

A New Treatment Option for Trichomoniasis: Single-Dose Secnidazole

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Scope of the problem

Trichomoniasis is the most prevalent nonviral sexually transmitted infection (STI) worldwide.¹ As a nonreportable STI, reported prevalence estimates of trichomoniasis have varied.² A recent epidemiological study found that trichomoniasis affects 1.8% of women and 0.5% of men aged 18 to 59 in the United States.² There are health disparities in the prevalence of this infection, which is 6.8% in African Americans vs. 0.4% among other racial/ethnic groups.² In addition to race, other risk factors for trichomoniasis in women include older age, lower socioeconomic status, and increased numbers of recent sexual partners. The epidemiology of trichomoniasis in men has not been studied extensively, and men are not routinely tested. However, a recent review found that population-based prevalence estimates of trichomoniasis in men ranged from 0.2% to 1.3%.³ Furthermore, the prevalence of trichomoniasis among men attending sexually transmitted disease

Trichomoniasis is estimated to be the most prevalent nonviral STI worldwide, affecting approximately 3.7 million people in the United States.

(STD) clinics ranges from 3% to 17%, and prevalence can be as high as 72% among men with infected sexual partners.⁴ Overall, despite its high prevalence, especially in those with at least one risk factor, trichomoniasis receives little attention in the public health sector.⁵⁻⁷

Risks and consequences

Trichomoniasis is associated with significant morbidity if not treated promptly and appropriately (**Table 1**). In women, trichomoniasis can cause vaginitis, cervicitis, and pelvic inflammatory disease.⁸⁻¹⁰ It is associated with cervical cancer,¹¹ infertility,^{12,13} and adverse birth outcomes, including premature rupture of membranes, preterm birth, and low birthweight infants.¹⁴⁻¹⁶ Although men are frequently asymptomatic and may only seek treatment after learning that their female partner(s) are infected, trichomoniasis may be associated with nongonococcal urethritis, epididymitis, prostatitis, and infertility.^{1,3,17,18}

TABLE 1. Adverse Outcomes Associated With Trichomoniasis

Adverse birth outcomes ¹⁶ <ul style="list-style-type: none"> ■ Low birth weight infants^{14,15} ■ Premature rupture of membranes¹⁵ ■ Preterm delivery^{14,15}
Increased risk for HIV acquisition ^{19,20} and transmission ¹
Increased risk for acquisition of other STIs ^{8,21}
Vaginitis ⁸ and pelvic inflammatory disease ^{9,10}
Non-gonococcal urethritis, ^{17,22,23} epididymitis, ²⁴⁻²⁶ prostatitis ^{23,27,28}
Infertility ^{12,13}
Increased risk of cervical cancer ¹¹

Women with trichomoniasis have a two- to three-fold increased risk for acquiring HIV.^{19,20} Women with HIV and trichomoniasis have an increased risk of transmitting HIV to an uninfected partner.¹

Trichomoniasis also increases the risk for the acquisition of other STIs, including chlamydia, gonorrhea, herpes simplex virus (types 1 and 2), and syphilis.^{8,21} Coexistence of bacterial vaginosis (BV) and *Trichomonas vaginalis* is common, with coinfection rates of 60% to 80%.²⁹

A recent systematic review and meta-analysis showed that the risk of acquiring trichomoniasis is two-fold higher among women who have BV compared with women who do not have BV.³⁰

Diagnosis and screening

Up to 70% to 85% of patients with trichomoniasis are asymptomatic.¹ For symptomatic women, examination findings can include an abnormal vaginal discharge, often described as yellow or even blood-tinged and frothy, along with findings of vaginal and cervical inflammation (ie, strawberry cervix). Although microscopy is still widely used to identify motile trichomonads on wet mount and has the advantage of immediate diagnosis, the American College of Obstetricians and Gynecologists (ACOG)⁸ and Centers for Disease Control and Prevention (CDC)¹ both stress the low sensitivity (40% to 60%) of this test.^{1,8} Nucleic acid amplification tests are highly sensitive, detecting three to five times more *T vaginalis* infections than wet

mount,³¹ and are considered the current gold standard test.¹ Other United States Food and Drug Administration (FDA)-cleared methods such as culture and point-of-care rapid antigen or nucleic acid probe tests may be useful but are less sensitive.^{8,32,33}

The CDC recommends diagnostic testing for trichomoniasis for all women seeking care for vaginal discharge and all women with HIV, including those who are pregnant.¹ Screening for trichomoniasis might be considered for women being screened for chlamydia and gonorrhea,³⁴ as well as asymptomatic women at high risk of infection, including those who have multiple recent sexual partners, have a history of or are currently being treated for other STIs, use drugs, or are sex workers. Repeat testing is recommended for all sexually active women within 3 months after treatment because of high rates of recurrent infection, either due to reinfection from an untreated sexual partner or persistent infection.¹ Women with trichomoniasis should also be tested for HIV and other STIs. Women with HIV should be screened for trichomoniasis at entry to care, at prenatal visits, and then at least annually.¹

Current recommendations and change in treatment guidelines for trichomoniasis

The old 2015 CDC STD Treatment Guidelines recommended a single 2-g dose of oral metronidazole (MTZ) or tinidazole (TDZ) for *T vaginalis*-infected women without HIV; for HIV-infected women, MTZ 500 mg orally twice daily for 7 days was preferred.¹ The recommendation to use the 7-day MTZ dose in women with HIV arose from results of a trial that found the 7-day MTZ dose had better efficacy in HIV+ women compared to the 2-g single dose (91.5% vs. 83.2%).³⁵ A more recent similarly designed study compared single-dose MTZ (n = 311) with the 7-day MTZ regimen (n = 312) for trichomoniasis among women without HIV. Efficacy in the 7-day MTZ group was 89% compared to 81% in the single-dose MTZ group.³⁶ The authors concluded that the 7-day dose of MTZ, as opposed to the single 2-g dose, should be the preferred treatment for trichomoniasis among all women. This recommendation has been adopted by ACOG⁸ and was just adopted in the new updated 2021 CDC STI Treatment Guidelines. As the recommended treatment for trichomoniasis in women has moved to the multidose MTZ regimen, patient adherence

Women with trichomoniasis have a two- to three-fold increased risk for acquiring HIV

could become a potential issue.³⁷ Secnidazole demonstrated an efficacy of 92.2% in a similarly designed trial and is newly approved for the treatment of trichomoniasis in adults while also covering BV simultaneously.

Secnidazole

Secnidazole (SEC), a potent 5-nitroimidazole, has been used to treat various bacterial and parasitic infections since the late 1960s and was first used to treat BV in 1976.³⁸ In 2017, SEC was approved by the FDA as the first single-dose oral treatment for BV in women based on two randomized controlled trials.³⁹⁻⁴¹ The updated 2020 ACOG Clinical Practice Bulletin includes SEC as a treatment option for women with BV, citing a 2010 noninferiority study conducted in France that found the efficacy and safety of 2-g single-dose SEC for treatment of BV comparable to that of the 7-day dose of oral MTZ.⁸ Considering BV treatment options comparable, ACOG encourages a patient-centered treatment approach based on factors such as patient preference, convenience, adherence, and adverse reaction to prior treatments.⁸

SEC has favorable pharmacokinetic (PK) attributes that may provide advantages over other options. Seminal in vitro and PK studies have shown that the half-life of SEC

CDC Diagnosis and Screening Recommendations:

- Perform diagnostic testing for all women seeking care for vaginal discharge.
- Consider screening for trichomoniasis among women being screened for chlamydia and gonorrhea.
- Consider screening in asymptomatic women at high risk for infection including those who have multiple recent sexual partners, have a history of or are currently being treated for other STIs, use drugs, or are sex workers.
- Repeat testing for all sexually active T vaginalis-infected women within 3 months of treatment

ranges from 17 to 19 hours,^{38,42-44} which is considerably longer than other 5-nitroimidazoles including MTZ (ie, 7-8 hours)⁴³ and TDZ (ie, 12-13 hours).^{38,42,43} These studies also demonstrated that the half-life of SEC is longer in men vs. women (20 hours vs. 14 hours).^{42,43,45}

The antimicrobial activity of SEC is similar to that of other drugs in the class of 5-nitroimidazoles. In general, SEC and MTZ have equipotent activity against *T vaginalis*

TABLE 2. Non-comparative Clinical Trials of SEC for *T vaginalis*

First author, year (country)	Treatment	M/F	Cure rate	AEs
Piato, 197750 (Brazil)	SEC 2 g SD	0/50	94%	Nausea/vomiting: 10% Dizziness: 2% Bitter taste: 2% Edema (eyelid, vulva): 2%
Rocha, 197751 (Brazil)	SEC 2 g SD	0/50	100%* 96%†	Transient epigastralgia: 2%
Siboulet, 197745 (France)	SEC 2 g SD	76/104	95.5%	Nausea/gastralgia: 9% Gastric burning: 1%
Bravo, 197848 (Brazil)	SEC 500 mg q12 h × 4 d SEC 2 g SD	48 49	97.9%*‡ 100%*‡	Mild GI effects: 8%
Videau, 197843 (France)	SEC 2 g SD	56/84	97.1%	Nausea: 4%
Dyudyun, 201649 (Ukraine)	SEC 2 g SD§ SEC 2 g MD (3 d)¶	34/33	97.0%	Dyspepsia: 4.5% Metallic taste: 3.0%

*Infection eradication.

†Clinical cure.

‡Presumed to reflect infection eradication and clinical cure.

§Treatment for patients experiencing their first occurrence of *T vaginalis*.

¶Treatment for patients with chronic trichomoniasis.

AE, adverse event; BID, twice daily; d, days; F, females; M, males; MD, multiple doses; SD, single dose; SEC, secnidazole.

lis.^{43,46} Notably, the minimal lethal concentration of SEC is 56% lower than that of MTZ against *T vaginalis*.^{41,47}

We recently reviewed studies of SEC for the treatment of trichomoniasis in men and women.⁴⁵⁻⁵⁴ We identified six noncontrolled trials of SEC for trichomoniasis,^{43,45,48-51} and four randomized controlled trials of SEC for trichomoniasis in men,⁵² women,⁵³ and both men and women.^{54,55}

**Secnidazole is now
FDA approved for men
with an efficacy
of 95-100%**

Noncomparative studies

A series of six non-comparative studies of SEC for *T vaginalis* was published in the late 1970s; none were conducted in the United States or published in English.^{43,45,48-51} Overall, in patients with *T vaginalis*, a single dose of 2-g oral SEC resulted in cure rates ranging from 94% to 100% (Table 2).

Randomized controlled trials

Several placebo- or active-controlled clinical trials have been conducted to evaluate the efficacy and safety of SEC for the treatment of *T vaginalis* (Table 3). In a controlled clinical trial of MTZ vs. SEC, 60 women (aged 18-50 years) were randomly assigned to three treatment groups in which a study drug was administered vaginally as ovules: MTZ 500 mg daily for 10 days, SEC 500 mg daily for three days, and SEC 500 mg daily for 7 days.⁵⁴ At the end of treatment, all women in the three groups had parasitological cure based on wet mount microscopy. Among patients who received MTZ, clinical remission occurred within a mean (SD) of 4.2 (1.4) days, and symptoms were significantly reduced in 70% of patients. Among those who received SEC for 3 days, clinical remission occurred within a mean (SD) of 7.0 (2.0) days, and symptoms were significantly reduced in 75% of patients. Among those who received SEC for 7 days, clinical remission occurred within a mean (SD) of 4.0 (1.0) days, and symptoms were significantly reduced in 90% of patients. Patient and physician ratings of effectiveness were significantly higher among those who received SEC vs. MTZ.⁵⁴

In a controlled clinical trial of *Mentha crispera* vs. SEC, 60 women (aged ≥ 18 years) with *T vaginalis* were randomly assigned to *M crispera* 24 mg or SEC 2 g as a single, oral dose. After 7 days, cure rates were 90% in the *M crispera* group and 97% in the SEC group. There were no significant between-group differences in the absence/presence

of signs and symptoms. The only adverse event (AE) that occurred with greater frequency in the SEC vs. *M crispera* group was a metallic taste (50% vs. 0%).⁵⁵ One of the studies only included men (n = 30) and reported that the cure rate after 5 days of treatment with SEC was 100%.⁵²

Recently, we conducted the first randomized, double-blind, placebo-controlled study in the United States evaluating the efficacy and safety of a single 2-g dose of oral SEC in 147 women with trichomoniasis.⁵³ At the test-of-cure (TOC) visit 6 to 12 days later, the microbiologic cure rate was 92.2% (95% CI, 82.7%–97.4%) in the SEC group and 1.5% (95% CI, 0.0%–8.0%) in the placebo group (*P* < .001). Subgroup analyses of women with HIV, BV, or vaginal symptoms at baseline showed cure rates of 100%, 92.9%, and 95.2%, respectively, after treatment with SEC. No patients in the placebo group had a negative *T vaginalis* culture at TOC (all *P* values < .001).

Thus, data show single-dose SEC to be an effective option for treatment of trichomoniasis in women. SEC is currently the only single-dose treatment available for both BV and trichomoniasis.

Comparing these clinical findings with data used to support currently recommended treatment options in the CDC 2021¹ and ACOG 2020 Guidelines,⁸ the efficacy of SEC was better and AEs were comparable to or less than MTZ. Single-dose treatment options are con-

TABLE 3. Controlled Clinical Trials of SEC for *T vaginalis*

First author, year (Country)	Treatment	M/F	Cure rate	AEs
Özbilgin, 1994 ⁵² (Turkey)	SEC 2 g SD	30/0	100%	NR
	MTZ 250 mg TID (7 d)	29/0	100%	
	ORZ 500 g BID (5 d)	26/0	100%	
Buitron Garcia Figueroa, 1997 ⁵⁴ (Mexico)	MTZ 500 mg QD (10 d)	0/20	70%	0%
	SEC 500 mg QD (3 d)	0/20	75%	0%
	SEC 500 mg QD (7 d)	0/20	90%	0%
Moraes, 2012 ⁵⁵ (Brazil)	<i>M crispera</i> 24 mg SD	0/30	90.0%	20%
	SEC 2 g SD	0/30	96.6%	70%
Muzny, 2021 ⁵³ (US)	SEC 2 g SD	0/147	92.2%	15%
	Placebo SD		1.5%	22%

AE, any adverse event; BID, twice daily; d, days; F, females; M, males; MTZ, metronidazole; NR, not reported; ORZ, ornidazole; SD, single dose; SEC, secnidazole; TID, three times daily.

venient and likely to improve patient adherence, especially in populations at risk for nonadherence.⁵⁶ Of note, adherence with multidose MTZ has been low (50%–63%) in some studies.⁵⁷ Factors that may affect adherence include gastrointestinal complaints, treatment duration, and lifestyle restrictions. In one study, 23% of patients reported nausea in the single-dose and multidose MTZ groups.³⁶ In the SEC trial, 2.7% of patients reported nausea with SEC.⁵³

Conclusions

Accurate diagnostic testing and appropriate screening

SEC is currently the only single-dose treatment option for both BV and trichomoniasis.

are needed for successful treatment of trichomoniasis. Treatment of trichomoniasis is recommended to relieve symptoms and reduce a patient's risk of transmission

and acquisition of HIV, other STIs, and adverse reproductive outcomes. Management of trichomoniasis should include shared decision-making and a patient-centered approach that individualizes treatment to encourage adherence. Now FDA-approved, oral 2-g SEC offers a new single-dose option for treating both BV and trichomoniasis,

which is likely to improve patient adherence, especially in populations at risk for medication nonadherence. ■

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