**PROFESSIONAL INFORMATION**

## SCHEDULING STATUS

**S4**

## 1 NAME OF THE MEDICINE

**ENDOSTIL 6 ml** (Gel – pre-filled syringe)

**ENDOSTIL 11 ml** (Gel – pre-filled syringe)

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

ENDOSTIL contains:

| | **6 ml syringe** | **11 ml syringe** |
|---|---|---|
| Lidocaine hydrochloride: | 117,6 mg | 215,7 mg |
| | (2,00 g per 100 g gel) | |
| Chlorhexidine digluconate: | 15,7 mg | 28,8 mg |
| | (0,05 g per 100 g gel) | |

*Preservatives:*

Methylhydroxybenzoate 0,060 % m/m

Propylhydroxybenzoate 0,025 % m/m

*For a full list of excipients, see section 6.1*

## 3 PHARMACEUTICAL FORM

ENDOSTIL is a clear, practically colourless, viscous liquid.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Instillation into the urethra prior to the insertion of a catheter or other instruments (catheterisation, cystoscopy) which require the use of a local anaesthetic.

### 4.2 Posology and method of administration

*Posology*

The content of one syringe is sufficient to fill the urethra.

The syringe contains 12,5 g of which 10 g is instilled into the urethra.

Do not exceed the recommended dosage.

Never instil more than one syringe as one syringe contains 200 mg lidocaine.

*Method of administration*

For instillation into the urethra 10 – 20 minutes prior to the instillation of instruments (by a medical practitioner or trained medical qualified personnel):

1. Clean the external orifice of the urethra with an appropriate antiseptic agent.
2. Peel off the paper from the blister back cover (possibly up to the waist of the transparent blister material).
3. The plastic rod at the top of the applicator cone is broken off (in the blister pack if required).
4. One drop of gel may be released for easier insertion of the applicator.
5. Instillation is completed by applying steady pressure to the syringe.

ENDOSTIL should be inserted approximately 10 – 20 minutes prior to instillation of an instrument or catheter to ensure that the medicine exerts an action prior to use.

**4.3 Contraindications**

- Hypersensitivity to the active ingredients (amide type anaesthetics, chlorhexidine and alkyl hydroxybenzoates) or any of the ingredients of ENDOSTIL (see section 6.1)
- Severe bradycardia.
- Children under the age of 18 years.
- Hypovolaemia, heart block or other conduction disturbances.
- Urethral trauma.
- Urethral inflammation.

**4.4 Special warnings and precautions for use**

ENDOSTIL must not be applied to, or near the eyes and ears.

Not to be used on the brain, meninges or other sensitive tissues.

Since the absorption of ENDOSTIL is greater if the mucous membrane has been damaged, ENDOSTIL should be used with caution in patients with bleeding wounds or damaged mucous membranes.

Before applying ENDOSTIL to the urethra it should therefore be ensured that trauma has not, or does not occur. This might give rise to rapid absorption of ENDOSTIL, causing serious side effects and systemic overdosage. If more than one syringe is applied and the gel enters into the bladder, or in the presence of severe inflammation of the urethra, an increase of lidocaine (lignocaine) absorption may lead to an overdose with depressant cardiovascular reactions, characterised by excessive hypotension, bradycardia and an increase in ventricular activation time.

If large amounts of the gel are applied to mucous membranes or damaged skin, overdosage of lidocaine (lignocaine) may occur. The systemic toxicity mainly involves the central nervous system (CNS) and the cardiovascular system:

- Excitation of the CNS manifests by yawning, restlessness, excitement, nervousness, dizziness, tinnitus, nystagmus, blurred vision, nausea and vomiting, muscle twitching, tremors and convulsions. Numbness of the tongue and perioral region and light-headedness followed by sedation may appear

as early signs of systemic toxicity. Excitation when it occurs may be transient and followed by depression with drowsiness, respiratory failure and coma.

- The effects on the cardiovascular system may manifest as myocardial depression and peripheral vasodilatation, resulting in hypotension and bradycardia; dysrhythmias and cardiac arrest may occur.

ENDOSTIL should be used with caution in patients with impaired cardiac conditions, including congestive heart failure, bradycardia or respiratory depression.

**In cases of severe bradydysrhythmia and under anaesthesia, preference should be given to a lubricant without lidocaine (lignocaine).**

ENDOSTIL should be used with caution in patients with epilepsy.

ENDOSTIL is metabolised in the liver and must be administered with caution to patients with hepatic insufficiency.

The decrease in sensation consequent to the use of ENDOSTIL may lead to inadequate reflex protective mechanisms.

ENDOSTIL contains Methylhydroxybenzoate and Propylhydroxybenzoate. This may cause allergic reactions (possibly delayed).

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

ENDOSTIL should be used with caution in patients receiving antidysrhythmic medicines (see section 4.4).

### 4.6 Fertility, pregnancy and lactation

*Pregnancy*

Safety in pregnancy has not been established.

*Breastfeeding*

It is not known whether ENDOSTIL passes into breast milk.

Breastfeeding should be suspended for 12 hours after administration.

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

No effects of the product on the ability to drive or use machine are known.

### 4.8 Undesirable effects

| | |
|---|---|
| **Immune system disorders** | |
| Less frequent: | Angioedema, allergic contact dermatitis |
| Unknown frequency: | Allergic reactions |
| **Renal and urinary disorders** | |
| Less frequent: | Urethritis |
| **General disorders and administration site conditions** | |
| Less frequent: | Burning, stinging, swelling or tenderness not present before therapy |

ENDOSTIL may produce systemic adverse effects as a result of raised plasma concentrations that occur when the rate of uptake into the circulation exceeds the rate of breakdown, for example after absorption of large amounts through mucous membranes or damaged skin (see section 4.2).

*Reporting of suspected adverse reactions*

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website: https://www.sahpra.org.za/Publications/Index/8

### 4.9 Overdose

***Symptoms of overdose:***

Cardiovascular system depression (increased sweating, low blood pressure, pale skin, slow or irregular heartbeat) – may lead to cardiac arrest.

CNS toxicity (blurred or double vision, confusion; convulsions; dizziness or light-headedness; drowsiness; feeling hot, cold or numb; ringing or buzzing in ears; shivering or trembling; unusual anxiety, excitement, nervousness or restlessness).

Methaemoglobinaemia (difficulty in breathing on exertion, dizziness, headache, tiredness, weakness).

***Treatment of overdose:***

Treatment of a patient suffering from systemic toxicity consists of arresting the convulsions and ensuring adequate ventilation with oxygen, if necessary, by assisted or controlled ventilation.

## 5 PHARMACOLOGICAL PROPERTIES

ATC code: A 13.3 Surface anaesthetics

### 5.1 Pharmacodynamic properties

Lidocaine (lignocaine) is a local anaesthetic of the amide type. Lidocaine (lignocaine) hydrochloride stabilises neuronal membranes and prevents the initiation and conduction of nerve impulses, thus effecting local anaesthetic action.

Chlorhexidine is a bisbiguanide antiseptic and disinfectant that is bactericidal or bacteriostatic against a wide range of gram-positive and gram-negative bacteria.

### 5.2 Pharmacokinetic properties

After application to mucous membranes lidocaine (lignocaine) is absorbed, but its blood concentrations after the instillation of doses up to 800 mg into the urethra remain in the low range, below toxic levels. The metabolism of lidocaine (lignocaine) takes place in the liver and the unchanged medicine is excreted renally.

The antiseptic action of chlorhexidine digluconate is potentiated by the combination with methyl- and propylhydroxybenzoates; the microbial organisms normally present in the distal region of the urethra are killed within 5 - 10 minutes.

### 5.3 Preclinical safety data

Not Applicable

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Hydroxymethylcellulose, propylene glycol and purified water.

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf life

5 years

### 6.4 Special precautions for storage

Store at or below 25 °C.

Keep in outer carton until used.

Do not refrigerate.

### 6.5 Nature and contents of container

A pre-filled syringe made of polypropylene with polypropylene plunger and a chlorobutyl rubber stopper piston, containing 6 ml or 11 ml of gel.

The syringes are packed in boxes of 10.

### 6.6 Special precautions for disposal and other handling

No special requirements for disposal.

## 7 HOLDER OF CERTIFICATE OF REGISTRATION

Gen-Eye Pty Ltd

Royal Palm Business Estate

Unit 7, 646 Washington Street

Halfway house, Midrand 1685

## 8 REGISTRATION NUMBER(S)

ENDOSTIL 6 ml: 42/13.3/0959

ENDOSTIL 11 ml: 42/13.3/0960

## 9 DATE O FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

23 November 2017

## 10 DATE OF REVISION OF THE TEXT

02 April 2024