1 NAME OF THE MEDICINAL PRODUCT

Octenisept 1mg/ml + 20mg/ml cutaneous spray, solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml solution contains:
Octenidine dihydrochloride 1 mg
Phenoxyethanol 20 mg

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Cutaneous spray, solution

Clear, colourless, almost odourless solution

4.1 Therapeutic indications

Octenisept is indicated for repeated short-term antiseptic treatment of mucous membranes and adjacent tissues prior to diagnostic procedures in the anogenital region including the vagina, vulva and glans penis as well as prior to bladder catheterization.

Octenisept is also indicated for antiseptic treatment of small superficial wounds and skin disinfection prior to non-surgical procedures.

Octenisept may be used in patients of all age groups.

4.2 Posology and method of administration

The solution is intended for cutaneous use.
Octenisept is applied to the area to be treated until complete moistening is achieved. Following application and prior to further measures, such as e.g. the application of a wound dressing, an exposure time of at least 1 to 2 minutes must be observed. These instructions must be carefully followed in order to achieve the desired effect. So far there is only experience of continuous use for no longer than 14 days, therefore Octenisept should only be used for a limited treatment period.

*Paediatric population*

The posology of Octenisept is identical in adults and children.

### 4.3 Contraindications

Octenisept must not be used in cases of hypersensitivity to the active substances or to any of the excipients listed in section 6.1.

Octenisept must not be used for rinses in the abdominal cavity (e.g. intra-operatively) or the bladder, nor on the tympanic membrane.

### 4.4 Special warnings and precautions for use

Do not allow Octenisept to pass into the circulation, e.g. as a result of accidental injection. The use of octenidine aqueous solutions (0.1%, with or without phenoxyethanol), for skin antisepsis prior to invasive procedures has been associated with serious skin reactions in low weight preterm neonates.

Remove any soaked materials, drapes or gowns before proceeding with the intervention. Do not use excessive quantities and do not allow the solution to pool in skin folds or under the patient or drip on sheets or other material in direct contact with the patient. Where occlusive dressings are to be applied to areas previously exposed to Octenisept, care must be taken to ensure no excess product is present prior to application of the dressing.

Usage of Octenisept in the eye should be avoided.

**To prevent possible tissue injury, the product must not be injected or applied to tissues with pressure.**

### 4.5 Interaction with other medicinal products and other forms of interaction

Do not use Octenisept concomitantly with PVP iodine-based antiseptics on adjacent areas of skin, as strong brown to violet discolorations can occur at the border areas.

The incompatibility of the medicine in the concomitant use with anionic surfactants (soap, detergent, etc) can reduce or nullify its activity.
4.6 Fertility, pregnancy and lactation

**Pregnancy**

There is a moderate amount of data (between 300 – 1000 pregnancy outcomes, gestational age $\geq$ 12 weeks) from the use of octenidine dihydrochloride / phenoxyethanol combinations in pregnant women. No adverse events have been reported during and after birth. Animal studies with octenidine dihydrochloride do not indicate reproductive toxicity (see section 5.3). Animal studies with dermal application of 2-phenoxyethanol do not indicate reproductive toxicity (see section 5.3).

The use of Octenisept may be considered during pregnancy, if necessary.

**Lactation:**

There are no adequate experimental animal and clinical data on the use of Octenisept during lactation. As octenidine dihydrochloride is only absorbed in very small amounts or not at all, it must be assumed that it does not pass into breast milk.

Phenoxyethanol is absorbed rapidly and almost completely. There are no data regarding the excretion of phenoxyethanol in breast milk. As a precaution, Octenisept should not be applied in the area of the breast during the nursing period.

**Fertility**

There are no human data regarding the effect of octenidine and phenoxyethanol on fertility. Octenidine did not affect fertility in rats and rabbits. Phenoxyethanol did not affect fertility in mice.

4.7 Effects on ability to drive and use machines

Octenisept has no influence on the ability to drive and use machines.

4.8 Undesirable effects

The evaluation of undesirable effects is based on the following rates of occurrences:

- Very common ($\geq 1/10$)
- Common ($\geq 1/100$ to $< 1/10$)
- Uncommon ($\geq 1/1,000$ 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)

General disorders and administration site conditions

Rare: burning, redness, itching and warmth at the application site

Very rare: allergic contact reaction, e.g. temporary redness at the application site

Paediatric population

Frequency, type and severity of adverse reactions in children are the same as in adults.

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 the Yellow Card Scheme.

Website: www.mhra.gov.uk/yellowcard

4.9 Overdose

There is no knowledge of cases of overdose. However, overdosing of a topical preparation is very unlikely. In the case of local overdose, the affected areas can be rinsed with plenty of Ringer's solution.

Accidental oral ingestion of Octenisept is not considered dangerous as acute toxicity of octenidine hydrochloride and 2-phenoxyethanol via oral administration route is low (section 5.3). However, in cases of oral ingestion of larger amounts of Octenisept irritation of the mucosa of the gastrointestinal tract cannot be ruled out.

The acute toxicity of octenidine hydrochloride and 2-phenoxyethanol via intravenous administration route is low (section 5.3). Taking the low concentrations of the active substances into account an intoxication appears very unlikely. However, Octenisept should not be allowed to pass into the circulation, e.g. as a result of accidental injection.

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antiseptics and disinfectants / Quaternary ammonium compounds / octenidine, combinations
ATC code: D08AJ57

Mechanism of action
Octenidine dihydrochloride is a cation-active compound and as a result of its two cationic centres possesses marked surface-active properties. It reacts with cell wall and membrane components of the microbial cell and thus leads to destruction of cell function.

The mechanism of antimicrobial action of phenoxyethanol is based, among other effects, on an increased permeability of the cellular membrane for potassium ions.

Pharmacodynamic properties
Octenisept displays the following range of in vitro efficacy:
- Gram-positive and Gram-negative bacteria
- Yeasts and fungi

Octenisept meets the criteria for chemical disinfectants and antiseptic products as established by European Standards:
- EN 1040 – basic bactericidal activity (Phase 1)
- EN 1275 – basic yeasticidal activity (Phase 1)
- EN 13727 – bactericidal activity (Phase 2/step 1)
- EN 13624 – fungicidal activity (Phase 2/step 1)

The spectra of efficacy of phenoxyethanol and octenidine dihydrochloride complement each other in this respect. Specific primary resistance to octenidine dihydrochloride / phenoxyethanol combinations and the formation of secondary resistance in cases of prolonged use as a result of its non-specific efficacy are not to be expected.
Table: *in vitro* microbiocidal efficacy against exemplary germs

<table>
<thead>
<tr>
<th>Strain</th>
<th>Contact time</th>
<th>Concentration tested</th>
<th>Conditions</th>
<th>Result</th>
<th>EN criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>0.5 min</td>
<td>90%</td>
<td>10% bovine albumin, 4.5%defibrinated sheep blood, 4.5% bovine albumin, 1% mucin</td>
<td>6.14 log reduction</td>
<td>EN 13727</td>
</tr>
<tr>
<td></td>
<td>0.5 min</td>
<td>90%</td>
<td>4.5%defibrinated sheep blood, 4.5% bovine albumin, 1% mucin</td>
<td>6.06 log reduction</td>
<td>EN 13727</td>
</tr>
<tr>
<td><em>Enterococcus faecalis</em></td>
<td>0.5 min</td>
<td>90%</td>
<td>10% bovine albumin, 4.5%defibrinated sheep blood, 4.5% bovine albumin, 1% mucin</td>
<td>6.51 log reduction</td>
<td>EN 13727</td>
</tr>
<tr>
<td></td>
<td>0.5 min</td>
<td>90%</td>
<td>4.5%defibrinated sheep blood, 4.5% bovine albumin, 1% mucin</td>
<td>6.68 log reduction</td>
<td>EN 13727</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>0.5 min</td>
<td>90%</td>
<td>10% bovine albumin, 4.5%defibrinated sheep blood, 4.5% bovine albumin, 1% mucin</td>
<td>6.85 log reduction</td>
<td>EN 13727</td>
</tr>
<tr>
<td></td>
<td>1.0 min</td>
<td>90%</td>
<td>4.5%defibrinated sheep blood, 4.5% bovine albumin, 1% mucin</td>
<td>6.13 log reduction</td>
<td>EN 13727</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>0.5 min</td>
<td>90%</td>
<td>10% bovine albumin, 4.5%defibrinated sheep blood, 4.5% bovine albumin, 1% mucin</td>
<td>6.26 log reduction</td>
<td>EN 13727</td>
</tr>
<tr>
<td></td>
<td>1.0 min</td>
<td>90%</td>
<td>4.5%defibrinated sheep blood, 4.5% bovine albumin, 1% mucin</td>
<td>5.63 log reduction</td>
<td>EN 13727</td>
</tr>
<tr>
<td><em>Candida albicans</em></td>
<td>10 min</td>
<td>90%</td>
<td>10% bovine albumin, 4.5%defibrinated sheep blood, 4.5% bovine albumin, 1% mucin</td>
<td>5.95 log reduction</td>
<td>EN 13624</td>
</tr>
<tr>
<td></td>
<td>10 min</td>
<td>90%</td>
<td>4.5%defibrinated sheep blood, 4.5% bovine albumin, 1% mucin</td>
<td>5.39 log reduction</td>
<td>EN 13624</td>
</tr>
<tr>
<td><em>Aspergillus brasiliensis</em></td>
<td>20 min</td>
<td>80%</td>
<td>n/a</td>
<td>4.8 log reduction</td>
<td>EN1275</td>
</tr>
</tbody>
</table>

**Paediatric population**

The efficacy and tolerability of the octenidine dihydrochloride / phenoxyethanol combination was demonstrated in 347 children aged 6 days to 12 years, as well as 73 premature infants with a gestational age of less than 36 weeks.
Treatment of the umbilical stump with an octenidine dihydrochloride / phenoxyethanol combination was studied in 1725 newborns demonstrating tolerability in this age group.

5.2 Pharmacokinetic properties

Absorption
Orally administered $^{14}$C-radioactively labelled octenidine dihydrochloride was absorbed only in very small amounts (0 - 6%) via the mucous membranes of the gastrointestinal tract in mouse, rat and dog. In mouse it was found that topically applied amounts of octenidine dihydrochloride were not absorbed during a 24-hour contact time under an occlusive dressing.

On the basis of in vitro studies, passage of octenidine dihydrochloride across the placenta can be ruled out.

Octenidine dihydrochloride was not absorbed either via the mucous membrane of the vagina (rabbit) or via wounds (humans, rat).

Orally administered $^{14}$C-phenoxyethanol is absorbed almost completely and is excreted with the urine in the form of phenoxyacetic acid.

Paediatric population
The oxidative metabolism of 2-phenoxyethanol was studied in 4 babies aged 1 week to 11 months, as well 24 premature infants with a gestational age of less than 36 weeks. It was shown that 2-phenoxyethanol is absorbed via the skin and completely or almost completely metabolised by oxidation to phenoxyacetic acid and eliminated via the kidneys.

5.3 Preclinical safety data

Non-clinical data from acute and repeated dose toxicity studies, as well as from reproductive toxicology, genotoxicity and carcinogenicity studies with octenidine revealed no specific hazard for humans at the intended therapeutic doses.

Non-clinical data from acute and repeated dose toxicity studies and from genotoxicity studies with phenoxyethanol revealed no specific hazard for humans at the intended therapeutic doses.

A study in which mice were treated with phenoxyethanol via the diet over the whole reproduction cycle revealed a decreased pup body weight after birth and during lactation and increased pup lethality during lactation. Because the results were obtained following oral administration, its clinical relevance is not clear. In a dermal embryofetal development study with phenoxyethanol in rabbits no adverse effects were found.

Phenoxyethanol was slightly irritating to rabbit skin.

No carcinogenicity studies were performed with phenoxyethanol.

The combination of octenidine and phenoxyethanol was slightly irritating to rabbit eyes.
6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cocamidopropylbetaine
sodium gluconate
glycerol 85 %
sodium chloride
sodium hydroxide solution (10 %)
purified water

6.2 Incompatibilities

With anionic surfactants, e.g. from detergents and cleaning preparations the octenidine cation can form insoluble complexes, which can reduce or nullify its activity.

6.3 Shelf life

250 ml: 5 years
50 ml: 3 years
After first opening: use within 1 year.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container
50ml: white moulded bottle of polyethylene (high density) provided with a white tamper proof manual spray pump of polyethylene (low density) and polypropylene packed in a folding box containing 50 ml of medicinal product
250ml: white round bottle of polyethylene (high density) provided with a white tamper proof manual spray pump of polyethylene (low density) and polypropylene containing 250 ml of medicinal product
Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Schülke & Mayr GmbH
Robert-Koch Str. 2
22851 Norderstedt
Germany

8 MARKETING AUTHORISATION NUMBER(S)

PL 05536/0001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORIZATION

12/08/2015
DATE OF REVISION OF THE TEXT

15/01/2018