CENTENE PHARMACY AND THERAPEUTICS
DRUG REVIEW
1Q18 January – February

BRAND NAME
Solosec™

GENERIC NAME
Secnidazole

MANUFACTURER
Symbiomix Therapeutics

DATE OF APPROVAL
September 15, 2017

PRODUCT LAUNCH DATE
First quarter of 2018

REVIEW TYPE
☒ Review type 1 (RT1): New Drug Review
Full review of new chemical or biologic agents

☐ Review type 2 (RT2): New Indication Review
Abbreviated review of new dosage forms of existing agents that are approved for a new indication or use

☐ Review type 3 (RT3): Expedited CMS Protected Class Drug Review
Expedited abbreviated review of Centers for Medicare & Medicaid Services protected class drugs (anticonvulsants, antidepressants, antineoplastic, antipsychotics, antiretrovirals, and immunosuppressants)

☐ Review type 5 (RT5): Abbreviated Review for Intravenous Chemotherapy Agents
Abbreviated review for intravenous chemotherapy agents which are usually covered under the medical benefit

FDA APPROVED INDICATION(S)[1]
Solosec is indicated for the treatment of bacterial vaginosis (BV) in adult women.

OFF LABEL USES
Not applicable

CLINICAL EFFICACY
Background
BV is the most common vaginal infection among girls and women ages 15-44.[2] Recommended treatment regimens from the Centers for Disease Control and Prevention (CDC) include a 7-day

regimen of twice daily oral metronidazole 500 mg, a 5-day regimen of intravaginal metronidazole 0.75% gel, and a 7-day regimen of intravaginal clindamycin 2% cream. Solosec is the first single-dose oral therapy approved by the Food and Drug Administration (FDA) for the treatment of BV in adult women.

	Schwebke J, et al. A phase-3, double-blind, placebo-controlled study of the effectiveness and safety of single oral doses of secnidazole 2 g for the treatment of women with bacterial vaginosis[3]
Study Design	Phase-3, multicenter, prospective, randomized (2:1), double-blind, placebo-controlled trial <u>Inclusion criteria</u> • Adult females or postmenarchal adolescent girls ≥ 12 years • Clinical diagnosis of BV, defined as meeting 4 Amsel criteria for BV (discharge; pH ≥ 4.7; ≥ 20% clue cells; and positive 10% potassium hydroxide [KOH] whiff test) • Nugent scores ≥ 4 <u>Exclusion criteria</u> • Are pregnant, lactating, menstruating, menopausal • Are suspected or confirmed clinically of having alternative causes of vaginal symptoms (e.g., candidiasis, C trachomatis, Trichomonas vaginalis, N gonorrhoeae, or herpes simplex infection) • History of secnidazole use or have received antifungal or antimicrobial therapy (systemic or intravaginal) within 14 days prior to baseline
N	189
Drug Regimen	Single-dose secnidazole 2 g or placebo
Primary Outcome(s)	Proportion of clinical outcome responders (CORs), defined as those with: • Normal vaginal discharge; • Negative 10% KOH whiff test; • Clue cells <20% of total epithelial cells on microscopic examination of the vaginal wet mount using saline at the test of cure (TOC)/end of study (EOS) visit (study days 21-30)
Secondary Outcome(s)	Clinical cure rates defined as: • Responders with normal discharge after treatment or abnormal discharge that is inconsistent with BV, likely due to Candida infection; • Negative KOH whiff test; • Clue cells <20% assessed at the interim visit (study days 7-14) and TOC/EOS (study days 21-30)
Results	Single-dose secnidazole 2 g was superior to placebo for the primary and all secondary efficacy measures in the modified intent-to-treat (mITT) population. The COR rate for single-dose secnidazole 2 g and placebo was

	53.3% (57/107) vs 19.3% (11/57), respectively (P < 0.001). Although it was prespecified that mITT was designated as the primary analysis population, the intent-to treat (ITT) population showed similar COR rates: 53.6% (67/125) in the single-dose secnidazole 2 g group and 21.9% (14/64) in the placebo group (P < 0.001). Clinical cure rates, based on an alternate definition of responder, which accounted for resolution of abnormal discharge consistent with bacterial vaginosis, were consistent with the COR rate analysis (58.9% vs 24.6%; P < 0.001) for single-dose secnidazole 2 g vs placebo.
# Withdrew due to Lack of Efficacy	None reported
# Withdrew due to Adverse Effects	None reported

	Hillier SL O., et al. Secnidazole Treatment for Bacterial Vaginosis: A Randomized Controlled Trial[4]
Study Design	Three-arm, phase 2, randomized (1:1:1), double-blind, dose-ranging, placebo-controlled trial <u>Inclusion criteria</u> • Non-pregnant women who were 18 years of age or older • Met the four Amsel criteria for bacterial vaginosis (discharge; pH 4.7 or greater; 20% or greater clue cells; positive whiff test). <u>Exclusion criteria</u> • Are pregnant • Bleeding at baseline • Allergic to metronidazole • Unable or unwilling to abstain from alcohol for 3 days after treatment • Receiving concomitant antimicrobial therapy (topical or oral), or received a recent course (within previous 14 days) of antimicrobial or antifungal therapy.
N	215
Drug Regimen	1 g or 2 g secnidazole or matching placebo granules
Primary Outcome(s)	Clinical cure 21-30 days after treatment, based on the 1998 FDA guidance regarding evaluation of treatment for bacterial vaginosis: • Normal vaginal discharge;

	• Negative 10% potassium hydroxide whiff test; and • Clue cells less than 20% of total epithelial cells on microscopic examination of the vaginal wet mount using saline at the test of cure visit The mITT was used for efficacy analyses.
Secondary Outcome(s)	• Microbiologic cure (defined as a Nugent score of 0–3) • Therapeutic cure, defined as meeting the criteria for both clinical and microbiologic cure
Results	In the mITT population, clinical, microbiologic, and therapeutic cure rates were 67.7%, 40.3%, and 40.3% for 2 g secnidazole and 51.6%, 23.4%, and 21.9% for 1 g secnidazole compared with 17.7%, 6.5%, and 6.5% for placebo, respectively (P<0.05 for secnidazole compared with placebo; all endpoints).
# Withdrew due to Lack of Efficacy	None reported
# Withdrew due to Adverse Effects	None reported

CONTRAINDICATIONS
Solosec is contraindicated in patients who have shown hypersensitivity to secnidazole, other ingredients of the formulation, or other nitroimidazole derivatives.

BLACK BOX WARNINGS
None reported

DRUG INTERACTIONS
There was no clinically significant drug interaction between secnidazole and the combination oral contraceptive, ethinyl estradiol plus norethindrone. Solosec can be co-administered with combination oral contraceptives (e.g., ethinyl estradiol plus norethindrone).

ADVERSE REACTIONS
Most common adverse reactions observed in clinical trials (incidence ≥ 2%) were vulvo-vaginal candidiasis, headache, nausea, dysgeusia, vomiting, diarrhea, abdominal pain, and vulvovaginal pruritus.

DOSAGE AND ADMINISTRATION
- The recommended dosage of Solosec is a single 2-gram packet of granules taken once orally, without regard to the timing of meals.

- The entire contents of the Solosec packet should be sprinkled onto applesauce, yogurt or pudding and consumed within 30 minutes without chewing or crunching the granules. A glass of water may be taken after the administration of Solosec to aid in swallowing.
- Solosec is not intended to be dissolved in any liquid.

PRODUCT AVAILABILITY
Oral granules: 2 g

THERAPEUTIC ALTERNATIVES

DRUG NAME	USAGE REGIMEN (route of admin/frequency of use)	COMMENTS
clindamycin (Clindesse® vaginal cream, Cleocin®)	Intravaginal 2% cream: 1 applicatorful (100 mg clindamycin/5 g cream) intravaginally at bedtime for 7 days* • The FDA-approved regimen for most products is 1 applicatorful (100 mg clindamycin/5 g cream) intravaginally at bedtime for 3 or 7 consecutive days in non-pregnant patients and for 7 days in pregnant patients. The dose for Clindesse vaginal cream is 1 applicatorful (100 mg clindamycin/5 g cream) intravaginally as a single dose at any time of the day. Intravaginal ovules/suppositories: 1 ovule (100 mg clindamycin) inserted intravaginally at bedtime for 3 days** Oral†: 300 mg PO BID for 7 days**	
metronidazole (Flagyl®, MetroGel-Vaginal®, Nuvessa®, Vandazole®)	0.75% vaginal gel (MetroGel-vaginal): 1 applicatorful (5 g of 0.75% metronidazole gel) intravaginally 1 to 2 times daily for 5 days 0.75% vaginal gel (Vandazole): One applicatorful (5 g of 0.75% metronidazole gel) intravaginally once daily for 5 days* 1.3% vaginal gel: One applicator (5 g of 1.3% gel containing 65 mg of metronidazole) administered intravaginally as a single dose at bedtime. Only approved for use in non-pregnant women. Regular-release tablet†: 500 mg PO BID for 7 days*	

tinidazole (Tindamax®)	2 g PO QD for 2 days or 1 g PO QD for 5 days**	

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
†Off-label indication
*Recommended regimen per CDC
**Alternative regimen per CDC

Utilization Management Recommendation
• There is not significant potential for inappropriate use. • It would be clinically appropriate to limit the quantity of Solosec to 1 packet/14 days.
Product Comparison
• CPAC score: 59 vs. metronidazole (oral) - Equal therapeutic outcomes anticipated • It would be clinically appropriate to provide equal access to Solosec, metronidazole (oral and vaginal), clindamycin (oral and vaginal), and tinidazole, or to require a trial of one before the others. o The aforementioned agents are recommended by the CDC and indicated for the treatment of BV. Comparative literature suggests that clinical cure rates are similar among the agents listed above.[5, 6]

REFERENCES

[1] Solosec Prescribing Information. Newark, NJ: Symbiomix Therapuetics LLC; September 2017. Available at: http://solosechcp.com/. Accessed September 24, 2017.
[2] Centers for Disease Control and Prevention. Bacterial vaginosis statistics. Available at: https://www.cdc.gov/std/bv/stats.htm. Accessed September 21, 2017.
[3] Schwebke JR, Morgan FG Jr, Koltun W, et al. A phase-3, double-blind, placebo-controlled study of the effectiveness and safety of single oral doses of secnidazole 2 g for the treatment of women with bacterial vaginosis. Am J Obstet Gynecol 2017.
[4] Hillier SL, Nyirjesy P, Waldbaum AS, et al. Secnidazole treatment of bacterial vaginosis: A randomized controlled trial. Obstet Gynecol. 2017 Aug;130(2):379-386.
[5] Ferris DG, Litaker MS, Woodward L, et al. Treatment of bacterial vaginosis: a comparison of oral metronidazole, metronidazole vaginal gel, and clindamycin vaginal cream [Abstract]. J Fam Pract. 1995 Nov;41(5):443-9.
[6] Bohbot JM, Vicaut E, Fagnen D, et al. Treatment of bacterial vaginosis: a multicenter, double-blind, double-dummy, randomised phase III study comparing secnidazole and metronidazole. Infect Dis Obstet Gynecol. 2010;2010.