, appropriate symptomatic treatment should be administered.

Symptoms of overdose may include nausea, vomiting, and gastrointestinal discomfort.

5. PHARMACOLOGICAL PROPERTIES**5.1. Pharmacodynamic properties**

Pharmacotherapeutic group: Throat preparations

ATC code: R02AX01

FLUREND[®] contains a non-steroidal anti-inflammatory agent with anti-inflammatory, analgesic, and antipyretic properties. Similar to other non-steroidal anti-inflammatory agents, the mechanism of action of flurbiprofen is not completely understood and is thought to be related with the inhibition of prostaglandin synthase.

Like other NSAIDs, flurbiprofen inhibits the cyclooxygenase (COX) enzyme including COX-1 and COX-2 isoenzymes in body tissues, leading to the inhibition of prostaglandin synthesis. Flurbiprofen is one of the most potent prostaglandin inhibitors among NSAID class of drugs.

5.2. Pharmacokinetic properties**Absorption:**

Flurbiprofen is absorbed through the buccal mucosa via passive diffusion. Buccal membrane is essentially a lipid membrane, and flurbiprofen is readily transported into the buccal mucosa

due to its high lipid solubility. Flurbiprofen is a weak acid, and therefore the rate of absorption is a function of pH.

Flurbiprofen is used for the treatment and prevention of periodontal diseases due to its anti-inflammatory effects. Since local administration into the oral cavity will have local effect, high systemic concentrations are not required. For this indication, weak buccal absorption is a desired effect.

FLUREND® oral spray is a topical agent that is used externally. Therefore it should not be swallowed. No significant systemic effects are expected with the use of FLUREND® oral spray. However, 50 to 100 mg of therapeutic doses of oral flurbiprofen display the following pharmacokinetic properties:

Distribution:

Plasma peak levels are reached within 1.5 to 2 hours. The apparent volume of distribution (V_z/F) of both R and S-flurbiprofen is approximately 0.12 L/kg. More than 99% of both enantiomers of flurbiprofen are bound to plasma proteins, mainly to albumin. Plasma protein binding is relatively stable with the typical average steady state concentrations achieved by the recommended doses ($\leq 10 \mu\text{g/ml}$).

Biotransformation:

A variety of flurbiprofen metabolites have been detected in human plasma and urine including the two major metabolites, ([2-(2-fluoro-4'-hydroxy-4-biphenyl) propionic acid] and [2-(2-fluoro-3'-hydroxy-4-methoxy-4-biphenyl)], as well as 4-hydroxy-flurbiprofen, 3,4-dihydroxyflurbiprofen, 3-hydroxy-4-methoxy-flurbiprofen, their conjugates, and conjugated flurbiprofen. In contrast with other arylpropionic acid derivatives (e.g. ibuprofen), metabolism of R-flurbiprofen to S-flurbiprofen occurs at a minimal rate. In vitro studies have shown that P450 2C9 plays an important role in the metabolism of the main metabolite 4-hydroxy-flurbiprofen. The 4-hydroxyflurbiprofen metabolite has demonstrated minimal anti-inflammatory activity in human models of inflammation. Flurbiprofen does not induce enzymes that alter its metabolism. The total plasma clearance of unbound flurbiprofen is not stereoselective, and clearance of flurbiprofen is independent of dose when used within the therapeutic range.

Elimination:

Elimination half-life of flurbiprofen ranges between 3 and 4 hours.

Following the use of flurbiprofen, less than 3% of flurbiprofen is excreted unchanged in the urine, with about 70% of the dose eliminated in the urine as the main drug and metabolites. Approximately 20% of the dose is excreted in the urine in free and conjugated form, while 50% is excreted as hydroxylated metabolites. Because renal elimination is a significant pathway of elimination of flurbiprofen metabolites, dosing adjustment in patients with moderate or severe renal dysfunction may be necessary to avoid accumulation of flurbiprofen metabolites. The mean terminal half-lives (t) of R- and S-flurbiprofen are similar, about 4.7 and 5.7 hours, respectively. There is minimal accumulation of flurbiprofen following multiple doses of flurbiprofen.

Linearity/non-linearity:

Flurbiprofen pharmacokinetics is linear. Plasma levels increase in proportion to the dose administered.

5.3. Preclinical safety data

Preclinical safety data have not shown any specific risks for humans based on conventional safety pharmacology, repeat dose toxicity, genotoxicity, carcinogenic potential, reproduction, and toxicity studies. In reproduction studies in rats and rabbits, no developmental abnormalities have been observed. However, animal studies may not always reflect human drug toxicity. No adequate and well controlled studies have been conducted in pregnant women.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Glycerin
Ethyl alcohol (96%)
Sorbitol (E420)
Cremofor RH40
Sodium saccharin
Sodium hydroxide
Sodium benzoate (E211)
Peppermint essence
Deionized water

6.2. Incompatibilities.

None reported until now.

6.3 Shelf life

24 months.

6.4. Special precautions for storage

Store in room temperature below 25°C in its original packing. Protect from direct light.

6.5. Nature and contents of container

FLUREND % 0,25 spray is available in white opaque bottles of 30 ml in cartoon boxes together with the spray pump and instructions for use.

6.6. Disposal of medicinal waste and other special precautions

Unused medicinal products or waste should be disposed of in accordance with the “Directives for the Control of Medicinal Waste” and “Directives for the Control of Pack Waste”.

7. MARKETING AUTHORISATION HOLDER

Santa Farma İlaç San. A.Ş.
Okmeydanı, Boruçiçeği Sok. No: 16
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0212 220 64 00

0212 222 57 59

8. MARKETING AUTHORISATION NUMBER

255/34

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

The date of initial approval: 25 Dec 2013

The date of the license renewal: ---

10. THE DATE OF THE RENEWAL FOR SmPC
