SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

MAXIMUS %0.25 oral rinse

2. QUALITATIVE and QUANTITATIVE COMPOSITION

Active Substance:

200 ml oral rinse 0.50 g flurbiprofen (0.25%).

Excipients:

Sodium benzoate	0.4 g
Glycerol	14 g
Saccharin sodium	0.2 g
Sorbitol liquid non-crystalline (70%)	50 g
Propylene glycol	30.0 g

See 6.1 for excipients.

3. PHARMACEUTICAL FORM

Oral rinse solution
Blue colored solution

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

It is use to relieve discomfort in pain due to oropharyngeal area (eg gingivitis, oral inflammations, pharynx) and also used in symptomatic treatment as anti-inflammatory. It is used as protective following dental treatments.

4.2 Posology and method of administration

Posology / Term and frequency of administration:

10 ml of oral rinse solution is added to half a glass of water and rinsing or mouthwashing two or three times a day.

Application Form:

MAXIMUS oral rinse is for mouth rinsing and / or mouthwashing. After gargling, the remaining part should be thrown out and not swallowed.

Additional information on special populations:

Renal failure:

It must be used carefully in patients with renal failure.

Liver failure:

It must be used carefully in patients with liver failure.

Pediatric population:

It must not be used in children younger than 12 years of age.

Geriatric Population:

There are not data related to the use in the elderly.

4.3 Contraindications

- In patients who are hypersensitive against flurbiprofen or any ingredient included in the composition of the product
- In patients who are hypersensitive against acetylsalicylic acid or other non-steroidal anti-inflammatory drugs,
- In patients who have had bronchospasm (breathing difficulty related to bronchial narrowing) or rhinitis or urticaria related to acetyl salicylic acid or other non-steroidal anti-inflammatory drugs,
- In patients who have peptic ulcer or if you had this disease in the past.

4.4 Special warnings and special precautions for use

For external use.

MAXIMUS oral rinse is for mouth rinsing and / or mouthwashing. After gargling, the remaining part should be thrown out and not swallowed.

It should be used with caution in patients with renal insufficiency, heart failure or liver failure.

It contains glycerol, saccharin sodium, sorbitol, propylene glycol. However, it does not require any warning due to the way of use.

4.5 Interaction with other medicinal products and other forms of interaction

Flurbiprofen can rarely decrease the diuretic activity of furosemide. In addition, flurbiprofen can rarely interact with anticoagulant drugs. Furthermore, flurbiprofen has no interaction with digoxin, tolbutamide and antacid.

4.6 Pregnancy and lactation

General recommendation

Pregnancy category is **C (D in third trimester).**

Women with childbearing potential / Contraception

There is no data on the use of flurbiprofen in women with potential for childbearing.

Pregnancy period

Although animal studies have shown that flurbiprofen does not have a teratogenic effect, flurbiprofen should be used if the potential benefit to pregnant women is greater than the potential damage to the fetus.

Lactation period

The use of flurbiprofen in lactation is not recommended due to potential side effects of prostaglandin inhibitor drugs on newborns.

Reproduction ability / Fertility

There is no known effect on fertility.

4.7 Effects on ability to drive and use machines

Effects of MAXIMUS on driving and using machines have not been studies; however, no effects are expected based on its pharmacodynamics properties end general safety profile.

4.8 Undesirable effects

The reported undesirable effects are listed according to the following frequency rating.

Very common (≥1/10); common (≥1/100 and <1/10); not common (≥1/1000 and <1/100); rare (≥1/10.000, and <1/1000); very rare (<1/10.000), unknown (can not be estimated on the basis of available data)

General disorders and application region related diseases:

Unknown:

Finding related to sensivity,

Local irritation

4.9 Overdose and treatment

Given the low availability of active substance and local use, it is unlikely that overdose conditions will be visible. In case of overdose, appropriate symptomatic treatment should be performed.

Symptoms of overdose may include nausea, vomiting, gastrointestinal disturbances.

5 .PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group : Throat preparations

ATC Code : R02AX01

MAXIMUS contains flurbiprofen, a nonsteroidal anti-inflammatory drug with anti-inflammatory, analgesic and antipyretic effects. The mechanism of action of flurbiprofen is not fully understood, as it is in other nonsteroidal anti-inflammatory drugs, and is thought to be related to prostaglandin synthetase inhibition.

As in other NSAID drugs; flurbiprofen inhibits prostaglandin synthesis by inhibiting cyclooxygenase (COX), including COX-1 and COX-2 isoenzymes, in body tissues. Flurbiprofen is one of the most potent prostaglandin inhibitor NSAID drugs.

5.2 Pharmacokinetic properties

General Properties

Absorption:

Flurbiprofen is absorbed buccally through the passive diffusion mechanism. The buccal membrane is essentially a lipid membrane and flurbiprofen passes easily through the buccal mucosa due to its high lipid solubility. Flurbiprofen is a weak acid and as a result the absorption rates vary depending on the pH.

Flurbiprofen is used in the treatment and prevention of periodontal diseases due to its anti-inflammatory effect. High systemic concentration is not required as the effect will be local when applied locally to the mouth. For this indication, weak bucal absorption is desired.

MAXIMUS oral rinse is a locally effective drug used externally. For this reason, it should not be swallowed in proper use. No significant systemic effect is expected in the use of MAXIMUS oral rinse. However, in the treatment doses of flurbiprofen administered orally at 50-100 mg, the following pharmacokinetic properties are found:

Distribution:

Within about 1.5-2 hours, it reaches the plasma peak level. The apparent volume of distribution (Vz / F) of both R- and S-flurbiprofen is about 0.12 L / Kg. Both flurbiprofen enantiomers binds to plasma proteins mainly albumin above 99%. Binding to plasma proteins is relatively constant at typical average steady-state concentrations (≤10 μg / ml) obtained at the recommended doses.

Biotransformation:

Numerous flurbiprofen metabolites have been identified in human plasma and urine.

Among these metabolites, the two major metabolites of flurbiprofen are [2- (2-fluoro-4-hydroxy-4-biphenyl)] and [2- (2-fluoro-3-hydroxy-4-methoxy-4-biphenyl also include 4'-hydroxy-flurbiprofen, 3',4'-dihydroxy-fluribiprofen, 3'-hydroxy-4'-methoxy-flurbiprofen and their conjugates and conjugated flurbiprofen. In contrast to other arylpropionic acid derivatives (for example, ibuprofen), the metabolism of R-flurbiprofen to S-flurbiprofen is minimal. In vitro studies have shown that cytochrome P450 2C9 acts an important role in the metabolism of 4'-hydroxy-flurbiprofen, the main metabolite of flurbiprofen. 4'-hydroxy-flurbiprofen metabolite showed low anti-inflammatory activity in animal inflammation models. Flurbiprofen does not induce enzymes that alter metabolism. The total plasma clrency of the unbound flurbiprofen is not stereoselective, and when used in the therapeutic range, the flurbiprofen chlrensis is dose-independent.

Elimination:

The elimination half-life varies from 3 to 4 hours.

After the use of the drug, less than 3% of flurbiprofen is excreted unchanged, and about 70% of the dose that is eliminated in the urine forms the parent drug and its metabolites. 20% in free and conjugated form, approximately 50% is excreted in the urine as hydroxylated metabolites. Because renal elimination is a significant elimination pathway of flurbiprofen metabolites, dosage adjustment may be required to prevent the accumulation

of flurbiprofen metabolites in patients with moderate or severe renal insufficiency. The mean terminal half-lives ($t_{½}$) of R- and S-flurbiprofen are 4.7 and 5.7 hours, respectively, similar to each other. After multiple dosing, flurbiprofen accumulation was minimal.

Linearity / Nonlinearity:

The pharmacokinetic of flurbiprofen is linear. Plasma levels increase depending on the given dose.

5.3. Preclinical safety data

Preclinical data revealed no specific hazards for humans based on conventional safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, reproductive toxicity. There were no developmental disorders in the reproductive studies in rabbits and rats. However, animal studies may not always reflect human response. There are no adequate and well-controlled studies in pregnant women.

6 . PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium benzoate
Macrogolglycerol Hydroxystearate 40
Sodium bicarbonate
Glycerol
Saccharin sodium
Sorbitol liquid noncrystallized (70%)
Ecocool MP
Peppermint Essence
Patent V blue
Propylene glycol
Purified water

6.2 Incompatibilities

There is no identified incompatibility to date.

6.3 Shelf Life

36 months

6.4 Special precautions for storage

Store below the room temperature 25°C.

6.5 Nature and contents of container

In 200 ml amber colored PET bottle with 15 ml PP cup in carton box.

6.6 Instructions for use and handling

Unused products or waste materials must be destructed in accordance with "Medical Products Control Directive" and "Package and Package Waste Control Directive".

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORIZATION NUMBER

2014/272

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION

Date of First Authorization: 07.04.2014
Renewal of the Authorzation: 05.11.2019

10. DATE OF REVISION OF THE TEXT

22/09/2017