## CLASSES

Gynecological Antibiotics and Sulfonamides

## DEA CLASS

Rx

## DESCRIPTION

Topical antiinfective agent for vaginal use. Only for treatment of vulvovaginal candidiasis due to Candida albicans. Specially compounded to a pH approximately equal to that of the normal vagina (about 4.3) which helps to encourage growth of Doderlein's bacilli.

## COMMON BRAND NAMES

AVC

## HOW SUPPLIED

AVC Vaginal Cream: 15%

## DOSAGE & INDICATIONS

**For the treatment of vulvovaginal candidiasis due to *Candida albicans*.**

**Intravaginal dosage (cream)**

**Adults**

Use 1 applicatorful (roughly 6 g) PV once or twice daily for 30 days.[47303] Sulfanilamide is not included in the CDC's sexually transmitted diseases guidelines for VVVC.

## MAXIMUM DOSAGE

**Adults**

2 applicatorfuls of cream/day PV; 2 suppositories/day PV.

**Elderly**

2 applicatorfuls of cream/day PV; 2 suppositories/day PV.

**Adolescents**

Safe and effective use has not been established.

**Children**

Safe and effective use has not been established.

## DOSING CONSIDERATIONS

**Hepatic Impairment**

No dosage adjustment appears needed. However, use with caution since sulfonamides are absorbed systemically via the vaginal mucosa and metabolized by the liver.

**Renal Impairment**

No dosage adjustment appears needed. However, use with caution since sulfonamides are absorbed systemically via the vaginal mucosa and some excretion via the kidney occurs.

## ADMINISTRATION

**Intravaginal Administration**

Sulfanilamide preparations are for intravaginal use only; do not apply to the eye, mouth, or skin.
Cream and suppositories: Use applicator(s) supplied by the manufacturer. Instruct patient on proper administration and treatment course (see Patient information).
If an adequate response is not achieved, the diagnosis should be reconfirmed and other pathogens commonly associated with vulvovaginitis ruled out.

## STORAGE

AVC:

- Store below 86 degrees F

## CONTRAINDICATIONS / PRECAUTIONS

### Sulfonamide hypersensitivity

Vaginally-administered sulfonamides are absorbed through the vaginal mucosa and should not be used in patients with history of sulfonamide hypersensitivity. Cross-sensitivity between sulfonamides can occur. Topical use of sulfonamides can lead to sensitization which can result in hypersensitivity reactions with subsequent use of topical or systemic sulfonamides. Patients known to have a history of sulfonamide hypersensitivity should not be treated with sulfonamide topical preparations.

### Carbonic anhydrase inhibitor hypersensitivity, sulfonylurea hypersensitivity, thiazide diuretic hypersensitivity

Sulfonamides, like sulfanilamide, are absorbed through the vaginal mucosa and cause systemic reactions. Because of structural similarity, sulfonamides should be used cautiously in patients with known history of oral sulfonylurea hypersensitivity, thiazide diuretic hypersensitivity or carbonic anhydrase inhibitor hypersensitivity. Despite the chemical similarities between furosemide and sulfonamides and the logical conclusion that cross-sensitivity would occur, a thorough review of the published literature and direct communication with the manufacturer revealed no data supporting the conclusion that patients with sensitivity to sulfonamides also develop sensitivity to furosemide. Less is known regarding the cross-sensitivity between sulfonamides and the other agents, although some clinicians doubt that significant risk exists.

### G6PD deficiency

Sulfonamides are absorbed through the vaginal mucosa and have been associated with acute hemolytic anemia in patients with glucose-6-phosphate dehydrogenase deficiency (G6PD deficiency). Although the development of hemolytic anemia appears to be dose-related, sulfanilamide should be used with caution in patients with G6PD deficiency.

### Hepatic disease, renal failure, renal impairment

Sulfonamides, like sulfanilamide, should be used with caution in patients with hepatic disease, renal impairment, or renal failure. Sulfonamides are absorbed through the vaginal mucosa and are metabolized in the liver and excreted by the kidneys. Excessive accumulation may occur in these patients.

### Children, infants, neonates

Sulfanilamide should not be used in infants and neonates less than 2 months of age because sulfonamides may increase the risk of kernicterus in young infants by displacing bilirubin from plasma proteins. There is no specific information regarding the use of sulfanilamide in female children <= 12 years of age; consult physician. Sulfanilamide has been used clinically in female adolescents.

### Pregnancy

Use sulfanilamide during pregnancy only when clearly needed as it is unknown if it can cause fetal harm. Sulfonamides should generally be avoided near term due to the potential for jaundice, hemolytic anemia, and kernicterus in the newborn. Sulfanilamide is absorbed through the vaginal mucosa, and sulfonamides readily cross the placenta with fetal concentrations averaging 70% to 90% of maternal concentrations. In a nested, case-control study (n = 87,020 controls; 8,702 cases) within the Quebec Pregnancy Cohort, sulfonamide use during early pregnancy was associated with an increased risk of spontaneous abortion (adjusted odds ratio (aOR) 2.01; 95% CI: 1.36 to 2.97; 30 exposed cases); residual confounding by severity of infection may be a potential limitation of this study. However, other studies such as the Collaborative Perinatal Project, which included 1,455 mothers with first trimester sulfonamide exposure and 5,689 with exposure anytime during pregnancy, found no evidence to suggest a relationship between sulfonamide use during and fetal malformations.

### Breast-feeding

According to the manufacturer, because of the potential risk to a nursing neonate, either breast feeding or sulfanilamide should be discontinued. Sulfonamides are absorbed through the vaginal mucosa and are excreted in breast milk in low concentrations. Sulfanilamide should not be used in mothers who are breast-feeding infants less than 2 months of age because sulfonamides may promote kernicterus in the newborn by displacing bilirubin from plasma proteins. Sulfanilamide may be considered for use when breast-feeding healthy infants; however, caution should be used in infants with jaundice, hyperbilirubinemia, or G-6-PD deficiency or in infants who are critically ill, stressed, or premature. Fluconazole is generally considered compatible with breast-feeding by the American Academy of Pediatrics (AAP) and may be a potential alternative to consider during breast-feeding. However, site of infection, patient factors, local susceptibility patterns, and specific microbial susceptibility should be assessed before choosing an alternative agent. Consider the benefits of breast-feeding, the risk of potential infant drug exposure, and the risk of an untreated or inadequately treated condition. If a breast-feeding infant experiences an adverse effect related to a maternally ingested drug, healthcare providers are encouraged to report the adverse effect to the FDA.

### Porphyria

Sulfonamides, like sulfanilamide, are absorbed through the vaginal mucosa and should not be used in patients with porphyria because they can precipitate an acute attack of porphyria.

## ADVERSE REACTIONS

### Mild

vaginal irritation / Early / 0.2-0.2

## DRUG INTERACTIONS

There are no drug interactions associated with Sulfanilamide products.

## PREGNANCY AND LACTATION

### Pregnancy

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## MECHANISM OF ACTION

Sulfonamides, including sulfanilamide, inhibit bacterial dihydropteroate synthase by competing with p-aminobenzoic acid (PABA). This action interferes with the conversion of PABA into folic acid, an essential component of bacterial development. Folic acid is a coenzyme responsible for the transport of one-carbon fragments from one molecule to another, and it is crucial during the synthesis of thymidine, purines, and certain amino acids. When used intravaginally, sulfanilamide is in a specially compounded base buffered to the pH (about 4.3) of the normal vagina to encourage the presence of the normally occurring Doderlein’s bacilli of the vagina.

## PHARMACOKINETICS

Sulfanilamide is administered intravaginally. Metabolism of any systemically-absorbed drug occurs in the liver, with renal excretion of the metabolites.

### Other Route(s)

Intravaginal Route
Like other vaginally administered sulfonamides, sulfanilamide is absorbed systemically through the vaginal mucosa. There are no pharmacokinetic data available describing how much of an intravaginal dose reaches the systemic circulation.