

## **NEW ZEALAND DATA SHEET**

### **1. LOCACORTEN-VIOFORM® (1% clioquinol and 0.02% flumetasone pivalate ear drops)**

LOCACORTEN-VIOFORM® 1% clioquinol and 0.02% flumetasone pivalate ear drops

### **2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

LOCACORTEN-VIOFORM® contains 1% clioquinol and 0.02% flumetasone pivalate.

For a full list of excipients, see section 6.1.

### **3. PHARMACEUTICAL FORM**

Ear drops.

A clear yellowish solution with a volume of 7.5ml ( $32 \pm 3$  drops per 1ml). Flumetasone is a synthetic difluorinated glucocorticoid. Clioquinol is a halogenated hydroxyquinolone derivative.

### **4. CLINICAL PARTICULARS**

#### **4.1 Therapeutic indications**

Eczema of the external auditory meatus in which secondary infection with micro-organisms sensitive to clioquinol has occurred.

- Otitis externa
- Otomycosis.

#### **4.2 Dose and method of administration**

Before application, the auditory meatus should be cleansed and dried carefully.

Instill 2 or 3 drops twice daily into the auditory meatus by gently squeezing the plastic bottle. The patient should be either sitting or lying down with the treated ear turned upwards during application. This position should be maintained for at least 1-2 minutes following the application.

Alternatively, a gauze or cotton wick saturated with the solution may be inserted into the ear canal. Keep the wick moistened by adding further solution. It should be replaced at least once every 24 hours.

The solution may be warmed to body temperature prior to each application (e.g. by holding the bottle

in the hands). Heating above body temperature should be avoided. Contamination of the dropper with material from the ear, fingers, or other sources should be avoided. Treatment should normally not exceed 10 days.

LOCACORTEN-VIOFORM® is dissolved in a polyethylene glycol vehicle which forms an inert, non-irritant, rather viscous medium. This medium has a softening effect on the cerumen and does not prevent drainage, thus ensures prolonged contact of the active ingredients with the surface of the ear canal.

If no improvement occurs within about 1 week, the therapy should be discontinued; it is then advisable to identify the pathogens and to institute an appropriate treatment.

Use of the product is not advisable in children under the age of 2 years.

#### **4.3 Contraindications**

- Perforation of the ear-drum (suspected or verified)
- Application to the eye
- Viral infections of the skin (e.g. varicella, herpes simplex, herpes zoster, common warts, plane warts, condylomata, mollusca contagiosa)
- Syphilitic skin affections, tuberculosis of the skin, bacterial skin infections (e.g. pyoderma)
- Fungal and yeast infections of skin
- Disorders associated with therapy-resistant secondary infections
- Known hypersensitivity to flumetasone pivalate, known hypersensitivity to clioquinol, hydroxyquinolines and other quinoline derivatives, to iodine, as well as to other components contained in LOCACORTEN-VIOFORM® ear drops.
- Use in children under 2 years of age.

#### **4.4 Special warnings and precautions for use**

Prior to the beginning of therapy, the ear-drum should be checked by the physician. If there is a risk that perforation of the ear-drum may occur or is perforated, LOCACORTEN-VIOFORM® ear drops should not be used.

If no improvement occurs within about 1 week, the therapy should be discontinued; it is then advisable to identify the pathogens and to institute an appropriate treatment (see also "Dosage and method of administration").

LOCACORTEN-VIOFORM® ear drops should not be allowed to come into contact with the conjunctiva, due to the possibility of contamination of the conjunctiva with the risk of developing open-angle glaucoma or subcapsular cataract.

Contact with LOCACORTEN-VIOFORM® ear drops may cause discolouration of the hair and of

clothing and bed linen.

Topical use of clioquinol-containing preparations may lead to a marked increase in protein-bound iodine (PBI) (see also "Overdose") in patients with normal thyroid function and therefore may interfere with tests of thyroid function (such as PBI, radioactive iodine and butanol extractable iodine). Other thyroid function tests, such as the T3 resin sponge test or T4 determination, are unaffected.

LOCACORTEN-VIOFORM® should not be used concomitantly with products containing heavy metals, as clioquinol forms coloured complex-bound salts with these substances.

In the event of suspected allergic skin reaction, LOCACORTEN-VIOFORM® should be withdrawn.

Topical corticosteroids are absorbed systemically, and the risk of systemic adverse reactions should be considered, especially with high dosage or long-term treatment. It will be necessary to stop the treatment and start appropriate therapy.

Corticosteroids may mask or exacerbate an existing infection. Long-term use may compromise the immune system, increasing the risk of secondary infections.

It is not advisable to use it continuously for more than five days without consulting the doctor. In cases of superinfection, the product should be withdrawn and appropriate measures should be taken.

Medicines should be kept out of the reach of children. Use of the product is not advisable in children under the age of 2 years (see also "Dosage and method of administration").

#### Visual disturbance

Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

#### Hearing loss

Hearing loss may be reported after the use of LOCACORTEN-VIOFORM®.

### **4.5 Interaction with other medicines and other forms of interaction**

Topical use of clioquinol-containing preparations may increase the amount of protein-bound iodine (PBI) in patients with normal thyroid function and therefore may interfere with tests of thyroid function (such as PBI, radioactive iodine and butanol extractable iodine). Such tests should therefore be performed no sooner than one month after cessation of therapy. Other thyroid function tests, such as the T3 resin sponge test or T4 determination, are unaffected.

The ferric chloride test for phenylketonuria may yield a false-positive result when clioquinol is present in the urine.

However, no similar reports with LOCACORTEN-VIOFORM® ear drops have been received to date.

#### **4.6 Fertility, pregnancy and lactation**

##### Pregnancy

There is limited information on use of LOCACORTEN-VIOFORM® ear drops in pregnant women. Animal experiments relevant to the safety assessment of corticosteroids, although not specifically conducted with LOCACORTEN-VIOFORM® ear drops, have shown either teratogenic potential or other adverse effects on the embryo and/or the foetus. However, no reports on adverse effects with LOCACORTEN-VIOFORM® ear drops in human pregnancy have been received to date.

The safety of use during pregnancy has not been demonstrated. Although systemic exposure to the active ingredients is expected to be low following local application in the ear. When using LOCACORTEN-VIOFORM® ear drops in pregnancy, the risk-benefit relationship must be carefully considered.

Corticosteroids are known to cross the placenta and therefore potentially influence the foetus. This will be significant predominantly when intensive treatment is administered to large areas using a potent or highly potent product.

##### Breast-feeding

It is not known whether the active substances of LOCACORTEN-VIOFORM® ear drops and/or their metabolite(s) pass into the breast milk when the preparation is applied topically.

For safety reasons caution is indicated.

##### Fertility

No data available on fertility for LOCACORTEN-VIOFORM®.

#### **4.7 Effects on ability to drive and use machines**

None known to date, but LOCACORTEN-VIOFORM® is not expected to have an effect.

#### **4.8 Undesirable effects**

The following adverse drug reactions have been derived from post marketing experience with LOCACORTEN-VIOFORM® ear drops. Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency which is therefore categorized as not known. The adverse drug reactions are listed according to system organ classes in

MedDRA. Within each system organ class, ADRs are presented in order of decreasing seriousness.

***Ear and labyrinth disorders:***

Not known: Hearing loss.

***Infections and infestations:***

Not known: Manifestations of bacterial infections, viral and fungal infections.

***Immune system disorders:***

Occasional: Hypersensitivity.

***Eye disorder:***

Not known: Increased risk of cataract\*, vision blurred (also see section “Special warnings and precautions for use”).

***Skin and subcutaneous tissue disorders:***

Not known: Skin atrophy\* (often irreversible), telangiectasia\*, purpura\*, skin striae\*, rosacea-like dermatitis and dermatitis (perioral) with or without skin atrophy\*, dermatitis contact (due to components of the vehicle or due to the corticosteroid itself)\*, skin depigmentation\*, hypertrichosis\*, hair colour changes (contact with LOCACORTEN-VIOFORM® ear drops).

***General disorders and administration site conditions:***

Occasionally: Application site irritation, application site burn, application site pruritus application site rash, rebound effect, which may lead to steroid dependence\*, impaired healing\*.

Treatment should be discontinued if severe irritation or sensitisation develops.

***Investigation:***

Not known: Intraocular pressure increased\*.

*\*The localised undesirable effects that have been reported after topical application of corticosteroids in general.*

**Side effects observed after prolonged periods of application**

***Endocrine disorders:***

Not known: Adrenal suppression

The risk of localised undesirable effects increases with potency of the product and duration of treatment. Application in skin folds increases this risk. The face, hairy skin and genital skin are especially sensitive to localised effects.

Incorrect use may mask and/or worsen bacterial, parasitic, fungal and viral infections.

In addition, the development of resistant organisms requires the initiation of appropriate treatment and, should this fail, cessation of treatment with the product.

Systemic undesirable effects due to topical application of corticosteroid preparations are rare in adults, but may be serious.

The risk of systemic effects is the greatest with:

- application under occlusion,
- application in skin folds,
- application on large areas of skin,
- prolonged application,
- application in children (thin skin and relatively large skin surface make children highly sensitive).

#### **4.9 Overdose**

Treatment with clioquinol-containing preparations applied to extensive or eroded areas of skin may already within 1-week lead to increased PBI values and to signs and symptoms resembling those of thyrotoxicosis. Elevated PBI values also occur where relatively small areas of skin are treated for more than 1 week.

However, no similar reports with LOCACORTEN-VIOFORM<sup>®</sup> ear drops have been received to date.

No cases of acute poisoning have been reported to date. However, the possibility of such an occurrence owing to accidental ingestion by children cannot be excluded. This would result in gastrointestinal disorders accompanied by vomiting and nausea. There are no known specific antidotes.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

### **5. PHARMACOLOGICAL PROPERTIES**

#### **5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: Otologicals corticosteroids and anti-infectives in combination, ATC code: S02CA02.

##### Mechanism of action

Flumetasone pivalate is a moderately potent glucocorticoid designed for local application. It exerts an anti-inflammatory, anti-allergic, vasoconstrictive, and anti-proliferative effect.

Experimental results show that the multiple effects of glucocorticoid drugs can be attributed to a complex molecular mechanism that includes binding to specific cytoplasmic receptors.

### Pharmacodynamic effect

In inflammatory skin diseases of the external auditory meatus it affords prompt relief and eliminates symptoms such as pruritus while at the same time reducing swelling.

Appropriate studies in various animal species demonstrated the anti-allergic and anti-anaphylactic properties of LOCACORTEN-VIOFORM® eardrops, solution.

### Clinical efficacy and safety

Clioquinol, the antimicrobial component of LOCACORTEN-VIOFORM® ear drops is a halogenated quinolinol derivative and is active against a broad spectrum of pathogenic micro-organisms, including fungi (e.g. *Candida albicans* and dermatophytes, Microsporum, Trichophyton) and gram-positive bacteria (e.g. staphylococci and streptococci).

Clioquinol has only a moderate inhibitory effect on gram-negative bacteria.

Clioquinol exerts a bacteriostatic, rather than a bactericidal action.

Microbiological testing demonstrated the antimicrobial and antimycotic activity of clioquinol, which is not influenced by the presence of the corticosteroid.

## **5.2 Pharmacokinetic properties**

No pharmacokinetic data on LOCACORTEN-VIOFORM® ear-drops are available.

### Absorption

Trials (including treatment under occlusive dressings) with different formulations of LOCACORTEN-VIOFORM® for topical application have shown that no demonstrable percutaneous absorption of flumetasone pivalate occurs, while clioquinol was absorbed to an extent of about 1.5% to 4%, as judged by the urinary excretion.

### Elimination

Investigations of different pharmaceutical forms for topical use have shown that clioquinol is absorbed and excreted in the urine mainly in glucuronide form and to a smaller extent as sulphate, whereas unchanged clioquinol is found in traces only.

## **5.3 Preclinical safety data**

### Teratogenicity

Some topical corticosteroids have been shown to be teratogenic in animals. The specific experimental teratogenic potential of glucocorticoid drugs in animals is known.

### Mutagenicity

Flumetasone pivalate was not tested for mutagenic potential. Information on the mutagenicity of other

corticosteroids suggests that this class of drug has minimal mutagenic potential. Clioquinol was shown to be non-mutagenic in studies using *Salmonella typhimurium*.

**Carcinogenicity**

Flumetasone pivalate has not been tested for carcinogenic potential. Another related topically-applied corticosteroid, fluticasone propionate, was negative for carcinogenicity following oral and topical administration. Clioquinol has not been tested for carcinogenicity.

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

Polyethylene glycol 300 base.

### **6.2 Incompatibilities**

None known to date.

### **6.3 Shelf life**

18 months

### **6.4 Special precautions for storage**

Store below 25°C.

### **6.5 Nature and contents of container**

Yellow coloured polyethylene 10ml bottles containing 7.5ml solution.

### **6.6 Special precautions for disposal and other handling**

Medicines should be kept out of the reach of children.

## **7. MEDICINE SCHEDULE**

Prescription Medicine

## **8. SPONSOR**

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## **9. DATE OF FIRST APPROVAL**

20 May 2010

## **10. DATE OF REVISION OF THE TEXT**

07 November 2019

Summary table of changes:

<b>Revision date</b>	<b>Section changed</b>	<b>Summary of new information</b>
November 2019	All	Correction of trade name
	4.4 & 4.8	Re-installment of “hearing loss” information to be in line with MARC notification dated September 2017
	4.9	Standard wording included for National Poisons Centre for completeness
	4.1, 4.2, 4.4, 4.7, 4.8, 5.1, 5.2, 6.1, 6.2, 6.4, 6.5, 6.6	Corrections made to general spelling, grammatical or typographical errors