

PRODUCT MONOGRAPH
INCLUDING PATIENT MEDICATION INFORMATION

^{Pr}**VABLYS™**

Dequalinium chloride vaginal tablets

Tablets, 10 mg, Vaginal

Anti-infective and Antiseptic Agent

Duchesnay Inc.
950 boul. Michèle-Bohec
Blainville, Quebec
Canada, J7C 5E2

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PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATION

Vablys (dequalinium chloride) is indicated for the treatment of bacterial vaginosis in adult women under 55 years of age. Other pathogens commonly associated with vulvovaginitis such as *Trichomonas vaginalis*, *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Candida albicans* and Herpes simplex virus should be ruled out.

1.1 Pediatrics

Pediatrics (< 18 years of age): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

1.2 Geriatrics

Geriatrics (> 55 years of age): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for use in women over 55 years of age.

2 CONTRAINDICATIONS

Dequalinium chloride is contraindicated in:

- Patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredients, or component of the applicator and container. For a complete listing, see Dosage Forms, Strengths, Composition and Packaging.
- Patients with ulceration of the vaginal epithelium and the vaginal portion of the cervix.
- Premenarchal patients.

3 DOSAGE AND ADMINISTRATION

3.1 Dosing Considerations

The following recommendations should be considered during treatment with Vablys:

- Menstruation
Since heavy bleeding during menses could result in a wash-out, the required local concentrations of dequalinium chloride cannot be ensured. Thus, it is recommended to start therapy 6 days before the next menses or directly after menses. In the event the treatment cannot be completed before the onset of menses, treatment should be interrupted and resumed afterwards.
- Treatment duration
Treatment should be continued for six consecutive days even when subjective discomfort (itching, discharge, odour) has resolved. Treatment for less than six days could result in increased risk of relapse.

- Sexual intercourse
There are no data regarding the effect of sexual intercourse on the efficacy of Vablys. It is recommended to refrain from sexual intercourse during treatment with Vablys.
- Contraception, conception, hygiene
Insufficient data are available to Health Canada regarding the compatibility of Vablys with condoms and other intravaginal devices and genitourinary products (e.g. diaphragms, menstrual tampons and cups, soaps, spermicides, vaginal douches (vaginal washes), natural health, herbal, cosmetic, etc.). The concomitant use of condoms and other intravaginal and genitourinary devices and products is not recommended.

3.2 Recommended Dose and Dosage Adjustment

One Vablys (dequalinium chloride) tablet intravaginally at bedtime for six consecutive days.

Health Canada has not authorized an indication for pediatric use. See **INDICATION, Pediatrics**.

3.3 Administration

One Vablys vaginal tablet is to be inserted deeply into the vagina, either with or without using the applicator provided as described below. The patient should wash her hands prior to opening the blister pack and after insertion of the tablet into the vagina. To ease insertion, it is recommended that the tablet be inserted while the patient is in a lying position, with legs slightly bent.

With Applicator

The patient should ensure that the applicator has been cleaned using a fragrance free soap, thoroughly rinsed and dried with a clean cloth. The inside piece of the applicator should be slightly pulled back to place the tablet into applicator. To prevent tablet from falling, ensure that approximately 2/3 of the tablet is inserted in the applicator. Holding the applicator in place, patient should gently push on the inside piece of the applicator to release the tablet deeply inside the vagina.

Without Applicator

One Vablys tablet is to be inserted deeply inside the vagina using the index and/or middle finger.

Vablys contains excipients that do not dissolve completely. Therefore, small tablet remnants may occasionally be found in undergarments.

In cases of severe vaginal dryness, vaginal tablet may not dissolve and may be discharged from the vagina intact. In such cases, the vaginal tablet should be moistened with a drop of water before re-insertion into the vagina.

3.4 Missed Dose

In the event that a dose is missed, treatment should be continued with the missed dose the following day. The patient should not double the dose to make up for a missed dose. The

patient should continue the full prescribed dosage schedule and use all 6 doses of Vablys.

4 OVERDOSAGE

No cases of overdose have been reported with the vaginal use of Vablys. However, the use of a higher daily dose or longer treatment duration might result in vaginal ulcerations. In the event of overdose, general symptomatic and supportive measures should be undertaken as required (e.g. vaginal lavage).

| |
|---|
| For management of a suspected drug overdose, contact your regional poison control centre. |
|---|

5 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 1 – Dosage Forms, Strengths, Composition and Packaging

| Route of Administration | Dosage Form / Strength/Composition | Non-medicinal Ingredients |
|-------------------------|------------------------------------|---|
| vaginal | tablet 10 mg | lactose monohydrate, magnesium stearate microcrystalline cellulose |

Vablys vaginal tablets are white or almost white, oval and biconvex. Vablys vaginal tablets are supplied in PVC/PE/PVDC blisters with a push-through aluminum foil. Boxes contain 6 tablets and a LDPE plastic applicator.

6 WARNINGS AND PRECAUTIONS

General

For vaginal use only.

There are no safety and efficacy data available on the re-treatment of patients who did not respond to or relapsed immediately after initial therapy with Vablys. Patients should be advised to consult their physician if symptoms persist at the end of the treatment or in case of recurrence.

Anionic substances such as soaps, detergents and surfactants may reduce the antimicrobial activity of dequalinium chloride. Thus, concomitant intravaginal use of soaps, spermicides or vaginal douches (vaginal washes) is not recommended.

Genitourinary

Increasing the daily dose or treatment duration of Vablys may increase the risk of vaginal ulcerations.

Sexual Health

Fertility

The effects of Vablys on fertility have not been studied. Vablys should not be used within 48 hours before sexual intercourse if you would like to conceive.

6.1 Special Populations

6.1.1 Pregnant Women

Limited data is available with Vablys use in pregnancy. Data from 7 clinical studies involving 481 pregnant patients did not demonstrate any adverse effect on the pregnancy or the foetus/neonate.

Vablys should not be used within 12 hours before birth to minimize exposure of the newborn.

In animals, no reproductive toxicity studies have been conducted due to low blood levels of dequalinium chloride in rabbits following vaginal administration.

6.1.2 Breast-feeding

No animal studies have been conducted to investigate if dequalinium chloride is excreted in breast milk.

It is not known whether dequalinium chloride is excreted in human breast milk. Because many drugs are excreted in human milk precaution should be exercised.

6.1.3 Pediatrics

Pediatrics (< 18 years of age): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

6.1.4 Geriatrics

Geriatrics (> 55 years of age): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for use in women over 55 years of age.

7 ADVERSE REACTIONS

7.1 Adverse Reaction Overview

In clinical trials, the most common adverse reactions reported in patients treated with Vablys were local reactions, including vaginal discharge, vulvovaginal pruritus, vaginal candidiasis and vulvovaginal burning sensation.

7.2 Clinical Trial Adverse Reactions

Because clinical trials are conducted under very specific conditions, the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.

Table 2 below presents adverse reactions occurring in $\geq 1\%$ of patients in one randomized, active-controlled, single-blind clinical trial involving women with bacterial vaginosis who were treated either with Vablys tablets for 6 days or Clindamycin vaginal cream for 7 days.

Table 2 – Adverse Reactions Occurring $\geq 1\%$ of Patients Receiving Vablys (Dequalinium Chloride 10 mg Once Daily for 6 Days) or Clindamycin Vaginal Cream 2% (5g [100 mg Clindamycin] Once Daily for 7 Days)

| | Vablys n = 163 (%) | Clindamycin n = 153 (%) |
|---|--------------------------|-------------------------------|
| Infections and Infestations | | |
| Vulvovaginal candidiasis | 4.9 | 5.2 |
| Bacterial vulvovaginitis | 0.6 | 3.9 |
| Reproductive System and Breast Disorders | | |
| Vaginal discharge | 9.2 | 4.6 |
| Vulvovaginal burning sensation | 1.8 | 3.3 |
| Vulvovaginal discomfort | - | 1.3 |
| Vulvovaginal pruritus | 4.9 | 8.5 |

One or more adverse reactions were experienced by 17.8% of Vablys-treated patients and 20.3% of clindamycin-treated patients.

Adverse reactions were most commonly classified as Reproductive System and Breast Disorders (reported by 11.0% and 13.1% of patients) and Infections and Infestations (reported by 7.4% and 8.5% of patients) in the Vablys and clindamycin groups, respectively. The most commonly reported adverse reactions in the Vablys group were vaginal discharge (reported by 9.2% of patients), followed by vulvovaginal pruritus and vulvovaginal candidiasis (each reported by 4.9% of patients). The most commonly reported adverse reactions in clindamycin-treated patients were vulvovaginal pruritus (8.5% of patients) and vulvovaginal candidiasis (5.2% of patients).

7.3 Less Common Clinical Trial Adverse Reactions

Other related adverse reactions occurring in $< 1\%$ of the Vablys group include:

Gastrointestinal disorders: nausea

Infections and infestations: bacterial vulvovaginitis, fungal skin infection, vulvitis, vulvovaginitis

Nervous system disorder: headache
Reproductive system and breast disorders: vaginal haemorrhage, vulvovaginal pain

7.4 Post-Market Adverse Reactions

The following adverse events were reported during post-marketing experience. Because these events are reported voluntarily by a population of uncertain size, it is not possible to reliably estimate their frequency or establish a causal relationship to drug exposure:

| | |
|---|---|
| Gastrointestinal disorders: | abdominal pain, vomiting |
| Immune System disorders | hypersensitivity with allergic symptoms like urticaria, erythema, swelling, rash or pruritus |
| General disorders and administration site conditions: | pyrexia |
| Infections and infestations: | cystitis |
| Reproductive system and breast disorders: | Vaginal ulceration and maceration of vaginal epithelium, uterine haemorrhage, vulvovaginal erythema, vulvovaginal dryness |

8 DRUG INTERACTIONS

8.1 Drug Interactions Overview

Drug interactions have not been established.

8.2 Drug-Drug Interactions

Interactions with other drugs have not been established. Due to low blood levels of dequalinium chloride in animal studies following vaginal administration, interactions with systemic drugs are not expected.

8.3 Drug-Food Interactions

Interactions with food have not been established. Due to low blood levels of dequalinium chloride in animal studies following vaginal administration, interactions with food are not expected.

8.4 Drug-Herb Interactions

Interactions with herbal product have not been established. Due to low blood levels of dequalinium chloride in animal studies following vaginal administration, interactions with systemic herbal products are not expected.

8.5 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

9 ACTION AND CLINICAL PHARMACOLOGY

9.1 Mechanism of Action

Dequalinium chloride is an antiseptic agent with anti-infective properties belonging to the class of quaternary ammonium compounds.

Dequalinium chloride is a surface-active substance. The antimicrobial activity of dequalinium chloride is primarily based on an increase in bacterial cell permeability and the subsequent loss of enzyme activity, finally resulting in cell death.

Dequalinium chloride exhibits a rapid bactericidal activity in *in vitro* studies.

Dequalinium chloride in vaginal tablets exerts its action locally within the vagina.

9.2 Pharmacodynamics

Based on evidence from *in vitro* studies, the minimal inhibitory concentration (MIC) for dequalinium chloride against relevant vaginal pathogens ranges from 0.2 to ≥ 1024 $\mu\text{g/mL}$. Gram-positive bacteria may be more sensitive to dequalinium chloride than gram-negative bacteria. No studies on samples from human subjects were performed.

9.3 Pharmacokinetics

The *in vitro* dequalinium chloride concentration in vaginal fluid was 2000 to 4000 mg/L after dissolution of one Vablys vaginal tablet (10 mg dequalinium chloride) in an estimated 2.5 to 5 mg/L of vaginal fluid.

Preclinical data in rabbits indicate that only a very small amount of dequalinium chloride is absorbed after vaginal application. No further pharmacokinetic data are available.

10 STORAGE, STABILITY AND DISPOSAL

Store at room temperature (15 to 30°C).

Keep out of the reach and sight of children.

11 SPECIAL HANDLING INSTRUCTIONS

There are no special handling instructions.

PART II: SCIENTIFIC INFORMATION

12 PHARMACEUTICAL INFORMATION

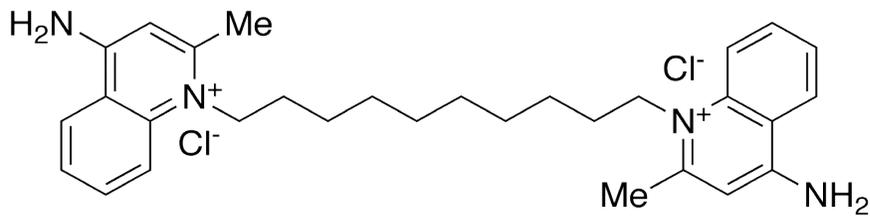
Drug Substance

Proper name: Dequalinium dichloride

Chemical name: 1,1'-Decamethylenebis[4-aminoquinaldinium chloride]

Molecular formula and molecular mass: $C_{30}H_{40}Cl_2N_4$, 527.6

Structural formula:



Physicochemical properties: Dequalinium chloride is slightly soluble in water and alcohol.

13 CLINICAL TRIALS

13.1 Trial Design and Study Demographics

Table 3 – Summary of patient demographics for pivotal clinical trial in the treatment of bacterial vaginosis (Intent-to-Treat Population)

| Study # | Trial design | Dosage, route of administration and duration | Study subjects (n) | Median age (Range) | Sex |
|---------|--|--|--|--|--------|
| 380104 | Randomized, single-masked, prospective, multi-center, two-arm, parallel group, active-controlled, two-stage adaptive, non-inferiority (15% margin) | Test: Vablys 10 mg dequalinium chloride tablet, intravaginal, one tablet daily for 6 days Active control: clindamycin 2% cream (100 mg clindamycin per dose), intravaginal, one dose daily for 7 days | Test: 163 163/163 Caucasian Active control: 152 150/152 Caucasian Total: 315 | Test: 32 (16-54) Active control: 31 (18-60) | Female |

Study 380104, conducted over 2007 to 2008, evaluated treatment in patients diagnosed with bacterial vaginosis based on 4 positive 'Amsel' criteria: vaginal pH > 4.5, presence of clue cells, KOH [potassium hydroxide] amine test and presence of grayish white, malodorous vaginal discharge. Subjects were postmenarchal women aged 16 to 60 years, who had not yet reached menopause. Treatment groups were comparable in demographics and baseline characteristics. The median age was approximately 30 years and all but two patients were Caucasian. At 3 to 14 days, and at two to six weeks after the end of the therapy, patients were assessed for clinical cure.

13.2 Study Results

The primary efficacy outcome, the clinical cure rate at Visit C1, performed 3 to 14 days after the end of the therapy, was tested for non-inferiority. The clinical cure was based on the Amsel criteria (vaginal pH > 4.5, presence of clue cells, KOH [potassium hydroxide] test, as well as grayish white, malodorous discharge) and defined as: clue cells and 2 other criteria being negative.

Based on the primary outcome, the treatment of bacterial vaginosis with a 6-day course of Vablys was found to be as effective as a 7-day course of clindamycin, with respective cure rates of 81.5% and 78.4%, showing no statistically significant difference (see Table 4).

Post-hoc sensitivity analysis regarding total non-failure rate was also performed. Total non-

failure rate was defined as no bacterial vaginosis recurrence, no treatment failures and no bacterial vaginosis as adverse event. The total non-failure rate in the Vablys group is in the range from 76.1 % to 85.2% and comparable to the range in the clindamycin group (75.7% to 87.9 %) (Table 4).

Table 4 – Results of study 380104 in the treatment of bacterial vaginosis

| Outcomes | Vablys | Clindamycin | Difference [95% Confidence Interval] p-value[†] |
|---|---|--------------------|---|
| Primary Endpoint Clinical cure rate at Visit C1* (clinical cure was defined as: clue cells and 2 other Amsel criteria** being negative) | <i>per-protocol analysis</i> | | |
| | (N=135) | (N=116) | 3.0% [-6.93%, 12.99%] 0.00019 |
| | 81.5% | 78.4% | |
| | <i>Intention-to-treat analysis</i> | | |
| | (N=163) | (N=152) | 1.0% [-8.21%, 10.26%] 0.00034 |
| | 79.7% | 78.7% | |
| Secondary Endpoint Non-failure rate at Visit C2*** (no BV recurrence, no treatment failures, no BV as adverse event) | <i>per-protocol analysis</i> | | |
| | (N=135) | (N=116) | 3.3% [-6.93%, 13.48%] 0.00022 |
| | 80.0% | 76.7% | |
| | <i>Intention-to-treat analysis</i> | | |
| | (N=163) | (N=152) | 0.4% [-9.03%, 9.86%] 0.00069 |
| | 76.1% | 75.7% | |

* Visit C1: Control 1, performed 3 to 14 days after the end of the therapy

** Amsel criteria: vaginal pH > 4.5, presence of clue cells, KOH test, and grayish white, malodorous discharge.

***Visit C2: Control 2, performed 2 to 6 weeks after the end of the therapy.

† Maximum likelihood estimation

14 MICROBIOLOGY

Resistance

There are no clinical studies on acquired antimicrobial resistance to dequalinium chloride. However, the development of resistance in microorganisms to dequalinium chloride is unlikely due to its multiple mode of action and has not been reported in *in vitro* studies.

Breakpoints

No breakpoints for dequalinium chloride are available by any recommending body and no relationship between minimal inhibitory concentrations (MIC) and clinical efficacy has been established.

15 NON-CLINICAL TOXICOLOGY

Systemic toxic effects of dequalinium chloride following intravaginal administration were not investigated; however, intravaginal administration in rabbits resulted in low blood dequalinium chloride concentrations suggesting minimal systemic exposure in this species.

Acute Toxicity

Single-dose toxicity studies with dequalinium chloride have been reported in dogs and rodents.

Following an oral dose of dequalinium chloride, Beagle dogs showed emesis after 1000 mg/kg dequalinium chloride whereas rats tolerated this dose. Mice tolerated an oral dose of 2000 mg/kg.

Overall, dequalinium chloride had low acute oral toxicity in all species tested.

Repeat-Dose Toxicity

A repeat-dose local tolerance of vaginally administered dequalinium chloride was studied in rabbits. This study showed no systemic, toxicologically relevant effects after administration of dequalinium chloride vaginal tablets (1 x 1.2 mg or 2 x 1.2 mg) per day for 4 weeks in rabbits with an average body weight of 3 kg. Thus, the No Observed Adverse Effect Level (NOAEL) was > 0.8 mg/kg/day for 28 days.

In mice, intraperitoneal doses of 6 to 7 mg/kg dequalinium chloride every second day (QOD) or 10 to 14 mg/kg every seventh day for 30 days resulted in the following reversible toxic effects: slightly laboured breathing; a 20 to 30% reduction in body weight; tubular cell necrosis and liver damage, with concomitant lung congestion; and the overall mortality was 40%. Higher doses of 13 and 14 mg/kg every 7 days and 8, 9 and 10 mg/kg QOD resulted in severe dyspnea, accompanied by cyanosis, a rapid and extreme decrease in body weight (40-45%), and eventual death.

No oral toxicity was seen in Wistar rats after administration of a 0.01 or 0.05% dequalinium chloride solution in drinking water for 26 weeks. All animals survived with no toxic effects or growth inhibition. The haematological profile (percentage haemoglobin, number of erythrocytes and leukocytes) was normal. There was no histological evidence of treatment-related changes

to major organs, including brain, stomach, small and large intestines, liver, thyroid, spleen, kidneys, heart, lungs and ovaries.

In tumour growth studies in rats, no overt toxic effects were observed after 8 subcutaneous injections of 4 mg/kg dequalinium chloride over 10 days, whilst 8 subcutaneous injections of 10 mg/kg, or 8 intraperitoneal injections of 4 and 10 mg/kg were lethal.

Local Tolerance

A repeat-dose local tolerance study of vaginally administered dequalinium chloride conducted in rabbits showed that dequalinium chloride is well tolerated by the vaginal epithelium. Although a minimal to mild increased vaginal irritation index was observed after treatment of rabbits with dequalinium chloride vaginal tablets (one or two administrations of 1.2 mg per day for 4 weeks), all epithelia were intact and no ulcerations were found. The total exposure (mg/kg) in rabbits was 11- to 22-fold higher than the indicated vaginal dose of Vablys in humans.

Genotoxicity

Dequalinium chloride showed no evidence of mutagenicity in the mammalian cell HPRT test (V79 Chinese Hamster cells), the *in vitro* cytogenetic test in human lymphocytes, or the *in vivo* mouse spot test. In the salmonella mutagenicity test (Ames test), a frameshift mutation was found in one bacterial strain (TA 1537). However, as this result in bacteria contrasts with the negative results from the *in vitro* and *in vivo* studies in mammalian cells, the overall conclusion from the genotoxicity studies is that dequalinium chloride showed no mutagenic potential in mammalian cells.

Carcinogenicity

No studies have been performed to evaluate Vablys' carcinogenic potential.

Reproductive and Development Toxicity

In Sprague-Dawley rats, no embryofetal effects were reported after topical administration of quaternary ammonium compounds with antimicrobial action.

The *in vivo* mouse spot test showed that high doses of dequalinium chloride (≥ 7 mg/kg intraperitoneal) reduce the number of pregnant female mice with litters and reduce litter size. Since single dose studies in mice have shown that toxicity depends on the route of administration (LD₅₀ in mice is ≥ 100 -fold higher for dequalinium chloride administered orally compared to intraperitoneal), an oral dose of ≥ 700 mg/kg would be required to achieve the same level of toxicity.

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE
PATIENT MEDICATION INFORMATION

VABLYS
Dequalinium chloride vaginal tablets

Read this carefully before you start taking **Vablys** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **Vablys**.

What is Vablys used for?

Vablys is used to treat an infection of the vagina, called bacterial vaginosis. It is used in adult women who are younger than 55 years of age.

How does Vablys work?

Vablys is inserted in the vagina. It is used to kill the bacteria that cause the infection.

What are the ingredients in Vablys?

Medicinal ingredient: dequalinium chloride

Non-medicinal ingredients: lactose monohydrate, magnesium stearate, microcrystalline cellulose.

Vablys comes in the following dosage forms:

As a 10 mg vaginal tablet.

Do not use Vablys if:

- You are allergic to dequalinium chloride or to any ingredient in Vablys.
- You have sores (ulcers) in your vagina.
- You have not had your first menstruation.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Vablys. Talk about your health situation or problems you may have, including if you:

- Are pregnant, think you might be pregnant or are planning to become pregnant.
- Are breastfeeding.
- Used Vablys in the past and did not respond to the treatment or if your infection reoccurred immediately after using Vablys.

Other warnings you should know about:

- Do not use products that go inside your vagina while you are using Vablys. These include: condoms, spermicides, soaps, vaginal douches (vaginal washes), diaphragms, tampons, menstrual cups or any other product that goes inside your vagina. These can make Vablys less effective.
- You should not use Vablys during your period. This is because bleeding can make Vablys less effective. Start your treatment with Vablys six days before your period starts. Or, wait until your period has stopped before starting Vablys. If you get your period while you are already taking Vablys, stop taking Vablys and start taking it again once your period has stopped.

- You should not have sex during treatment with Vablys.

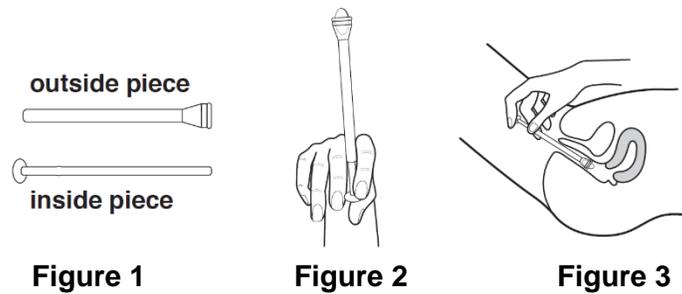
Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

How to take Vablys:

- Always use Vablys exactly as your healthcare professional has told you to.
- Wash your hands before opening the blister pack and inserting Vablys.
- Insert one tablet into your vagina at bedtime.
- You should insert the tablet while lying down with your legs slightly bent. You can use the vaginal applicator included with Vablys or your index and/or middle finger. See the detailed instructions for using the applicator or using without applicator, below.
- If your vagina is dry, the vaginal tablet might not dissolve and may come out of your vagina intact (in once piece). In this case, moisten the tablet with a drop of water before inserting it into your vagina.
- If a tablet is accidentally split, insert both halves of the tablet one after the other or both at once, if possible. For your comfort, insert both halves by their rounded parts.
- Vablys contains ingredients that do not dissolve completely. You may find remains of a tablet in your underwear. The tablet will not change the colour of your underwear. For your own comfort, you may wish to use a sanitary napkin or panty liner.
- Use Vablys every night for 6 days in a row even if you are no longer feeling discomfort such as itching, discharge or smell. If you take Vablys for less than 6 days your infection might return.

Using the applicator:

- Make sure both pieces of the applicator have been cleaned using a fragrance-free soap, rinsed and dried with a clean cloth (**Figure 1**). To clean the applicator, pull apart inside and outside pieces. Once completely dry, gently push the inside piece into the outside piece of the applicator.
- Delicately remove one tablet from the blister pack.
- Gently pull back the inside piece of the applicator until you feel slight resistance. Place the tablet vertically in the top of the applicator (**Figure 2**). To prevent the tablet from falling, be sure that approximately 2/3 of the tablet fits within the top of applicator.
- In a lying position, gently insert the applicator into your vagina as far as it will comfortably go. This is to ensure that the tablet is inserted into your vagina well. Hold the applicator in place and gently push the inside piece of the applicator (**Figure 3**) to release the tablet into your vagina. Remove the applicator from your vagina.
- Wash your hands and clean both pieces of the applicator with warm water and fragrance-free soap after each use. Make sure to keep them clean until next use.
- The applicator is for personal use only. It should not be shared with others.
- Discard the applicator once you have completed your 6 day treatment with Vablys.



Without applicator:

- Delicately remove one tablet from the blister pack.
- In a lying position, insert one Vablys tablet into your vagina, as far as it will comfortably go using your index and/or middle finger. This is to ensure that the tablet is inserted into your vagina well.
- Wash your hands thoroughly after inserting a Vablys vaginal tablet.

Usual dose:

Insert one Vablys vaginal tablet into the vagina at bedtime for 6 days in a row.

Overdose:

Using a dose that is higher than the usual daily dose or for a longer treatment duration may cause vaginal sores (ulcers).

If you think you have used too much Vablys, contact your healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

If you miss a dose, insert the missed dose the following day. Do not take two doses in one day to make up for a forgotten dose. Never insert more than one tablet a day. Continue using one tablet at bedtime until you have used all 6 tablets.

What are possible side effects from using Vablys?

Side effects may include:

- inflammation of your vulva or vagina
- vaginal discharge
- vaginal discomfort
- rash on your vulva or vagina
- burning sensation in your vulva or vagina
- vaginal dryness
- vaginal pain
- redness of the vulva or vagina
- headache
- abdominal pain
- nausea
- vomiting

These are not all the possible side effects you may feel when taking Vablys. If you experience any side effects not listed here, contact your healthcare professional.

| Serious side effects and what to do about them | | | |
|---|--------------------------------------|--------------|---|
| Symptom / effect | Talk to your healthcare professional | | Stop taking drug and get immediate medical help |
| | Only if severe | In all cases | |
| UNCOMMON | | | |
| · Allergic reactions: rash, fever, itchiness, hives, swelling. | | ✓ | |
| · Fever | | ✓ | |
| · Infection of vagina or vulva: itching, burning, pain, redness, swelling or irritation of the vagina or vulva, a thick, white vaginal discharge with a cottage cheese appearance | | ✓ | |
| · Inflammation of the bladder: pain or burning sensation while urinating, frequent urination, blood in urine, cloudy or strong-smelling urine, pain in pelvis, pressure in lower abdomen, fever. | | ✓ | |
| · Irritation and sores (ulcers) in the vagina | | ✓ | |
| · Vaginal bleeding | | ✓ | |
| · Skin Fungus: redness, itching or burning, peeling, cracking or scaly skin, swelling or irritation, blisters. | | ✓ | |

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Store at room temperature (15 to 30°C).

Keep out of reach and sight of children.

If you want more information about Vablys:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website <http://www.hc-sc.gc.ca/index-eng.php>; the manufacturer's website www.duchesnay.com, or by calling 1-888-666-0611.

This leaflet was prepared by Duchesnay Inc.

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