Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Instillagel 6 ml Urethral, vaginal, rectal and oropharyngeal gel

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

6 ml gel contains:

Active substances	
Lidocaine Hydrochloride	125.40 mg
Chlorhexidine Digluconate	3.14 mg
Methyl Parahydroxybenzoate (E218)	3.76 mg
Propyl Parahydroxybenzoate (E216)	1.57 mg

Excipients with known effect
Propylene Glycol (E1520)(Ph. Eur.) 3140.00 mg

For full list of excipients see section 6.1.

3 PHARMACEUTICAL FORM

Urethral, vaginal, rectal and oropharyngeal gel

Instillagel 6 ml is a clear, practically colourless, slightly opalescent, viscous gel.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

As a lubricant gel, disinfectant, and local anaesthetic e.g. in catheterizations and internal examinations, also intraoperatively; all forms of endoscopy, changes of fistula catheters, intubations, also in artificial respiration, for the prevention of iatrogenic injuries to the rectum and colon, and in paediatrics.

Instillagel must not be used in children under 2 years.

4.2 Posology and method of administration

Unless otherwise prescribed:

a) For urethral probe examination and catheterization:
Instil 6 or 11 ml. After the normal cleaning of the glans and the external urethral orifice, instil Instillagel slowly into the urethra, keeping the glans compressed, until the local anaesthetic and disinfectant action has set in.

b) For cystoscopy:
Instil 11 ml, and possibly an additional 6 or 11 ml. The entire urethral including the external sphincter must be covered with the lubricating film and anaesthetized for germ-free and painless introduction of instruments. A penis clamp is attached in the region of the sulcus coronarius.

In women, children (2-12 years) and adolescents (under 18 years) the effect of Instillagel with lidocaine is not so well demonstrated and therefore the need to use it should be assessed by the doctor. Specific dosage recommendations cannot be given for these groups of patients, but as a general rule, the amount of gel instilled is adapted to the individual anatomical conditions of the urethra.

The systemic absorption of lidocaine can be increased in children and caution is accordingly required. In general, the maximum dose in children aged 2 to 12 years of 2.9 mg/kg lidocaine hydrochloride should not be exceeded.

Instillagel with lidocaine must not be used in children under 2 years (see section 4.3).

Full local anaesthetic and disinfectant action develops in 5 - 10 min.

4.3 Contraindications

Hypersensitivity to the active substances (including amide-type anaesthetics, chlorhexidine or alkyl hydroxybenzoates) or to any of the excipients listed in section 6.1.

The gel should not be used in children under 2 years (see section 4.2).

4.4 Special warnings and precautions for use

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

Chlorhexidine should be only used in intact skin.

Products containing local anesthetics should also be used with caution in patients with impaired cardiac conditions, in epileptics and in those with liver problems (hepatic insufficiency, liver failure, cirrhosis).

The decrease in appreciation of sensation consequent to use of this product may lead to inadequate reflex protective mechanisms.

In the presence of severe damage to the urethra, an excessive hypotensive response may occur.

Parahydroxybenzoates and their esters
Instillagel contains Methyl Parahydroxybenzoate (E218) and Propyl Parahydroxybenzoate, (E216) which may cause allergic reactions (possible delayed).

Propylene Glycol
This medicine contains 3.14 g Propylene Glycol in each syringe of 6 ml. This is equivalent to 522.5 mg/ml.

Propylene Glycol may cause skin irritation.

While propylene glycol has not been shown to cause reproductive or developmental toxicity in animals or humans, it may reach the foetus and was found in milk. As a consequence, administration of propylene glycol to pregnant or lactating patients should be considered on a case by case basis (see section 4.6)

Medical monitoring is required in patients with impaired renal or hepatic functions because various adverse events attributed to propylene glycol have been reported such as renal dysfunction (acute tubular necrosis), acute renal failure and liver dysfunction.

4.5 Interaction with other medicinal products and other forms of interactions

Instillagel should be used with caution in patients receiving antiarrhythmic drugs.
Due to possible additive effects on the heart, lidocaine should be used with caution in patients taking antiarrhythmic drugs at the same time.

4.6 Fertility, pregnancy and lactation

Pregnancy
During the first 3 months of pregnancy Lidocaine should be used only if absolutely necessary.

Breast-feeding
Since it is not known whether Lidocaine passes into milk, breastfeeding should be suspended for 12 hours after administration.

Fertility
There is no data available on the effects of Instillagel on fertility in humans.

Administration of propylene glycol to pregnant or lactating patients should be considered on a case by case basis (see section 4.4).

4.7 Effects on ability to drive and use machines

The ability to drive and to operate machinery can be impaired after the use of Instillagel.

4.8 Undesirable effects

a) Summary of the safety profile

In very rare cases, hypersensitivity to amide-type local anaesthetic preparations and/or one of the other active substances has been reported. The most important serious adverse reaction is anaphylaxis.

In the cases of mucosal damage, hypotensive response may occur (see section 4.4).

Treatment must be stopped immediately if symptoms of intolerance occur.

b) Tabulated summary of adverse reactions

Adverse drug reactions derived from the literature, post-marketing surveillance and spontaneous reporting with Instillagel sorted by categories of frequency are listed below.

Undesirable effects are listed below by frequency convention and system organ class database.
Frequencies are defined as:

Very common (≥1/10)
Common (≥1/100 to <1/10)
Uncommon (≥1/1,000 to <1/100)
Rare (≥1/10,000 to <1/1,000)
Very rare (<1/10,000)
not known (cannot be estimated from the available data)

Possible undesirable effects:

Immune system disorders Very rare Not known	Hypersensitivity (in severe cases anaphylaxis) caused by lidocaine or other amide type local anaesthetics and / or by chlorhexidine containing medicinal products. Hypersensitivity caused by methyl hydroxybenzoate and/or propyl hydroxybenzoate (possibly delayed).
Injury, poisoning and procedural complications Not known	Systemic absorption may occur in cases of severe injury to the mucosa. Possible systemic undesirable effects are e.g. decrease in blood pressure, bradycardia or seizures.

c) Description of selected adverse reactions

The very rare cases of hypersensitivity reactions are mostly attributed to chlorhexidine. However, related adverse reactions with the combination of chlorhexidine and lidocaine as well as with lidocaine alone were also reported.

Most reported hypersensitivity reactions to chlorhexidine are immediate type, but also delayed hypersensitivity reactions are possible. Onset of symptoms of immediate type hypersensitivity reactions might be delayed, as time is required for topically administered chlorhexidine to pass the mucous membrane and reach the vascular system. In general, symptoms related to chlorhexidine allergy may present up to 40 minutes or more after exposure. Symptoms of type IV (delayed) hypersensitivity reactions may manifest up to seven days after exposure.

Type I hypersensitivity reactions to lidocaine are uncommon, and type IV hypersensitivity reactions are reported even less frequently.

In very rare cases with deep wounds, undesirable effects may occur, due to potential lidocaine absorption (see section 4.4). The necessary therapeutic measures should be decided upon by a physician.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Website: www.hpra.ie

4.9 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 (respiration). If convulsions occur, they must be treated promptly by intravenous injection of thiopentone (100 or 200 mg) or diazepam (5 to 10 mg). Alternatively, succinylcholine (50 to 100 mg i.v.) may be used, providing the clinician is capable of performing endotracheal intubation and managing a fully paralysed patient. If ventricular fibrillation or cardiac arrest occurs, effective cardiovascular resuscitation must be instituted. Epinephrine in repeated doses and sodium bicarbonate should be given as rapidly as possible.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group:
Anaesthetics, local-Amides-lidocaine combinations
Antiseptics and disinfectants, Biguanides and amidines, chlorhexidine, combinations.

ATC-Code: N01BB52, D08AC52.

The anaesthetic ingredient of Instillagel is Lidocaine, which stabilizes neuronal membranes and prevents the initiation and conduction of nerve impulses, thus effecting local anaesthetic action.

The antiseptic action of chlorhexidine gluconate is so potentiated by the combination with Methyl - and Propyl Parahydroxybenzoates that the microbial organisms normally present in the distal region of the urethra are killed within 5-to 10 minutes. Ascent of microbial microorganisms following urological interventions, or their upward displacement, is thereby largely prevented.

Chlorhexidine and methyl and propyl hydroxybenzoates have antiseptic properties.

5.2 Pharmacokinetic properties

After the product's application to mucous membranes Lidocaine is absorbed, but its blood concentrations after the instillation of doses of up to 800 mg into the urethra remain in the low range, below toxic levels. The metabolism of Lidocaine takes place in the liver and unchanged drug is excreted renally.

5.3 Preclinical safety data

None stated.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hydroxyethylcellulose, Propylene Glycol (E1520), Sodium Hydroxide, Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Unopened: 3 years.
For single use only.
Discard any unused gel.

6.4 Special precautions for storage

Do not store above 25 °C.

6.5 Nature and contents of container

A pre-filled syringe made of polypropylene with a butyl rubber stopper piston, and containing 6 ml of gel. The syringes are packed inboxes of 10 x 6 ml.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Farco-Pharma GmbH
Gereonsmuhlengasse 1-11
Koln
Germany

8 MARKETING AUTHORISATION NUMBER

PA0328/001/001

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