April 2019

New Medicine Review

Fortacin® (Lidocaine / Prilocaine) Spray

Treatment of primary premature ejaculation in adult men

Recommendation: Rag Status BLACK

Fortacin® (Lidocaine / Prilocaine) is not recommended for the treatment of primary premature ejaculation in adult men.

Compared with placebo, Fortacin® (Lidocaine / Prilocaine) statistically significantly increased the intravaginal ejaculation latency time. However, there are no trials against the active licensed comparator (dapoxetine).

Summary of supporting evidence:

- Currently, there is no consensus as to what level of intravaginal ejaculation latency time (IELT) constitutes a meaningful improvement in premature ejaculation (PE).
- The results from the two pivotal phase III trials support the use of Lidocaine / Prilocaine (Fortacin®) in the treatment of subjects with premature ejaculation.
- The results of the studies also demonstrate that, versus placebo, Lidocaine / Prilocaine was as effective in delaying ejaculation, improving ejaculatory control and sexual satisfaction, and reducing distress at the end of the open label treatment period (month 12) as at the end of the double blind treatment period (month 3).
- Two hundred and fifty-six men with premature ejaculation were randomized from 38 centres in the USA, Canada and Poland in phase III studies [1] during 2010. The geometric mean IELT over the 3-month treatment period increased and there were significantly greater increases in the scores for the domains of ejaculatory control, sexual satisfaction and distress in the Lidocaine / Prilocaine group than in the placebo group. This was supported by improvements in all secondary endpoints.[1]
- In European phase III trials [2] during 2009, Lidocaine / Prilocaine (Fortacin®) applied topically 5-minutes before intercourse improved ejaculatory latency and significantly improved ejaculatory control and sexual satisfaction, factors relevant for acceptance of a PE treatment by both patient and physician. Lidocaine / Prilocaine was well tolerated by both patients and partners, with no systemic side-effects and a low incidence of localized effects, and was rated favourably by most users.[2]

Details of Review

Name of medicine (generic & brand name)**:** [3]

Lidocaine & Prilocaine (Fortacin®) spray.

Strength(s) and form(s): [3]

Cutaneous spray, colourless to light yellow solution.

Each ml of solution contains 150mg lidocaine and 50mg prilocaine.
Each container delivers a minimum of 20-doses (6.5ml) or 12-doses (5.0ml).
Each actuation delivers 50microlitres which contains 7.5mg lidocaine and 2.5mg prilocaine.

Dose and administration: [3]

The spray container should be briefly shaken and then primed before initial use, by spraying it into the air 3-times and then re-primed by spraying it once, before each subsequent use.

Once the can is held upright (valve up), any foreskin should be retracted from the glans penis before the recommended dose of 3-actuations containing a total of 22.5mg lidocaine and 7.5mg prilocaine, is applied. One third of the gland penis should be covered with each actuation. After 5-minutes any excess spray should be wiped off prior to intercourse.

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

BNF therapeutic class / mode of action: Anaesthetics, amides. As Fortacin® is only recently marketed in the UK, it doesn't appear in the BNF / online BNF, but does now appear in MIMS.

Licensed indication(s): [3]

Treatment of primary premature ejaculation in adult men.

Proposed use (if different from, or in addition to, licensed indication above):

Course and cost: [4]

A 5ml container containing 12 doses = £59.99

NICE Clincal Knowledge Summary:

No NICE CKS is currently available for premature ejaculation.

Relevant NICE guidance:

No NICE / SMC guidance / guideline is currently available for Fortacin®.

AWMSG (2014) - In the absence of a submission from the holder of the marketing authorisation, lidocaine/prilocaine (Tempe®) cannot be endorsed for use within NHS Wales for the treatment of primary premature ejaculation in adult men

Background and context [5]

PE is the most common form of male sexual dysfunction, sometimes referred to as ejaculation praecox. The sexual response cycle consists of four different stages: desire, arousal, orgasm and resolution. In men, the fourth stage of orgasm is usually coincident with ejaculation and it is disruption of this fourth stage that is described as ejaculatory dysfunction, as shown in Figure 1.

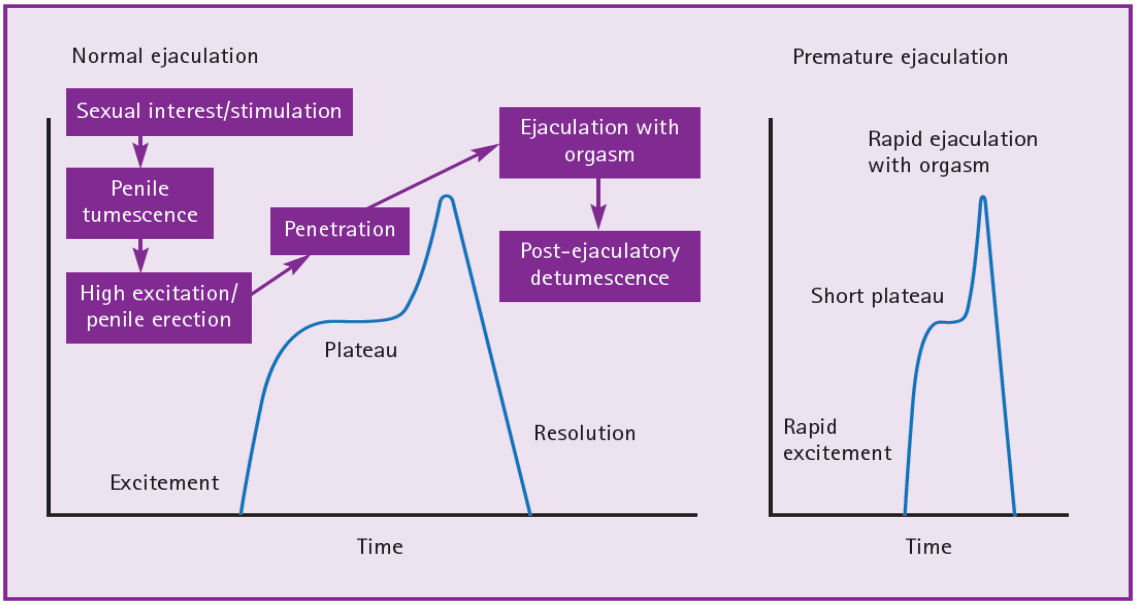

Figure 1: Premature ejaculation compared with the normal male sexual response [4]

The International Society for Sexual Medicine (ISSM) has suggested that there are four PE syndromes:

- lifelong PE (LPE)
- acquired PE (APE)
- natural variable PE (NVPE)
- premature-like ejaculatory dysfunction (PLED)

Lifelong PE is described as:

- a male sexual dysfunction characterised by ejaculation that always or nearly always occurs prior to, or within about one minute, of vaginal penetration
- the inability to delay ejaculation on all, or nearly all, vaginal penetrations
- negative personal consequences such as distress, bother, frustration and / or the avoidance of sexual intimacy

In men with LPE, ejaculation occurs in the majority of cases (80 per cent) within 30–60 seconds, or between one and two minutes (20 per cent). This will have been the situation since the first sexual encounter with nearly every woman with whom sexual intercourse has taken place. Ejaculation occurs too early in nearly every episode of sexual intercourse and remains rapid throughout the lifetime of the subject, suggesting a neurobiological / genetic cause.

APE has an additional key defining component, the presence of a clinically significant and bothersome reduction in latency time (often to around 3-minutes or less). APE may be the result of urological / thyroid dysfunctions or psychological / relationship problems.

In NVPE, the ejaculation time may be short or normal. Psychological support should be considered as first-line treatment in these men.

PLED has been described when the Intravaginal ejaculation latency times (IELT) is in the normal range, or may even be of longer duration. Subjective perception of consistent or inconsistent rapid ejaculation occurs. Consideration should be given as to whether the preoccupation with ejaculation is not better accounted for by another psychiatric disorder.[4]

When erectile dysfunction (ED) occurs in conjunction with PE it can lead to performance anxiety, and fear of losing the erection can contribute to early ejaculation. It is therefore important to

enquire about erectile difficulties in men presenting with PE.

From stopwatch studies, PE is characterised by a short ejaculation latency time, with approximately 90 per cent of men having an IELT of less than 60 seconds. However, 5–10 per cent of men without PE ejaculate in less than 2-minutes, whereas up to one-third of men with PE ejaculate within a timeframe of 2–5 minutes, providing a significant overlap of men with and without PE, as shown in Figure 2.

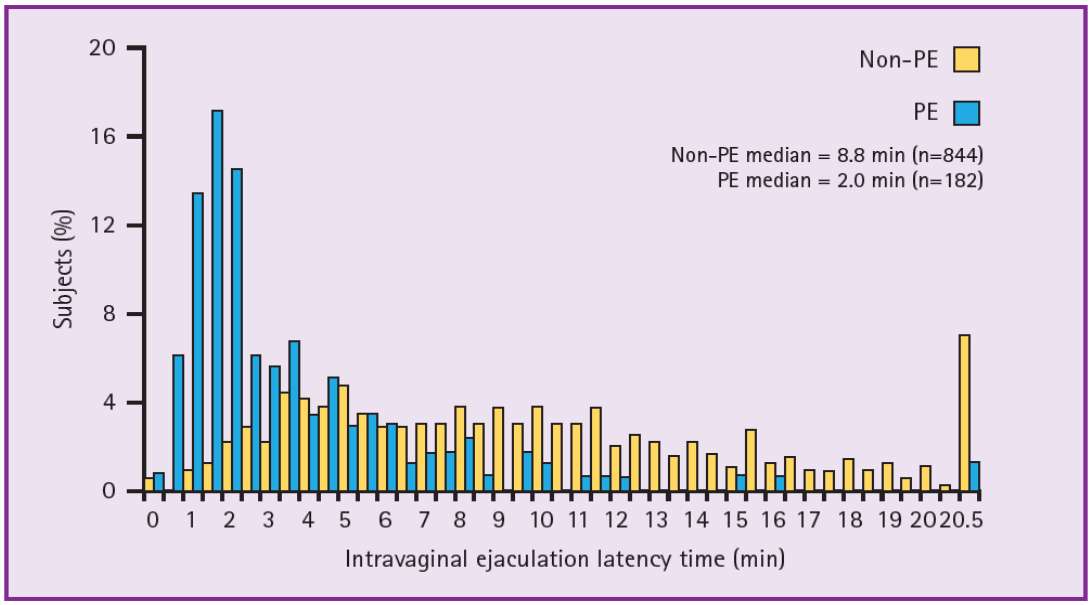

Figure 2: Intravaginal ejaculation latency times overlap between subjects with and without premature ejaculation (PE), especially in the 1–4 minute timeframe [4]

PE has been recognised as the most common male sexual dysfunction, with a prevalence of 20% to 30%.

In spite of relatively high prevalence rates, PE is the disorder for which patients are least likely to seek professional assistance. Most patients who present to an outpatient clinic with a complaint of PE suffer from LPE or APE.

The British Society for Sexual Medicine (BSSM) has produced a useful algorithm for the management of this prevalent and important condition; it recommends taking a careful and detailed medical and sexual history, asking six important questions about the PE and an enquiry about ED:

- Establish presenting complaint
- Time taken to ejaculate after vaginal penetration
- Perceived degree of ejaculatory control
- Degree of patient/partner distress
- Onset and duration of premature ejaculation
- Psychological history
- Medical history [4]

The algorithm suggests specific management plans according to the type of PE determined by the history taking. In the majority of patients, research has shown that in head-to-head studies, pharmacotherapy is generally superior to behavioural therapy, even in APE.

Treatment options for premature ejaculation

<u>Oral therapies</u>

- Short half-life on-demand selective serotonin-reuptake inhibitors (SSRIs) specifically

suggesting a role in treating PE, eg dapoxetine, which is the only oral licensed medication for the treatment of PE
- Off-label SSRIs and tricyclic antidepressants that have been used as a daily treatment for PE, eg paroxetine, sertraline, fluoxetine, citalopram and clomipramine
- Phosphodiesterase type 5 inhibitors used on demand as a combination treatment with SSRIs, when PE coexists with erectile dysfunction
- Tramadol, an opiate derivative (usually used as an analgesic) but could be used where PE coexists with a need for analgesia

Topical therapies

- Off-label lidocaine/prilocaine

Behavioural/psychological therapies

- Therapies have been incorporated for a number of years, but quantitative research shows benefit is not forthcoming. Nevertheless many patients are understandably anxious and may appreciate psychotherapy

There is a consensus that behavioural therapy is ineffective in LPE, which, in some cases, is genetic with neurobiological causes. Long-term studies have shown poor results after initial success. Combination therapy is superior to monotherapy. The use of topical anaesthetics such as lidocaine or prilocaine can be helpful but may be associated with significant penile hypoanaesthesia and possible transvaginal absorption.

Summary of evidence

Summary of efficacy data in proposed use: [6]

Clinical efficacy of lidocaine / prilocaine in males with PE was demonstrated in two multi-centre, multinational, randomised, double blind, placebo controlled studies, both followed by an open label phase. In the general population of patients with PE, lidocaine / prilocaine was shown to increase the time to achieve ejaculation after penetration (IELT); it also increased control over ejaculation and reduced the feelings of distress in patients with PE as measured by the Index of Premature Ejaculation (IPE). During the 3 months of the double blind treatment phase, the average IELT increased from 0.58 to 3.17 minutes in the lidocaine / prilocaine group and from 0.56 to 0.94 minutes in the placebo group. The clinically significant increases in IELT were paralleled by significant differences in the IPE score ($p<0.0001$).

Studies PSD502-PE-002 [1] and PSD502-PE-004 [2]

These were randomised, double blind, placebo controlled, parallel design, multinational studies. The duration of the study was 12 weeks for the double blind phase and then an open label extension to up to 9 months provides a total exposure of 12 months.

The open label design allowed all study subjects an opportunity for treatment with the active treatment.

Long term efficacy is based on a safety extension of this pivotal study. No controlled data further to 12 weeks to support efficacy is available.

Male subjects aged 18 years and over with lifelong PE were considered suitable for the study if they met the specified criteria. Subjects were eligible to enrol in the study if they had documented an IELT ≤ 1 minute in at least 2 of the first 3 sexual encounters in the baseline period, perceived control over ejaculation and satisfaction with sexual intercourse of ‘poor’ or ‘very poor’ and to personal distress and interpersonal difficulty related to ejaculation of ‘quite a bit’ or ‘extremely’.

The placebo was a metered dose aerosol spray that was identical in appearance to the Lidocaine / Prilocaine spray and contained the same propellant gas. No active control was included.

Eligible subjects were randomised to either Lidocaine / Prilocaine or placebo in a 2:1 ratio with stratification by centre.

The primary objective of the studies was to determine the effect of Lidocaine / Prilocaine on IPE and IELT.

The secondary objective of the studies was to evaluate the safety and tolerability of Lidocaine / Prilocaine in subjects with PE and their sexual partners and to evaluate the effect of Lidocaine / Prilocaine on the subject and partner Premature Ejection Profile (PEP).

Outcomes

Efficacy was primarily assessed by quantitative measures based on time to ejaculation (IELT) and qualitative evaluation of the personal impact as patient reported outcomes (IPE).

The primary measures of efficacy were the:

- Change in mean IELT from baseline to during the 3 months of the double blind treatment
- Change in the IPE domain of ejaculatory control from baseline to month 3
- Change in the IPE domain of sexual satisfaction from baseline to month 3
- Change in the IPE domain of distress from baseline to month 3 (in study PE-004 it was measured as a secondary variable).

The secondary measures of efficacy were the:

- Proportion of subjects with mean IELT > 1 minute and > 2 minutes during the 3 months of double blind treatment
- Change in mean IELT from baseline to each month of double blind treatment
- Change in the IPE domains of ejaculatory control, distress and sexual satisfaction from baseline to months 1 and 2 separately
- Scores for perceived control over ejaculation, personal distress related to ejaculation, satisfaction with sexual intercourse and interpersonal difficulty related to ejaculation based on the subject PEP and the partner at months1,2 and 3.

Results
Study PE-002 [1]

Of the 256 patients enrolled a total of 29 subjects withdrew during the double blind treatment phase. A median of 13 doses of Lidocaine / Prilocaine and 12 doses of placebo were administered in the double blind phase.

Primary Endpoints

IELT – over the 3 month double blind treatment phase the mean IELT for subjects had increased to 2.59 minutes in the Lidocaine / Prilocaine group and to 0.8 minutes in the placebo group. Subjects who received Lidocaine / Prilocaine had a 4.66 fold increase in their adjusted geometric mean IELT, whereas those who received placebo demonstrated a 1.53 fold increase. The analysis of the ratio to baseline over the 3 month treatment phase for Lidocaine / Prilocaine / placebo demonstrated a statistically significant 3.05 fold (95%CI: 2.29, 4.06) treatment benefit in favour of Lidocaine / Prilocaine ($p<0.0001$).

IPE – Substantial improvement was observed in all 3 domains at month 3 in the Lidocaine / Prilocaine group compared with the placebo group.

Secondary Endpoints

Mean IELT response of >1 and >2 minutes during months 1-3 – At the end of each month of study treatment, a greater proportion of subjects who received Lidocaine / Prilocaine than placebo attained a mean IELT >1 minute and >2 minutes.

Change from baseline to each month of double blind treatment – At the end of each month of

the double blind treatment phase, the geometric mean IELT for all subjects in the ITT population had increased more from baseline in the Lidocaine / Prilocaine treatment group than in the placebo group. At the end of months 1 and 2, subjects treated with Lidocaine / Prilocaine had larger changes in their adjusted mean change from baseline scores for each of the IPE domains than subjects who received placebo.

PEP- The PEP scores for subjects and partners followed a similar pattern of improvement to the IELT and IPE scores. At the end of each of months 1,2 and 3, more subjects treated with Lidocaine / Prilocaine than placebo had at least a 1 point category improvement in each of the PEP domains. At month 3 the proportion of Lidocaine / Prilocaine treated subjects who indicated a response of 'very good' or 'good' was 33.4% for control, 41% for satisfaction compared to 2.5% and 10.1% respectively for placebo. The proportion of Lidocaine / Prilocaine treated subjects with a response of 'not at all' or ' a little bit' was 43.6% for distress and 59% for interpersonal difficulty compared with 13.9% and 31.6% respectively for placebo treated subjects.

Study PE-004 [2]

300 study subjects were randomised and of these 22 withdrew during the double blind treatment phase. A median of 15 doses of Lidocaine / Prilocaine and placebo were administered in the double blind phase.

Primary Endpoints

IELT – over the 3 month double blind treatment phase the mean IELT for subjects in the ITT population had increased to 3.79 minutes in the Lidocaine / Prilocaine group and to 1.07 minutes in the placebo group. Subjects who received Lidocaine / Prilocaine had a 6.3 fold increase in their adjusted geometric mean IELT, whereas those who received placebo demonstrated a 1.74 fold increase. The analysis of the ratio to baseline over the 3 month treatment phase for Lidocaine / Prilocaine / placebo demonstrated a statistically significant 3.62 fold (95%CI: 2.8, 4.67) treatment benefit in favour of Lidocaine / Prilocaine ($p<0.0001$).

IPE – A substantial improvement was observed in all 3 domains at month 3 in the Lidocaine / Prilocaine group compared with the placebo group. The improvements in the scores for all 3 domains were slightly higher in this study than those in the PE-002 study, even though the baseline scores for all 3 domains were also higher in this study.

Secondary Endpoints

Mean IELT response of >1 and >2 minutes during months 1-3 - At the end of each month of study treatment, a greater proportion of subjects who received Lidocaine / Prilocaine than placebo attained a mean IELT >1 minute and >2 minutes. Ahigher proportion of subjects in this study attained a mean IELT >1 minute and > 2 minutes than in the PE-002 study.

Change from baseline to each month of double blind treatment – At the end of each month of the double blind treatment phase, the geometric mean IELT for all subjects in the ITT population had increased more from baseline in the Lidocaine / Prilocaine treatment group than in the placebo group. At the end of months 1 and 2, subjects treated with Lidocaine / Prilocaine had larger changes in their adjusted mean change from baseline scores for each of the IPE domains than subjects who received placebo. The changes from baseline were generally slightly larger in this study than in PE-002.

PEP- The PEP scores for subjects and partners followed a similar pattern of improvement to the IELT and IPE scores. At the end of each of months 1,2 and 3, more subjects treated with Lidocaine / Prilocaine than placebo had at least a 1 point category improvement in each of the PEP domains. At month 3 the proportion of Lidocaine / Prilocaine treated subjects who indicated a response of 'very good' or 'good' was 40.7% for control, 51.1% for satisfaction compared to 8.4% and 9.4% respectively for placebo. The proportion of Lidocaine / Prilocaine treated subjects with a response of 'not at all' or 'a little bit' was 55.4% for distress and 69.5% for interpersonal

difficulty compared with 18.8% and 32.3% respectively for placebo treated subjects.

Open label extension

At the end of the double blind treatment phase subjects had the option to participate in the open label treatment phase in which all subjects received treatment with Lidocaine / Prilocaine.

The duration of the open label phase was 5 months in PE-002 and 9 months in PE-004.

A total of 497 subjects (98.4% of those completing the double blind treatment phase) entered the open label phase of the studies. 90.3% of the subjects completed the open label phase.

For all subjects in the open label treatment phase, the ratio to baseline geometric mean IELT ranged from 5.62 (visit 6) to 6.73 (visit 7) in PE-002 and from 8.39 (visit 6) to 10.39 (visit 7) in PE-004.

For those subjects who had received placebo in the double blind phase and switched to Lidocaine / Prilocaine during the open label phase, marked improvements in IELT were observed at the first assessment after initiating treatment with Lidocaine / Prilocaine. Subjects who had received Lidocaine / Prilocaine in the double blind treatment phases of both studies had slightly higher ratio to baseline geometric mean IELTs at visits 6-8 in the open label treatment phase than those who had received placebo. However, at visit 10 in PE-004 this difference was no longer apparent.

Improvement was also seen in IPE domain scores from the end of the double blind treatment phase to the end of the open label treatment phase. The mean change from baseline for ejaculatory control, sexual satisfaction and distress score was 12.3, 10.9 and 5.3 points respectively at the end of the open label phase.

Summary of safety data:

Clinical safety [3]

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.

There is limited data on the efficacy and safety of Fortacin® in patients 65 years and over.

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.

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
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

Common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100)

Table 1 : Adverse Drug Reactions in Male Glans-penis-treated Subjects [3]

Adverse Drug Reactions in Female 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 parasthesia
Renal and urinary disorders	Uncommon	Dysuria
Reproductive system and breast disorders	Common	Vulvovaginal burning sensation, hypoaesthesia
	Uncommon	Vulvovaginal discomfort, vaginal pain, vulvovaginal pruritus

Common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100)

Table 2 : Adverse Drug Reactions in Female Partners [3]

Interaction with other medicinal products [3]

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.

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.

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

In vitro interaction studies with topical antifungal (clotrimazole, econazole, imidazole, nystatin, miconazole, ketoconazole), antibacterial (clindamycin, metronidazole) and antiviral medicinal products (aciclovir), showed no effect on antimicrobial activity.

Fertility, pregnancy and lactation [3]

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

Deterioration was observed when lidocaine / prilocaine was used with polyurethane based male and female condoms. A statement is included in the package leaflet that polyurethane based barrier contraceptives do not provide effective contraception when lidocaine / prilocaine cutaneous spray is used.

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 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. 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.

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. This medicinal product may reduce the possibility of pregnancy, but should not be used as a contraceptive.

Strengths and limitations of the evidence:

Limitations

- No active comparator
- Lack of elderly subjects in studies (there is limited data on the efficacy and safety of Fortacin® in patients 65 years and over).
- Subjects suffered from lifelong PE only, not APE, NVPE or PLED
- Although the trials were double blind, the numbing effect of lidocaine / prilocaine may have led to inadvertent un-blinding and subsequent bias.
- Both trials adjusted their statistical tests to account for multiple endpoints
- No controlled data further to 12 weeks to support efficacy is available.
- Improvement with placebo seen

Strengths

- Two multi-centre, multinational, randomised, double-blind, placebo controlled studies, both followed by an open-label phase.
- Consistent results
- Adequate number of subjects randomised

Summary of evidence on cost effectiveness:

Comparative health economic evidence

A 5ml container costs £59.99.[4]

Each container of 5ml delivers a minimum of 12 doses (1 dose = 3 actuations)

The only other available licensed treatment for premature ejaculation is Dapoxetine tablets with a maximum of one daily dose of either 30mg or 60mg (dependent on response), 1 to 3 hours before sexual activity.

NHS List price Dapoxetine 30mg tablets x 3 = £14.71
Dapoxetine 30mg tablets x 6 = £26.48
Dapoxetine 60mg tablets x 3 = £19.12
Dapoxetine 60mg tablets x 6 = £34.42

From November 2017-November 2018 the total usage within the Lancashire and South Cumbria CCGs of dapoxetine equates to an expenditure of £5,226.80 (1,021 x 30mg tablets and 81 x 60mg tablets).

This usage is despite dapoxetine having an LMMG RAG rating of BLACK [7] (Amber 0 for Chorley / South Ribble CCG and Amber for West Lancashire).

12 doses (5ml) of Fortacin® NHS List price = £59.99
12 x 30mg tablets dapoxetine NHS List price = £52.96
12 x 60mg tablets dapoxetine NHS List price = £68.84

Neither the Greater Manchester Medicines Management Group (GMMMG) [8] nor the Pan Mersey Area Prescribing Committee [9] currently have Fortacin® listed as a product available for prescribing, in their formularies.

Prior to Fortacin® being licensed, pharmacological treatment options for premature ejaculation included 'on demand' dapoxetine, daily use of a longer-acting SSRI (off-label use), daily use of clomipramine (off-label use), 'on demand' topical local anaesthetic agents (off-label use) or 'on demand' tramadol (off-label use). [10]

Commissioning considerations:

Associated additional costs or available discounts:

There are no known currently available manufacturer discounts.

Productivity, service delivery, implementation:

N/A

Anticipated patient numbers and net budget impact:

There are no reliable estimates of the prevalence in the UK of persistent PE associated with marked personal distress or interpersonal difficulty.

A GP based study suggests that the lifetime prevalence of self reported PE in England may be as high as 31%, with 14% of responders reporting current problems. [11]

However, another study using a more stringent definition estimated the prevalence over a four week period as 3.7%.[12]

The manufacturer of dapoxetine has estimated that based on a GP-registered population of

100,000 people, 5851 men aged 18 to 64 will be affected by premature ejaculation with 1151 men severely affected.[10] The manufacturer further estimates that 25% of the men severely affected by premature ejaculation will seek treatment and 70% of those seeking treatment could be prescribed dapoxetine. The manufacturer therefore estimates that based on a GP-registered population of 100,000, 202 men aged 18 to 64 may potentially be prescribed dapoxetine over a 5-year period.[10]

The estimated current population of Lancashire / South Cumbria is 1.7 million people. If the above calculation is used, this would suggest that 99,467 men aged 18-64 will be affected by premature ejaculation across Lancashire / South Cumbria and that 19,569 men will be severely affected. Of the men severely affected 4,892 could potentially seek treatment and 3,424 could be prescribed dapoxetine.

This number is far higher than the currently prescribed amount of dapoxetine would suggest, however dapoxetine currently has an LMMG RAG Rating of BLACK.

However, with the advantage of being able to be applied just prior to sexual activity (allowing more spontaneity) there may be an increased demand for Fortacin®.

Innovation, need, equity:

Fortacin® offers another licensed treatment for premature ejaculation alongside dapoxetine. Some men may prefer to use Fortacin® as it only needs to be applied just before sexual activity (5 minutes) whilst dapoxetine needs to be taken approximately 1-3 hours prior to sexual activity. Both medications are for use only as on demand treatment before anticipated sexual activity.

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