

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Fortacin 150 mg/ml + 50 mg/ml cutaneous spray, solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of solution contains 150 mg lidocaine and 50 mg prilocaine.

Each actuation delivers 50 microlitres which contains 7.5 mg lidocaine and 2.5 mg prilocaine.

1 dose is equal to 3 actuations.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Cutaneous spray, solution

Colourless to light yellow solution

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Fortacin is indicated for the treatment of primary premature ejaculation in adult men.

4.2 Posology and method of administration

Posology

The recommended dose is 3 actuations applied to cover the glans penis. Each dose consists of a total of 22.5 mg lidocaine and 7.5 mg prilocaine per application (1 dose is equal to 3 actuations).

A maximum of 3 doses can be used within 24 hours with at least 4 hours between doses.

Special populations

Elderly

Dose adjustments are not required in the elderly (see section 5.1).

Renal impairment

Clinical studies have not been performed in patients with impaired renal function, however due to its method of administration and very low systemic absorption, no dosage adjustment is required.

Hepatic impairment

Clinical studies have not been performed in patients with impaired hepatic function, however due to its method of administration and very low systemic absorption, no dosage adjustment is required. Caution is advised in case of severe hepatic impairment (see section 4.4).

Paediatric population

There is no relevant use of Fortacin in the paediatric population for the indication of treatment of primary premature ejaculation.

Method of administration

Cutaneous use.

Fortacin is only indicated for application to the glans penis.

Before initial use, the spray container should be briefly shaken and then primed by spraying it into the air three times.

Before each subsequent use, it should be briefly shaken and then the spray container should be re-primed by spraying into the air once.

Any foreskin should be retracted from the glans penis. The spray container should be held in an upright position before use. Fortacin should be applied to the entire glans penis, by actuating the valve 3 times. One third of the glans penis should be covered with each actuation. After 5 minutes any excess spray should be wiped off prior to intercourse.

4.3 Contraindications

Hypersensitivity of the patient or their partner to the active substances or to any of the excipients listed in section 6.1.

Patients or their partner with a known history of sensitivity to local anaesthetics of the amide type.

4.4 Special warnings and precautions for use

Precautions for use

Premature ejaculation may be due to a condition requiring medical supervision. If this product used as directed does not provide relief, the patient should discontinue use and seek medical advice.

Avoid contact with the eyes and ears

When applied in the vicinity of the eyes, Fortacin may cause eye irritation. Also the loss of protective reflexes may allow corneal irritation and potential abrasion. If eye contact occurs, the eye should immediately be rinsed with water or sodium chloride solution and protected until sensation returns. When applied to an impaired tympanic membrane, Fortacin may cause ototoxicity of the middle ear.

Risk of injury

Fortacin sprayed onto mucous membranes of the patient or their partner, such as the mouth, nose and throat, or transferred onto female genitalia or anal lining, could be absorbed and temporary local numbness/anaesthesia is likely to result. This hypoaesthesia may mask normal pain sensations and, therefore, increase the dangers of localised injury.

Use with condoms

Fortacin must not be used with polyurethane-based female and male condoms as deterioration was observed and protection from sexually transmitted diseases or pregnancy may be reduced. Fortacin can be used with contraceptive devices made of latex rubber, polyisoprene, nitrile and silicone as no deterioration has been shown with these materials.

A higher rate of erectile dysfunction and male genital hypoaesthesia may be experienced when using Fortacin with male condoms.

Anaemia related conditions

Patients or their partner with glucose-6-phosphate dehydrogenase deficiency or congenital or idiopathic methaemoglobinaemia are more susceptible to medicinal product-induced methaemoglobinaemia (see section 4.5).

Although the systemic availability of prilocaine by cutaneous absorption of Fortacin is low, caution should be exercised in patients with anaemia, congenital or acquired methaemoglobinaemia or patients on concomitant therapy known to produce such conditions.

Hypersensitivities

Patients allergic to paraaminobenzoic acid derivatives (procaine, tetracaine, benzocaine, etc.) have not shown cross sensitivity to lidocaine and/or prilocaine; however, Fortacin should be used with caution in patients with a history (or partner with a history) of sensitivities to medicinal products, especially if the aetiologic medicinal product is uncertain.

Skin effects

In case the patient or their partner develop a rash or skin irritation, treatment with Fortacin should be discontinued. If symptoms persist, the patient should consult a doctor.

Patients with severe hepatic impairment

Patients with severe hepatic disease, because of their inability to metabolise local anaesthetics normally, are at greater risk of developing toxic plasma concentrations of lidocaine and prilocaine (see section 4.2).

4.5 Interaction with other medicinal products and other forms of interaction

Methaemoglobinaemia may be accentuated in patients already taking medicinal products known to induce the condition, e.g. sulphonamides, acetanilid, aniline dyes, benzocaine, chloroquine, dapsone, metoclopramide, naphthalene, nitrates and nitrites, nitrofurantoin, nitroglycerin, nitroprusside, pamaquine, para-aminosalicylic acid, phenobarbital, phenytoin, primaquine and quinine (see section 4.4).

The risk of additional systemic toxicity should be considered when large doses of Fortacin are applied to patients already using other local anaesthetics or structurally related medicinal products, e.g. class I anti-arrhythmics such as mexiletine.

Specific interaction studies with lidocaine/prilocaine and anti-arrhythmic medicinal products class III (e.g. amiodarone) have not been performed, but caution is advised due to the potential increase of antiarrhythmic effect.

Medicinal products that inhibit cytochrome P450 (CYP) 1A2 reduce the clearance of lidocaine (e.g. fluvoxamine, cimetidine or betablockers) and may cause potentially toxic plasma concentrations when lidocaine is given intravenously in repeated high doses over a long time period (30 hours).

4.6 Fertility, pregnancy and lactation

Fortacin is not indicated for use by women. However, there may be some exposure in female partners of men treated with Fortacin.

Women of childbearing potential / contraception in male and females

Patients hoping to achieve conception should either avoid using Fortacin, or, if it is essential to achieve penetration, should wash the glans penis as thoroughly as possible 5 minutes after applying the spray but prior to intercourse.

Pregnancy

There are no or limited amount of data from the use of lidocaine and prilocaine in pregnant women. Animal studies do not indicate reproductive toxicity (see section 5.3). As a precautionary measure, it is preferable to avoid the use of Fortacin during pregnancy unless effective male barrier contraceptive measures are taken in order to avoid potential foetal exposure.

Breast-feeding

Lidocaine and prilocaine are excreted in human milk, but at therapeutic doses of Fortacin no effects on the breastfed newborns/infants are anticipated due to active substance transfer from the male patient to his female partner. Fortacin can be used during breast-feeding if clinically needed.

Fertility

There are no adequate data from the use of lidocaine and prilocaine on fertility in humans. A study in rats showed that Fortacin caused a reduction in sperm motility (see section 5.3). This medicinal product may reduce the possibility of pregnancy, but should not be used as a contraceptive.

4.7 Effects on ability to drive and use machines

Fortacin has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

The most frequent adverse reactions reported with the use of this medicinal product in male patients were local effects of genital hypoaesthesia (4.5%) and erectile dysfunction (4.4%). These adverse reactions caused discontinuation of treatment in 0.2% and 0.5% of patients, respectively.

The most frequent adverse reactions reported with the use of this medicinal product in female partners were vulvovaginal burning sensation (3.9%), and genital hypoaesthesia (1.0%). Vulvovaginal discomfort or burning sensation caused discontinuation of treatment in 0.3% of subjects.

Tabulated list of adverse reactions

Frequency of the adverse reactions is defined as: very common ($\geq 1/10$), common ($\geq 1/100$ to $< 1/10$), uncommon ($\geq 1/1\ 000$ to $< 1/100$), rare ($\geq 1/10\ 000$ to $< 1/1\ 000$), very rare ($< 1/10\ 000$), not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Adverse drug reactions in male glans-penis-treated subjects		
System organ class	Frequency	Adverse reactions
Psychiatric disorders	Uncommon	Abnormal orgasm
Nervous system disorders	Uncommon	Headache
Respiratory, thoracic and mediastinal disorders	Uncommon	Throat irritation
Skin and subcutaneous tissue disorders	Uncommon	Skin irritation

Adverse drug reactions in male glans-penis-treated subjects		
System organ class	Frequency	Adverse reactions
Reproductive system and breast disorders	Common	Hypoaesthesia of male genital, Erectile dysfunction, Genital burning sensation
	Uncommon	Genital erythema, Ejaculation failure, Paraesthesia of male genital, Penile pain, Penis disorder, Pruritus genital
General disorders and administration site conditions	Uncommon	Pyrexia

Adverse drug reactions in sexual partners		
System Organ Class	Frequency	Adverse Reactions
Infections and infestations	Uncommon	Vaginal candidiasis
Nervous system disorders	Uncommon	Headache
Respiratory, thoracic and mediastinal disorders	Uncommon	Throat irritation
Gastrointestinal disorders	Uncommon	Anorectal discomfort, Oral paraesthesia
Renal and urinary disorders	Uncommon	Dysuria
Reproductive system and breast disorders	Common	Vulvovaginal burning sensation, Hypoaesthesia
	Uncommon	Vulvovaginal discomfort, Vaginal pain, Vulvovaginal pruritus

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 national reporting system listed in Appendix V](#).

4.9 Overdose

It is unlikely that Fortacin at the recommended dosages to result in an overdose.

However, should symptoms of systemic toxicity occur, the signs are anticipated to be similar in nature to those following the administration of local anaesthetics by other routes. Local anaesthetic toxicity is manifested by symptoms of nervous system excitation (e.g. restlessness, vertigo, hearing and visual disorders, nausea, vomiting, tremor and muscle twitching) and, in severe cases, central nervous and cardiovascular depression (e.g hypotension, bradycardia and circulatory collapse which may lead to cardiac arrest).

Severe neurological symptoms (convulsions, CNS depression) must be treated symptomatically by respiratory support and the administration of anticonvulsive medicinal products.

Prilocaine in high doses may cause an increase in the methaemoglobin level particularly in conjunction with methaemoglobin-inducing medicinal products (e.g. sulphonamides). Clinically significant methaemoglobinaemia should be treated with a slow intravenous injection of methylthioninium chloride.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anaesthetics, amides, ATC code: N01BB20

Mechanism of action

Fortacin provides topical anaesthesia to the glans penis. The active substances lidocaine and prilocaine block the transmission of nerve impulses in the glans penis, reducing the sensitivity of the glans penis. This is translated into a delaying of the ejaculatory latency time without adversely affecting the sensation of ejaculation.

Pharmacodynamic effects

Clinical studies have shown Fortacin to increase the intra-vaginal ejaculatory latency time (IELT), increase control over ejaculation and reduce the feelings of distress in patients with premature ejaculation as measured by the Index of Premature Ejaculation (IPE). The medicinal product has a rapid onset of action and is effective within 5 minutes of application. The effectiveness of the medicinal product has been demonstrated to persist on repeat use over time.

Clinical efficacy and safety

The efficacy of Fortacin was demonstrated in two multi-centre, multinational, randomised, double-blind, placebo controlled studies (PSD502-PE-002 and PSD502-PE-004) both followed by an open-label phase. Men satisfying the International Society for Sexual Medicine (ISSM) criteria for premature ejaculation (PE) who had a baseline IELT \leq 1 minutes in at least 2 of the first 3 sexual encounters during screening were eligible to enrol.

The ITT population for the two combined pivotal studies comprised 539 patients, with 358 and 181 patients in the Fortacin and placebo groups, respectively (2:1 ratio) for the initial, three month DB phase. The Per Protocol population comprised 430 patients (284 and 146 patients in the Fortacin and placebo groups, respectively).

Demographic characteristics for the ITT population of PSD502-PE-002 and PSD502-PE-004 individually are summarised in table below.

Demographics: ITT population (PSD502-PE-002 and PSD502-PE-004 individual results)

Demographic	PSD502-PE-002			PSD502-PE-004		
	PSD502 N = 167	Placebo N = 82	Total N = 249	PSD502 N = 191	Placebo N = 99	Total N = 290
Age (years)						
n	167	82	249	191	99	290
Mean	39.1	37.9	38.7	34.6	35.2	34.8
SD	11.71	11.97	11.97	9.56	11.20	10.13
Range	18 - 67	18 - 68	18 - 68	19 - 65	20 - 60	19 - 65
Median	39.0	36.0	38.0	33.0	33.0	33.0
Age group (years)						
18 to < 25	14 (8.4%)	12 (14.6%)	26 (10.4)	27 (14.1%)	19 (19.2%)	46 (15.9%)
25 to < 35	53 (31.7%)	26 (31.7%)	79 (31.7)	82 (42.9%)	36 (36.4%)	118 (40.7%)
35 to < 45	44 (26.3%)	18 (22.0%)	62 (24.9)	50 (26.2%)	20 (20.2%)	70 (24.1%)
45 to < 55	39 (23.4%)	18 (22.0%)	57 (22.9)	24 (12.6%)	19 (19.2%)	43 (14.8%)
55 to < 65	13 (7.8%)	7 (8.5%)	20 (8.0)	7 (3.7%)	5 (5.1%)	12 (4.1%)
≥ 65	4 (2.4%)	1 (1.2%)	5 (2.0)	1 (0.5%)	0	1 (0.3%)
Race/ethnic origin						
Caucasian	133 (79.6%)	74 (90.2%)	207 (83.1%)	188 (98.4%)	99 (100%)	287 (99.0%)
Afro-American/Caribbean	17 (10.2%)	4 (4.9%)	21 (8.4%)	1 (0.5%)	0	1 (0.3%)
Hispanic	9 (5.4%)	2 (2.4%)	11 (4.4%)	0	0	0
Asian	5 (3.0%)	2 (2.4%)	7 (2.8%)	1 (0.5%)	0	1 (0.3%)
Other	3 (1.8%)	0	3 (1.2%)	1 (0.5%)	0	1 (0.3%)

Abbreviations: BMI = body mass index; ITT = intention-to-treat; SD = standard deviation

The effectiveness of Fortacin in treating PE was assessed by measuring IELT and the co primary endpoints of ejaculatory control, sexual satisfaction, and distress using the IPE. During the 3 months of the double-blind treatment phase, the geometric mean IELT increased from 0.58 to 3.17 minutes in the Fortacin group and from 0.56 to 0.94 minutes in the placebo group.

85.2% of subjects in the Fortacin group achieved a mean IELT of > 1 minute over the course of 3 months of treatment with it, whereas 46.4% of the placebo subjects had a mean IELT of > 1 minute. 66.2% of Fortacin-treated subjects and 18.8% of placebo-treated subjects achieved a mean IELT > 2 minutes.

The clinically significant increases in IELT were paralleled by significant differences in the IPE scores ($p < 0.0001$). Adjusted mean change scores (Fortacin vs. placebo) at Month 3 were 8.2 vs. 2.2 for the ejaculatory control score, 7.2 vs. 1.9 for the sexual satisfaction score, and 3.7 vs. 1.1 for the distress score.

In Fortacin-treated subjects, IELT and IPE scores increased at the first measured timepoint. Both IELT and IPE scores continued to increase slightly more throughout the remainder of the double-blind phase. The positive changes in IELT and IPE domain scores were maintained during the open-label treatment phase.

At each of the three monthly assessments all subjects completed a Premature Ejaculation Profile (PEP) questionnaire relating to perceived control over ejaculation, personal distress related to ejaculation, satisfaction with sexual intercourse, and interpersonal difficulty relating to ejaculation. The PEP scores followed a similar pattern of improvement to the IELT and IPE scores. For all of the three monthly assessments completed by the subjects, there was a significant difference between Fortacin and placebo ($p < 0.0001$). Partners completed the PEP questionnaire at month three. There was also a significant difference over placebo in all domains for the responses from the partners ($p < 0.0001$).

Elderly patients

Patients recruited into the clinical trials ranged from 18- 68 years of age. In the pivotal clinical studies, subgroup analysis of the efficacy response in different age groups showed that the efficacy and safety profiles were quite consistent between the different age groups.

There is a large safety database for lidocaine and prilocaine, due to their established use. This does not indicate a safety concern for elderly

Paediatric population

The European Medicines Agency has waived the obligation to submit the results of studies with Fortacin in all subsets of the paediatric population in primary premature ejaculation (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Absorption

The plasma levels of lidocaine and prilocaine in male and female subjects were below the level associated with toxicity (5 000 ng/ml). Male volunteers had maximum plasma concentrations of lidocaine which were less than 4% of toxic levels, and prilocaine which were less than 0.4% of toxic levels, after repeat dosing. Female volunteers receiving repeated doses directly to the cervix and vagina of up to five times the recommended dose for the male partner, had maximum plasma levels of lidocaine which were less than 8% of toxic levels, and prilocaine which were less than 1% of toxic levels.

Systemic exposure to lidocaine and prilocaine and their metabolites (respectively 2,6-xylidine and *o*-toluidine), is low following application to the glans penis in male patients and application to the cervix/vagina fornices in female subjects, at doses higher than recommended.

Distribution

Lidocaine

The steady-state volume of distribution is 1.1 to 2.1 L/kg after intravenous administration. Lidocaine is reported to be 66% bound by plasma proteins, including alpha-1-acid glycoprotein. Lidocaine can cross the blood brain barrier and the placenta and is distributed in breast milk.

Prilocaine

Following intravenous administration, the steady state volume of distribution of prilocaine is 0.7 to 4.4 L/kg. Prilocaine is reported to be 55% bound to plasma proteins, including alpha-1-acid glycoprotein. Prilocaine crosses the blood-brain barrier and also crosses the placenta. Prilocaine is also distributed in breast milk.

Biotransformation

Lidocaine is largely metabolised in the liver by cytochrome P450 (CYP 3A4) and probably to a minor extent in the skin. First pass metabolism is rapid and extensive and bioavailability is about 35% after oral doses.

Prilocaine is rapidly metabolised in both the liver, by cytochrome P450, and in the kidneys by amidases.

The metabolism of lidocaine and prilocaine results in the formation of 2,6-xylidine and *o*-toluidine, respectively, amongst other metabolites. Plasma levels of these metabolites detected after administration of Fortacin in clinical trials were low in both male and female subjects, even after doses of it many times in excess of the clinical dose were applied. No 2,6-xylidine or *o*-toluidine was detectable at any time-point in vaginal fluids following local application of the medicinal product in female volunteers.

Elimination

Lidocaine

The terminal elimination half-life of lidocaine from the plasma following intravenous administration is approximately 65 - 150 minutes and the systemic clearance is 10 - 20 mL/min/kg. Lidocaine is excreted in the urine mainly as metabolites, with only a small proportion excreted unchanged.

Prilocaine

The elimination half-life of prilocaine following intravenous administration is approximately 10 - 150 minutes. The systemic clearance is 18 - 64 mL/min/kg. Prilocaine is excreted in the urine mainly as its metabolites, with only a small proportion excreted unchanged.

5.3 Preclinical safety data

Reproductive toxicity

Lidocaine

No teratogenic effects were observed in studies of embryonic/foetal development in rats and rabbits receiving doses during organogenesis. Embryotoxicity was observed in rabbits at doses toxic to the mother. The postnatal survival time of the offspring of rats treated during pregnancy and lactation with a dose toxic to the mother was shown to be reduced.

Prilocaine

In a study of pregnant rats receiving a combination of lidocaine and prilocaine during organogenesis, no effects on embryonic/foetal development were observed. There are however no systemic exposure data available for comparison with clinical exposure.

Genotoxicity and carcinogenicity

Lidocaine

Lidocaine was not genotoxic and the carcinogenic potential of lidocaine has not been studied. The lidocaine metabolite 2,6-xylylidine has genotoxic potential *in vitro*. In a carcinogenicity study of rats exposed to 2,6-xylylidine in utero, postnatally and throughout their lifetime, tumours in the nasal cavity, subcutaneous tumours and liver tumours were observed. The clinical relevance of tumour findings in relation to short-term/intermittent use of lidocaine in humans is unknown. Human exposure from Fortacin is 20-30 fold less than the minimum dose that did not result in tumours and 200 fold less than the minimum dose that did result in tumours.

Prilocaine

Prilocaine was not genotoxic and the carcinogenic potential of prilocaine has not been studied. The prilocaine metabolite *o*-toluidine has genotoxic potential *in vitro*. In carcinogenicity studies of *o*-toluidine in rats, mice and hamsters, tumours were observed in several organs. The clinical relevance of tumour findings in respect of short-term/intermittent use of prilocaine in humans is unknown. Human exposure is 1 000 fold less than the minimum dose studied. Note, this dose did result in tumours.

Effect on fertility

In an *in vitro* study of rats Fortacin has shown a reduction in sperm motility when 22.5 mg lidocaine and 7.5 mg prilocaine (i.e. the amount in 1 human dose) was in direct contact with rat sperm. However this study did not reproduce the circumstances of clinical use, as the concentration of Fortacin in direct contact with the sperm would be many fold lower. The potential for reduction of sperm motility following the clinical use of the medicinal product can not be excluded; therefore it is not possible to state whether Fortacin would prevent pregnancy.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Norflurane

6.2 Incompatibilities

Deterioration was observed when Fortacin was used with polyurethane-based female and male condoms (see section 4.4). Patients should be advised to use alternative methods of contraception.

6.3 Shelf life

18 months.

After first use: 12 weeks

6.4 Special precautions for storage

Store below 25 °C. Do not freeze.

6.5 Nature and contents of container

Aluminium spray container with metering valve.

The metering valve's components are the stainless steel, POM, TPE, polypropylene, chlorobutyl rubber and HDPE.

Each pack contains one spray container with 6.5 ml or 5 ml solution.

Each spray container of 6.5 ml delivers a minimum of 20 doses (1 dose is equal to 3 actuations).

Each spray container of 5 ml delivers a minimum of 12 doses (1 dose is equal to 3 actuations).

6.6 Special precautions for disposal and other handling

The metal container is pressurised. It should not be punctured, broken or burnt, even when apparently empty.

A residual volume of fluid that is not usable will remain in the container after all doses have been administered.

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

7. MARKETING AUTHORISATION HOLDER

Recordati Ireland Limited
Raheens East
Ringaskiddy Co. Cork P43 KD30
Ireland

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/13/881/001

EU/1/13/881/002

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 15 November 2013

Date of latest renewal: 15 September 2023

10. DATE OF REVISION OF THE TEXT

{MM/YYYY}

Detailed information on this medicinal product is available on the website of the European Medicines Agency <http://www.ema.europa.eu>

ANNEX II

- A. MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE**
- B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**
- C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION**
- D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

A. MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturers responsible for batch release

Genetic S.p.A.
Via Canfora, 64
84084 Fisciano (SA)
Italy

Recordati Industria Chimica e Farmaceutica S.p.A.
Via Matteo Civitali 1
20148 Milano
Italy

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product not subject to medical prescription.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III
LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Fortacin 150 mg/ml + 50 mg/ml cutaneous spray, solution
lidocaine/prilocaine

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each ml of solution contains 150 mg lidocaine and 50 mg prilocaine.
Each actuation delivers 50 microlitres which contains 7.5 mg lidocaine and 2.5 mg prilocaine

3. LIST OF EXCIPIENTS

Also contains: norflurane.
Contains fluorinated greenhouse gases.

4. PHARMACEUTICAL FORM AND CONTENTS

Cutaneous spray, solution
Each spray container of 6.5 ml delivers minimum 20 doses (**1 dose is equal to 3 actuations**)
Each spray container of 5 ml delivers minimum 12 doses (**1 dose is equal to 3 actuations**)
6.5 ml
5 ml

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Only cutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP
Discard 12 weeks after first use.

9. SPECIAL STORAGE CONDITIONS

Store below 25 °C. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Recordati Ireland Ltd.
Raheens East
Ringaskiddy Co. Cork
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/13/881/001
EU/1/13/881/002

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product not subject to medical prescription.

15. INSTRUCTIONS ON USE

Treatment of premature ejaculation in men older than 18 years occurring from first sexual intercourse.
The dose is 3 sprays on the head of the penis at least 5 minutes before sexual intercourse.
A maximum of 3 doses a day with at least 4 hours between doses.

Avoid contact with eyes, nose, mouth and ears.
Do not use Fortacin with polyurethane condoms.

QR code www.fortacin.eu

16. INFORMATION IN BRAILLE

fortacin

17. UNIQUE IDENTIFIER – 2D BARCODE

Not applicable

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA
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Not applicable

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING

SPRAY CONTAINER LABEL

1. NAME OF THE MEDICINAL PRODUCT

Fortacin 150 mg/ml + 50 mg/ml cutaneous spray, solution
lidocaine/prilocaine

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each ml of solution contains 150 mg lidocaine and 50 mg prilocaine.
Each actuation delivers 50 microlitres which contains 7.5 mg lidocaine and 2.5 mg prilocaine
1 dose is equal to 3 actuations

3. LIST OF EXCIPIENTS

Also contains: norflurane

4. PHARMACEUTICAL FORM AND CONTENTS

Cutaneous spray, solution
6.5 ml
5 ml

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Only cutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP
Discard 12 weeks after first use.

9. SPECIAL STORAGE CONDITIONS

Store below 25 °C. **Do not freeze.**

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

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Ringaskiddy Co. Cork
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12. MARKETING AUTHORISATION NUMBER(S)

EU/1/13/881/001
EU/1/13/881/002

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY**15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE****17. UNIQUE IDENTIFIER – 2D BARCODE****18. UNIQUE IDENTIFIER – HUMAN READABLE DATA**

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Fortacin 150 mg/ml + 50 mg/ml cutaneous spray, solution lidocaine/prilocaine

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

Always use this medicine exactly as described in this leaflet or as your doctor or pharmacist have told you.

- Keep this leaflet. You may need to read it again.
- Ask your pharmacist if you need more information or advice.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.
- You must talk to a doctor if you do not feel better or if you feel worse.

What is in this leaflet

1. What Fortacin is and what it is used for
2. What you need to know before you use Fortacin
3. How to use Fortacin
4. Possible side effects
5. How to store Fortacin
6. Contents of the pack and other information

1. What Fortacin is and what it is used for

Fortacin is a combination of two medicines: lidocaine and prilocaine. These belong to a group of medicines called local anaesthetics.

Fortacin is indicated for the treatment of premature ejaculation occurring in adult men (aged 18 years and over) from first sexual intercourse. This is when you always, or nearly always, have ejaculated within one minute of sexual intercourse and this causes you negative emotional effects. Fortacin works by decreasing the sensitivity of the head of the penis to increase time before ejaculation.

2. What you need to know before you use Fortacin

Do not use Fortacin

- if you or your partner are allergic to lidocaine or prilocaine or any of the other ingredients of this medicine (listed in section 6);
- if you or your partner have a history of allergy or sensitivity to other local anaesthetics with a similar structure (known as amide-type local anaesthetics).

Warnings and precautions

Talk to your doctor or pharmacist before using Fortacin

- if you, or your partner, have been diagnosed with a genetic disease or other condition affecting your red blood cells (glucose-6-phosphate deficiency, anaemia or methaemoglobinaemia);
- if you have a history of medicine sensitivities, especially if you are not certain which medicine causes sensitivity;
- if you suffer from severe liver problems.

Premature ejaculation may be due to a condition requiring medical supervision. If this product used as directed does not provide relief, consult a doctor.

Use with condoms

- Fortacin must not be used with latex-free female and male condoms made of polyurethane as these condoms may deteriorate when used together with Fortacin and therefore may fail to protect from sexually transmitted disease or pregnancy. Fortacin can be used with contraceptive devices made of latex rubber, polyisoprene, nitrile and silicone as no deterioration has been shown. Carefully check the material that your contraceptive or your partner's contraceptive is made of before using this product. Ask your pharmacist if you are unsure.
- If you use Fortacin with condoms, you may be more likely to be unable to develop or maintain an erection. You may also be more likely to have reduced feeling in and around the penis.

Avoid accidental contact

- When you use this medicine, particularly during priming of the container, aim the container away from the face to avoid accidental contact with ears, eyes, nose and mouth.
- If some medicine accidentally gets into your eyes or your partner's eyes, rinse them immediately with cold water or sodium chloride solution and keep them closed as much as possible until any effects, such as numbness, wear off. Be aware that normal protective mechanisms, such as blinking, or sensation of a foreign body in the eye, may not occur until the numbness has worn off.
- Fortacin should not come into contact with a damaged ear drum.

Contact with other mucous membranes

- Fortacin may also come into contact with other mucous membranes such as your, or your partner's, mouth, nose and throat, causing them to feel slightly numb for a short while. As this will reduce the ability to feel pain in these areas, extra care should be taken not to injure them until the numbness has worn off.

Possible transfer to partner, e.g. to vagina or the anus

- During sexual intercourse, a small amount of this medicine may be transferred, e.g. to the vagina or the anus. Therefore, both you and your partner may feel slight numbness for a short while and should take care not to injure yourselves, particularly during sexual activity. For more information regarding possible side effects in sexual partners, see section 4.

If you or your partner develop a rash or irritation, discontinue use of Fortacin. If symptoms persist, consult a doctor.

Children and adolescents

This medicine should not be used in children or adolescents under 18 years of age.

Other medicines and Fortacin

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. It is particularly important that you talk to a doctor before using Fortacin if you are taking any of the following medicines which may interact with Fortacin:

- other local anaesthetics as benzocaine and procaine
- heart medicines (anti-arrhythmic medicines as mexiletine and amiodarone)
- fluvoxamine, cimetidine or beta-blockers, which may cause an increase in the blood levels of lidocaine.
- medicines known to increase the risk of a disorder reducing the amount of oxygen in the blood (methaemoglobinaemia), such as those listed below:
 - Benzocaine – a local anaesthetic used to treat pain and itching
 - Chloroquine, pamaquine, primaquine, quinine - used to treat malaria
 - Metoclopramide – used to treat feelings of sickness (nausea) and vomiting, including in patients with migraine
 - Glyceryl trinitrate (GTN, nitroglycerin), isosorbide mononitrate, erythrityl tetranitrate, pentaerythritol tetranitrate and other nitrate and nitrite medicines - used to treat angina (chest pain caused by the heart)

- Sodium nitroprusside, isosorbide dinitrate – used to treat high blood pressure and heart failure
- Nitrofurantoin – an antibiotic used to treat urinary and kidney infections
- Sulphonamides (also called sulpha medicines), e.g. sulfamethoxazole – an antibiotic used to treat urinary infections, and sulfasalazine – used to treat Crohn’s disease, ulcerative colitis and rheumatoid arthritis
- Dapsone – used to treat skin conditions such as leprosy and dermatitis and also to prevent malaria and pneumonia in high-risk patients
- Phenobarbital, phenytoin – used to treat epilepsy
- Para-aminosalicylic acid (PAS) – used to treat tuberculosis

The risk of methaemoglobinaemia can also be increased by the use of certain dyes (aniline dyes), or the pesticide naphthalene, so let your doctor know if you work with any dyes or chemical pesticides.

Pregnancy, breast-feeding and fertility

Fortacin is not approved for use by women.

Ask your doctor or pharmacist for advice before taking any medicine.

Pregnancy

Fortacin should not be used whilst your partner is pregnant unless you use an effective male condom, as listed above in section 2 “Use with condoms”, to prevent exposure of the unborn child.

Breast-feeding

This medicine may be used while your partner is breast-feeding.

Fertility

Fortacin may reduce the possibility of pregnancy. Therefore, patients hoping to achieve conception should either avoid using Fortacin, or, if this medicine is essential to achieve penetration, should wash the penis as thoroughly as possible five minutes after Fortacin has been applied, but prior to intercourse.

Driving and using machines

Fortacin has no or negligible influence on the ability to drive and use machines when used at the recommended doses.

3. How to use Fortacin

Always use this medicine exactly as described in this leaflet. Check with your doctor or pharmacist if you are not sure.

The recommended dose of Fortacin is 3 sprays (3 sprays = 1 dose) on the head of the penis at least 5 minutes before sexual intercourse. A maximum of 3 doses can be used within 24 hours with at least 4 hours between doses.

The maximum recommended dose (3 doses within 24 hours) should not be exceeded.

Instructions for use

- Before initial use, briefly shake the spray container and then prime the pump mechanism by spraying the valve three times into the air. Aim the container away from faces to avoid contact with eyes, nose, mouth and ears.
- Before each subsequent dose, briefly shake the spray container and then re-prime the pump by spraying 1 time into the air.
- Retract any foreskin from the head of the penis. Holding the can upright (valve up), apply 1 dose (3 sprays) of Fortacin to the entire head of the penis, by covering one third with each spray.

- Wait 5 minutes then wipe off any excess spray prior to having sexual intercourse. It is important that you wipe off any excess spray also if you use a condom (see also section 2 for other important information regarding use with condoms).

If you use more Fortacin than you should

If you do apply too much, wipe it off.

Symptoms of using too much Fortacin are listed below. Contact your doctor or pharmacist if you experience any of these. They are very unlikely to happen if it is used as instructed:

- Feeling light-headed or dizzy
- Tingling of the skin around the mouth and numbness of the tongue
- Abnormal taste
- Blurred vision
- Ringing in the ears
- There is also a risk of a disorder reducing the amount of oxygen in the blood (methaemoglobinaemia). This is more likely when certain medicines have been taken at the same time. If this happens, the skin becomes bluish-grey due to a lack of oxygen.

In serious cases of overdose, symptoms may include fits, low blood pressure, slowed breathing, stopped breathing and altered heart beat. These effects may be life-threatening.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The following side effects have been reported with Fortacin in male patients:

Common (may affect up to 1 in 10 people)

- Inability to develop or maintain an erection
- reduced feeling in and around the penis
- feeling of burning in and around the penis

Uncommon (may affect up to 1 in 100 people)

- headache
- local irritation of the throat (if inhaled)
- irritation of the skin
- redness on and around the penis
- failure to ejaculate during sexual intercourse
- abnormal orgasm
- tingling in and around the penis
- pain or discomfort in and around the penis
- itching in and around the penis
- a high temperature

The following side effects have been reported with Fortacin in sexual partners:

Common (may affect up to 1 in 10 people)

- feeling of burning in and around the vagina
- reduced feeling in and around the vagina

Uncommon (may affect up to 1 in 100 people)

- headache
- local irritation of the throat (if inhaled)

- vaginal thrush (Candida) infection
- discomfort in the anus and rectum
- loss of feeling in the mouth
- difficulty or pain passing urine
- pain in the vagina
- discomfort or itching in the vulva and vagina

Reporting of side effects

If you or your sexual partner get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via **the national reporting system** listed in [Appendix V](#). By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Fortacin

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the spray container label and the carton after “EXP”. The expiry date refers to the last day of that month.

Store below 25 °C. Do not freeze. You must throw away the container 12 weeks after you first use it. The metal container is pressurised. Do not puncture, break or burn it even when apparently empty. A residual volume of fluid that is not usable will remain in the container after all doses have been administered.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Fortacin contains

- The active substances are lidocaine and prilocaine.
- Each ml of solution contains 150 mg lidocaine and 50 mg prilocaine.
- Each spray delivers 50 microlitres which contains 7.5 mg lidocaine and 2.5 mg prilocaine.
- 1 dose is equal to 3 actuations.
- The other ingredient is norflurane.
- This medicine contains fluorinated greenhouse gases (HFA-134a).
- Each spray container of 5 ml contains 5.06 g of HFA-134a corresponding to 0.00724 tonne CO₂ equivalent (global warming potential GWP = 1.430).
- Each spray container of 6.5 ml contains 6.5 g of HFA-134a corresponding to 0.0093 tonne CO₂ equivalent (global warming potential GWP = 1.430).

What Fortacin looks like and contents of the pack

Fortacin is a colourless to light yellow cutaneous spray, solution in an aluminium spray container with metering valve.

The metering valve's components are the stainless steel, POM, TPE, polypropylene, chlorobutyl rubber and HDPE.

Each pack contains 1 spray container with 6.5 ml or 5 ml of solution.

- Each spray container of 6.5 ml delivers a minimum of 20 doses.
- Each spray container of 5 ml delivers a minimum of 12 doses.

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Other sources of information

Detailed and updated information on this medicine is available by scanning the QR code below and the outer carton with a smartphone.

The same information is also available on the following URL: www.fortacin.eu

QR code www.fortacin.eu

Detailed information on this medicine is available on the European Medicines Agency web site:

<https://www.ema.europa.eu>.