HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use PHEXXI® safely and effectively. See full prescribing information for PHEXXI.

PHEXXI (lactic acid, citric acid, and potassium bitartrate) vaginal gel
Initial U.S. Approval: 2020

----------INDICATIONS AND USAGE----------
PHEXXI is a combination of lactic acid, citric acid, and potassium bitartrate indicated for the prevention of pregnancy in females of reproductive potential for use as an on-demand method of contraception. (1)

Limitations of Use: PHEXXI is not effective for the prevention of pregnancy when administered after intercourse.

----------DOSAGE AND ADMINISTRATION----------
- Administer one (1) pre-filled single-dose applicator of PHEXXI (5 grams) vaginally immediately before (or up to one hour before) each episode of vaginal intercourse (2.1)
- May use during any part of the menstrual cycle (2.2)

----------DOSAGE FORMS AND STRENGTHS----------
Each pre-filled single-dose vaginal applicator delivers 5 grams of gel containing lactic acid (1.8%), citric acid (1%), and potassium bitartrate (0.4%). (3)

----------WARNINGS AND PRECAUTIONS----------
- Cystitis and Pyelonephritis: Avoid use in women with a history of recurrent UTI or urinary tract abnormalities (5.1)

----------ADVERSE REACTIONS----------
Most common adverse reactions (≥2%) were vulvovaginal burning sensation, vulvovaginal pruritus, vulvovaginal mycotic infection, urinary tract infection, vulvovaginal discomfort, bacterial vaginosis, vaginal discharge, genital discomfort, dysuria, and vulvovaginal pain. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Evofem at toll-free phone 1-833-EVFMBIO or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 06/2023

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

PHEXXI is indicated for the prevention of pregnancy in females of reproductive potential for use as an on-demand method of contraception.

Limitations of Use

PHEXXI is not effective for the prevention of pregnancy when administered after intercourse *[see Dosage and Administration (2.1)].*

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage

Administer one pre-filled applicator of PHEXXI (5 grams) vaginally immediately **before** or up to one hour **before** each act of vaginal intercourse. If more than one act of vaginal intercourse occurs within one hour, an additional dose must be applied. Five grams of PHEXXI contains 90 mg of lactic acid, 50 mg of citric acid, and 20 mg of potassium bitartrate.

2.2 Timing of PHEXXI Use

May use PHEXXI during any part of the menstrual cycle. May use PHEXXI as soon as it is safe to resume vaginal intercourse after childbirth, abortion, or miscarriage.

2.3 Use of PHEXXI with Other Contraceptive Methods

PHEXXI may be used concomitantly with hormonal contraceptives; latex, polyurethane, and polyisoprene condoms; and vaginal diaphragms. Avoid PHEXXI use with vaginal rings.

2.4 Use of PHEXXI with Other Vaginal Products

PHEXXI may be used concomitantly with other products for vaginal infections including miconazole, metronidazole, and tioconazole.

3 DOSAGE FORMS AND STRENGTHS

Vaginal gel: 18 mg of lactic acid, 10 mg of citric acid, and 4 mg of potassium bitartrate in each gram (1.8%, 1%, and 0.4%, respectively) of off-white to tan color gel supplied in a pre-filled single-dose (5 grams) vaginal applicator

5 WARNINGS AND PRECAUTIONS

5.1 Cystitis and Pyelonephritis

Among 2804 subjects who received PHEXXI in Studies 1 and 2, 0.36% (n=10) reported adverse reactions of cystitis, pyelonephritis, or other upper urinary tract infection (UTI). Of these, one case of pyelonephritis was considered serious and required hospitalization. Avoid use of PHEXXI in females of reproductive potential with a history of recurrent urinary tract infection or urinary tract abnormalities.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Cystitis and Pyelonephritis *[see Warnings and Precautions (5.1)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of PHEXXI (pre-filled applicator with 5-gram dose) has been evaluated in two clinical trials (Study 1 and Study 2) in 2804 subjects (over 19,000 cycles of exposure). The racial/ethnic distribution was 66% White, 27% Black or African American, 2% Asian, 1% American Indian or Alaska Native, 0.3% Native Hawaiian or Pacific Islander, and 5% other; 32% of the study population was Hispanic. Study 1 included a one-year extension phase where 342 U.S. subjects were exposed to PHEXXI for 13 cycles.

Hypersensitivity Reaction

Of the 2804 PHEXXI-treated subjects in Studies 1 and 2, one subject reported a suspected drug hypersensitivity. Avoid PHEXXI use in females of reproductive potential with suspected hypersensitivity to the ingredients in PHEXXI.

The most common adverse reactions (≥10%) in the U.S. population in Studies 1 and 2 (n = 2480) were: vulvovaginal burning sensation (18.0%) and vulvovaginal pruritus (14.5%). The majority of these adverse reactions were mild and few led to discontinuation. Table 1 summarizes the most common adverse reactions (≥2%) reported by subjects using PHEXXI in the U.S.

Table 1. Adverse Reactions that Occurred in ≥ 2% of Subjects Who Used PHEXXI to Prevent Pregnancy (Studies 1 and 2 – U.S. population only)

Adverse Reaction	PHEXXI (N=2480) (%)
Vulvovaginal Burning Sensation	18.0
Vulvovaginal Pruritus	14.5
Vulvovaginal Mycotic Infection*	9.1
Urinary Tract Infection† ‡	9.0
Vulvovaginal Discomfort	9.0
Bacterial Vaginosis	8.4
Vaginal Discharge	5.5
Genital Discomfort	4.1
Dysuria	3.1
Vulvovaginal pain	2.1

* Includes preferred terms (PT) vulvovaginal mycotic infection and vulvovaginal candidiasis.
† Includes PTs urinary tract infection, streptococcal urinary tract infection, Escherichia urinary tract infection, and urinary tract infection bacterial.
‡ Does not include PTs cystitis, kidney infection, and pyelonephritis [see *Warnings and Precautions (5.1)*].

Among subjects who used PHEXXI in Studies 1 and 2, 1.6% discontinued from the clinical trials due to an adverse reaction. The most common adverse reactions leading to study discontinuation were vulvovaginal burning sensation (0.7%); and vulvovaginal pruritus and vulvovaginal discomfort (0.1% each).

Adverse Reactions in Male Partners
Among male partners of subjects who used PHEXXI for contraception in Study 2, 9.8% (131 of 1330) reported symptoms of local discomfort (burning, itching, pain, and “other”). Of these local discomfort symptoms, 74.7% were mild, 21.4% were moderate, and 3.9% were severe. Two subjects discontinued participation in the study due to male partner symptoms.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary
There is no use for PHEXXI in pregnancy; therefore, discontinue PHEXXI during pregnancy. There are no data with the use of PHEXXI in pregnant women or animals. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4 percent and 15 to 20 percent, respectively.

8.2 Lactation

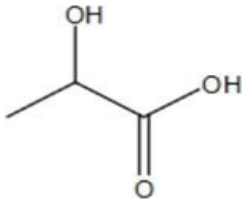
Risk Summary
There are no data on the presence of lactic acid, citric acid, and potassium bitartrate or their metabolites in human milk, the effects on the breastfed infant, or the effects on milk production.

8.4 Pediatric Use
The safety and effectiveness of PHEXXI have been established in females of reproductive potential. Efficacy is expected to be the same for post-menarchal females under the age of 17 as for users 17 years and older. The use of PHEXXI before menarche is not indicated.

11 DESCRIPTION
PHEXXI (lactic acid, citric acid, and potassium bitartrate) is a vaginal gel.

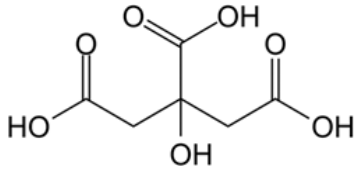
PHEXXI is an off-white to tan in color gel of uniform consistency, containing three active ingredients: lactic acid, citric acid, and potassium bitartrate.

The structural formula for lactic acid is:



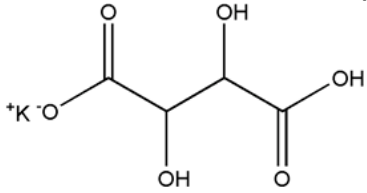
Lactic acid is designated chemically as 2-hydroxypropanoic acid with an empirical formula of $C_3H_6O_3$ and a molecular weight of 90.08 g/mol.

The structural formula for citric acid is:



Citric acid is designated chemically as 2-hydroxypropane-1,2,3-tricarboxylic acid with an empirical formula of $C_6H_8O_7$ and a molecular weight of 192.124 g/mol.

The structural formula for potassium bitartrate is:



Potassium bitartrate is designated chemically as potassium; (2*R*, 3*R*)-2,3,4-trihydroxy-4-oxobutanoate with an empirical formula of $KC_4H_5O_6$ and a molecular weight of 188.177 g/mol.

Each 5 gram dose is provided in a pre-filled single-dose applicator containing lactic acid USP (1.8% w/w), citric acid USP (1% w/w), and potassium bitartrate USP (0.4% w/w). Inactive ingredients present in the gel are: glycerin, alginic acid, xanthan gum, sodium hydroxide, benzoic acid, and purified water.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action
In *in vitro* studies, Phexxi produced a normal vaginal pH range (pH 3.5 – 4.5) in the presence of semen. In clinical studies, post-coital testing demonstrated pH < 5 in the majority of subjects, and sperm motility reduction.

12.2 Pharmacodynamics
Pharmacodynamic studies in humans have not been performed.

12.3 Pharmacokinetics
Pharmacokinetic studies in humans have not been performed. Systemic exposures of lactic acid, citric acid, and potassium bitartrate following vaginal administration of PHEXXI are not expected to lead to safety concerns.

In vitro studies with commonly used vaginal preparations (miconazole, metronidazole, tioconazole, and a product for maintaining normal vaginal pH) showed no significant effect on the pH or buffering capacity of PHEXXI.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
Carcinogenesis
Long-term carcinogenicity studies have not been performed with PHEXXI.

Mutagenesis
Mutagenic studies have not been performed with PHEXXI.

Impairment of Fertility
Reproductive studies have not been performed with PHEXXI. Upon discontinuation of PHEXXI, pregnancy may occur.

14 CLINICAL STUDIES

The efficacy of PHEXXI for the prevention of pregnancy was evaluated in a multi-center, open-label, single-arm clinical trial in the United States (AMP002; NCT03243305). The study enrolled females of reproductive potential 18 to 35 years of age with regular menstrual cycles (21 to 35 days). The median age was 27.8 years. The racial distribution was 70.6% White, 23.7% Black or African American, 2.5% Asian, 0.4% American Indian or Alaska Native, 0.2% Native Hawaiian or Pacific Islander, and 2.7% other. Subjects agreed to engage in at least 3 acts of heterosexual, vaginal intercourse per cycle. Subjects self-administered a 5 gram dose of PHEXXI intravaginally up to one hour before each episode of intercourse for up to 7 cycles.

The primary efficacy endpoint was the 7-cycle typical use cumulative pregnancy rate as derived by Kaplan-Meier life-table analysis. A total of 101 on-treatment pregnancies occurred in 1183 subjects contributing 4769 evaluable natural cycles. The 7-cycle cumulative pregnancy rate was 13.7% (95% CI: 10.0%, 17.5%), excluding cycles with back-up contraception, cycles <21 days or >35 days in length and cycles in which no intercourse was reported. The estimated Pearl Index, calculated based on data from the 7-cycle study, was 27.5 (95% CI: 22.4%, 33.5%).

16 HOW SUPPLIED/STORAGE AND HANDLING

PHEXXI (lactic acid, citric acid, and potassium bitartrate) vaginal gel is an off-white to tan color gel of uniform consistency containing lactic acid (1.8%), citric acid (1%), and potassium bitartrate (0.4%), supplied as individually wrapped 5 gram pre-filled single-dose vaginal applicators in sealed foil pouches along with a plunger, and are available as follows:

- NDC 69751-100-12 Box of 12 units
- NDC 69751-100-03 Sample box of 3 units

Store in the original foil pack at room temperature 20°C to 25°C (68°F to 77°F); excursion permitted between 15°C to 30°C (59°F to 86°F) [*see USP Controlled Room Temperature*].

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the Patient Information and FDA-approved patient labeling (Instructions for Use). Advise the patient:

- To intravaginally administer the contents of one pre-filled single-dose applicator of PHEXXI before **each** episode of vaginal intercourse and to administer an additional dose if intercourse does not occur within one hour of administration [*see Dosage and Administration (2.1)*].
- To consult their healthcare provider for severe or prolonged genital irritation [*see Adverse Reactions (6.1)*].
- To discontinue PHEXXI if they develop a local hypersensitivity reaction [*see Adverse Reactions (6.1)*].
- To contact their healthcare provider if experiencing urinary tract symptoms [*see Warnings and Precautions (5.1)*].
- That PHEXXI does not protect against HIV infection and other sexually transmitted infections.

Manufactured for Evofem, Inc., a wholly owned subsidiary of Evofem Biosciences, Inc., 12636 High Bluff Drive, Suite 400, San Diego, CA 92130