For the use only of a Registered Medical Practitioner or a Hospital.

Metronidazole 1%w/w,Chlorhexidine gluconate 1%w/w & Lignocaine Hydrochloride 2%w/w Gel

METROFLIX™

1. Generic Name

Metronidazole 1%w/w,Chlorhexidine gluconate 1%w/w & Lignocaine Hydrochloride 2%w/w Gel

2. Qualitative and quantitative composition

Each gram of gel contains:-
Metronidazole Benzoate I.P.
Equivalent to Metronidazole ... 1%w/w
Chlorhexidine gluconate solution I.P.
Equivalent to Chlorhexidine gluconate ... 1%w/w
Lignocaine Hydrochloride IP ... 2%w/w
Sodium Hyaluronate, Hydroxy Propyl Cellulose,
Poly Ethylene Glycol 400, Methyl paraben, Menthol,
Polysorbate 20, Sucralose, Butylated Hydroxy Toluene,
Tartaric Acid, Sodium Tartrate, Purified Water

3. Dosage form and strength

Gel and 1% w/w + 1% w/w + 2% w/w

4. Clinical particulars

4.1 Therapeutic indication

Metroflix gel indicated in Periodontal infections (Gingivitis, Periodontal surgery, subgingival infection & Scaling & Root Planning, Periodontal Abscess), Implant surgery, Surgical Tooth extraction.

4.2 Posology and method of administration

After cleaning teeth, properly rinse the mouth cavity and apply small quantity of gel on the finger and rub on the gums and interdental parts.
Upto 30 minutes post application the patient should not eat or rinse mouth cavity.
Metroflix gel is applied on the gums 2 times a day. The course of treatment on average is 7-10 days. Prophylactic courses of treatment can be taken 1-2 times a year.

4.3 Contraindications

Known hypersensitivity to the product or any of its components, especially in those with a history of possible chlorhexidine, lignocaine related allergic reactions.
Known hypersensitivity to Metronidazole, nitroimidazoles and/or hydroxybenzoates or any of the excipients.

4.4 Special warnings and precautions for use

Chlorhexidine in Metroflix gel is known to induce hypersensitivity, including generalised allergic reactions and anaphylactic shock. The prevalence of chlorhexidine hypersensitivity is not known, but available literature suggests this is likely to be very rare.
It should not be administered to anyone with a potential history of an allergic reaction to a chlorhexidine-containing compound.
Metronidazole in Metroflix gel is a nitroimidazole and should be used with care in patients with evidence of, or history of blood dyscrasias.
Metroflix gel is for oral use only. Keep away from the eyes and ears. If the gel comes into contact with the eyes, rinse well with water.
Keep out of the reach and sight of children. Do not swallow. If symptoms persist, stop using and consult your doctor or dentist.

4.5 Drugs Interactions

Chlorhexidine digluconate is incompatible with anionic agents which are usually present in conventional dentrifices. These should therefore be used before the mouthwash.
Rinse the mouth thoroughly with water before using the mouthwash.
Oral metronidazole has been reported to potentiate the anticoagulant effect of coumarin and warfarin resulting in a prolongation of prothrombin time. The effect of topical metronidazole on prothrombin time is not known.
Due to possible interferences (opposite action or inactivation) the simultaneous or consecutive use of antiseptics should be avoided.

4.6 Use In special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

In chlorhexidine, no harmful effects in human pregnancy or during lactation have been reported. Nevertheless, like all medicines, care should be exercised and the mouthwash should only be used on the advice of a doctor or dentist.
There has been no experience to date with the use of Metroflix gel in pregnant patients. Metronidazole crosses the placental barrier and enters the fetal circulation rapidly. No fetotoxicity was observed after oral metronidazole in rats or mice. However, because animal reproduction studies are not always predictive of human response and since oral metronidazole has been shown to be a carcinogen in some rodents, this drug should be used during pregnancy only if clearly needed.
After oral administration, metronidazole is secreted in breast milk in concentrations similar to those found in the plasma. Even though Metroflix gel blood levels are significantly lower than those achieved after oral metronidazole, a decision should be made whether to discontinue nursing or to discontinue the gel, taking into account the importance of the gel to the mother.
Lignocaine is excreted in breast milk but in small quantities that there is generally no risk of the infant being affected at therapeutic dose levels. There is no data on excretion of chlorhexidine in breast milk.

4.7 Effects on ability to drive and use machine
Metroflix gel has no influence on the ability to drive and use machines.

4.8 Undesirable effects
Chlorhexidine should be taken into account that rare allergic reactions of the skin and mucous membrane, which are caused by contact with anaesthetics of the amide-type, such as lignocaine can occur.
Prolonged and continuous use of chlorhexidine can cause brown-discoloration of the teeth. However, this brown-discoloration is removable.
The following adverse experiences have been reported with the topical use of Chlorhexidine, Metronidazole, Lignocaine combination: burning, irritation, dryness, transient redness, metallic taste, staining of teeth, tingling or numbness of extremities and nausea.

4.9 Overdose
Metroflix gel is poorly absorbed by the oral route; therefore, systemic effects are unlikely even if large volumes are swallowed. However, gastric lavage followed by supportive measures may be used as appropriate.

5 Pharmacological properties
5.1 Mechanism of Action
Chlorhexidine is a cation-active antiseptic agent. It possesses a powerful bactericidal effect against both gram-positive and gram-negative bacteria and an antimycotic effect on dermatophytes and yeasts.
Lignocaine hydrochloride is a local peripheral anesthetic of the amide group, which has a superficial analgesic effect without interfering with motor functions at the point of application.
It acts locally in the form of non-ionised base.
Metroflix gel contains metronidazole, at a concentration of 10mg per gram (1%). Metronidazole is classified therapeutically as an antiprotozoal and antibacterial agent.
The mechanism by which topical metronidazole acts, is not known but appears to include an antimicrobial and/or anti-inflammatory effect.

5.2 Pharmacodynamic properties
Chlorhexidine digluconate is a bisbiguanide antiseptic and disinfectant, which is bactericidal or bacteriostatic against a wide range of gram negative and gram positive vegetative bacteria, yeasts, dermatophyte fungi and lipophilic viruses. The antimicrobial activity covers most of the important species occurring in the oral microflora.
Metronidazole have the selective action against anaerobes and anoxic and hypoxic cells is due to the mode of action. The nitro group of metronidazole acts as electron acceptor and is thus reduced to a chemically reactive drug form. This produces biochemical lesions in the cells, thus causing death. The major site of action is believed to be DNA, where it causes loss of the helical structure and inhibits synthesis.
Lignocaine is a local anesthetic used in a wide variety of superficial and invasive procedure.

5.3 Pharmacokinetic properties
Chlorhexidine
Due to its cationic nature, chlorhexidine digluconate binds strongly to skin, mucosa and other tissues and is thus very poorly absorbed. No detectable blood levels have been found following oral use.
Small amounts may enter the digestive system if saliva is swallowed.

Absorption
In oral or topical use, absorption of chlorhexidine is insignificant.
In topical use on intact skin, chlorhexidine is adsorbed on the outside layers of the skin, providing long-term antimicrobial effect.
Pharmacokinetic research has shown that after rinsing the oral cavity, approximately 30% of chlorhexidine is retained, which is then slowly released into the saliva.

Distribution
Chlorhexidine binds tightly to saliva proteins.

Biotransformation
Chlorhexidine is not accumulated in the body. Very little of it is metabolised.

Elimination
Following ingestion of a 300 mg dose of chlorhexidine gluconate approximately 90 % is excreted in faeces via biliary routes and less than 1 % is eliminated into urine.

Metronidazole
It is readily absorbed from the gastro-intestinal tract and widely distributed in body tissues. Half life in plasma is about 8-10 hours. About 10% is bound to plasma proteins.
It penetrates well into body tissues and fluids, including vaginal secretions, seminal fluid, saliva and breast milk. Therapeutic concentrations are also achieved in cerebrospinal fluid.
Unchanged metronidazole and several metabolites are excreted in the urine, the liver is the main site of metabolism and the major metabolites are as a result of side chain oxidation, forming glucuronides.

Lignocaine
Absorption
Lidocaine absorption varies, depending on the site and the method of use. It is quickly resorbed from the digestive organs, mucous membranes and through damaged skin.
In healthy adults, no detectable plasma lignocaine levels were noted after use of a 2 % mouth rinse. Children and immune impaired adults do resorb lidocaine from the oral mucosa into the plasma. The levels were approximately 0,2 µg/ml but the toxic plasma concentration is 5 µ g/ml. The anaesthetic effect of lidocaine after topical use appears 2 to 5 minutes after a application and lasts 30 to 45 minutes.
The anaesthetic effect is limited to the surface and does not extend to the submucosal structures.

Distribution
Lignocaine is distributed well in the tissues (kidneys, lungs, liver, heart, adipose tissue).
Lignocaine passes through the blood-brain barrier and placenta and into mother's milk.

Biotransformation
it is metabolised during the first pass through the liver and the bioavailability is about 35 % after oral administration. 90 % is deethylated in the liver to monoethylglycinexylide and glycinexylide.
Both primary metabolites are pharmacologically active. Further cleavage of the amide bonds forms the metabolites xylidine and 4-hydroxyxylidine.

Elimination
Lignocaine is eliminated in the form of metabolites through the kidneys. Approximately 10% is eliminated unchanged. The biological half-life of lidocaine is one and a half to two hours in adults.
The biological half-life of the primary metabolites is two to ten hours.

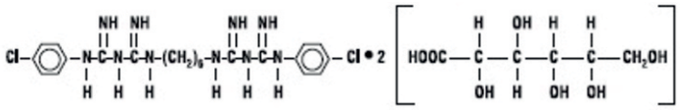
6 Nonclinical properties

6.1 Animal Toxicology or Pharmacology

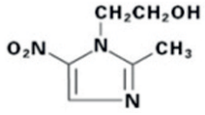
Chlorhexidine and lignocaine effects in non-clinical studies were observed only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use and development.
Metronidazole has been shown to be carcinogenic in the mouse and in the rat following chronic oral administration however similar studies in the hamster have given negative results.
Epidemiological studies have provided no clear evidence of an increased carcinogenic risk in humans.
Metronidazole has been shown to be mutagenic in bacteria in vitro. In studies conducted in mammalian cells in vitro as well as in rodent or humans in vivo, there was inadequate evidence of a mutagenic effect of metronidazole, with some studies reporting mutagenic effects, while others studies were negative.

7 Description

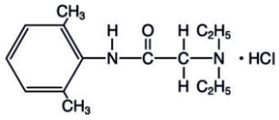
Chlorhexidine gluconate is a salt of chlorhexidine and gluconic acid. Its chemical name is $C_{22}H_{30}Cl_2N_{10}2C_6H_{12}O_7$ and molecular weight is 897.72.



Metronidazole Chemically is 2-methyl-5-nitro-1H-imidazole-1-ethanol. The molecular formula for metronidazole is $C_6H_9N_3O_3$ and molecular weight of 171.16.



Lignocaine hydrochloride, chemical name: acetamide, 2-(diethylamino)-N-(2,6-dimethylphenyl),monohydrochloride has the following structural formula:



8 Pharmaceutical particulars

8.1 Incompatibilities

None

8.2 Shelf-life

24 months

8.3 Packaging information

Tube of 20 grams

8.4 Storage and handing instructions

Store at Cool and Dark place. Store below 30˚C.
Keep out of reach of children.
Do not swallow. Keep the cap tightly closed after use.

9 Patient Counselling Information

Metroflix gel is used fo treat gum inflammation (gingivitis) and mouth ulcers. Gingivitis is the inflammation of gum caused by bacteria; if left untreated it can lead to periodontitis (gum infection that damages gums and can destroy the jawbone). This can cause the gum to separate from teeth leading to loss of teeth.
Metroflix gel inhibits the growth of bacteria and helps in the healing of ulcers. It exerts anti-microbial action on the infection causing micro-organisms. Thereby treats gum inflammation.
It is advised not to use during pregnancy unless clearly needed.
It has been reported to cause tearing of the eyes. Therefore, contact with the eyes should be avoided.
After cleaning teeth, properly rinse the mouth cavity and apply small quantity of gel on the on finger and rub on the gums and interdental parts. Upto 30 minutes post application the patient should not eat or rinse mouth cavity.
Metroflix gel is applied on the gums 2 times a day. The course of treatment on average is 7-10 days. Prophylactic courses of treatment can be taken 1-2 times a year.

10 Marketed by:

CURFLIX PHARMA PRIVATE LIMITED
Regd.Office: H.No. 437-A,Jaggi Garden Colony,
Ambala City,Haryana-134003
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