

Jazz Pharmaceuticals  
AVC (sulfanilamide) Vaginal Cream 15%  
Supplemental New Drug Application – CBE-30 Days

1.14 Labeling

AVC<sup>®</sup> (sulfanilamide)

Cream

## DESCRIPTION

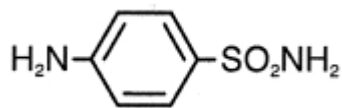
AVC<sup>®</sup> is a preparation for vaginal administration for the treatment of *Candida albicans* infections and available in the following forms:

### AVC Cream

Each tube contains:

Sulfanilamide.....15.0%  
in a water-miscible, non-staining base made from lactose, propylene glycol, stearic acid, diglycol stearate, methylparaben, propylparaben, trolamine, and water; buffered with lactic acid to an acid pH of approximately 4.3.

Sulfanilamide is an anti-infective agent. It is *p*-amino-benzenesulfonamide with the chemical structure:



Sulfanilamide occurs as a white odorless crystalline powder with a slightly bitter taste and sweet aftertaste. It is slightly soluble in water, alcohol, acetone, glycerin, propylene glycol, hydrochloric acid, and solutions of potassium and sodium hydroxide. It is practically insoluble in chloroform, ether, benzene, and petroleum ether.

## CLINICAL PHARMACOLOGY

Sulfanilamide has been a useful ingredient of vaginal formulations for about four decades. It blocks certain metabolic processes essential for the growth of susceptible bacteria. In AVC, the 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 Döderlein's bacilli of the vagina.

The use of AVC for the treatment of vulvovaginitis caused by *Candida albicans* is supported by three clinical investigations. The three studies show AVC with sulfanilamide to be significantly more effective ( $p \leq 0.01$ ) than placebo as follows:

In Study I, the ratio of effectiveness was 71% for the AVC with sulfanilamide versus 49% for placebo with 30 days of treatment;

In Study II, the percentages were 48% and 24%, respectively, with 15 days of treatment;

In Study III, the percentages were 66% versus 33%, respectively, with 30 days of treatment.

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## INDICATIONS AND USAGE

For the treatment of vulvovaginitis caused by *Candida albicans*. (See CLINICAL PHARMACOLOGY.)

## CONTRAINDICATIONS

AVC should not be used in patients known to be sensitive to this product or to the sulfonamides.

## PRECAUTIONS

### General

Because sulfonamides are absorbed from the vaginal mucosa, the usual precautions for oral sulfonamides apply. Patients should be observed for skin rash or evidence of systemic toxicity, and if these develop, the medications should be discontinued.

Deaths associated with administration of oral sulfonamides have reportedly occurred from hypersensitivity reactions, agranulocytosis, aplastic anemia, and other blood dyscrasias.

Goiter production, diuresis, and hypoglycemia have reportedly occurred rarely in patients receiving oral sulfonamides. Cross-sensitivity may exist with these agents. Rats appear to be especially susceptible to the goitrogenic effects of sulfonamides, and long-term administration has reportedly produced thyroid malignancies in this species.

Vaginal applicators or inserters should be used with caution after the seventh month of pregnancy.

### Information For Patients

The doctor should advise the patient that in the event unusual local itching and burning occur, or other unusual symptoms develop, medication should be discontinued and not restarted without further consultation.

### Drug Interactions

Drug interactions have not been documented with AVC.

### Carcinogenesis, Mutagenesis, Impairment of Fertility

No data are available on long-term potential of AVC for carcinogenicity, mutagenicity, or impairment of fertility in animals or humans.

### Pregnancy

**Teratogenic Effects. Pregnancy Category C:** Animal reproductive studies have been conducted with sulfonamides, including sulfanilamide (see below). It is not known whether AVC can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. AVC should be given to a pregnant woman only if clearly needed.

Sulfonamides, including sulfanilamide, readily pass through the placenta and reach fetal circulation. The concentration in the fetus is from 50-90% of that in the maternal blood and if high enough, can cause toxic effects. The safe use of sulfonamides, including sulfanilamide, in pregnancy has not been

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established. The teratogenic potential of most sulfonamides has not been thoroughly investigated in either animals or humans. However, a significant increase in the incidence of cleft palate and other bony abnormalities of offspring has been observed with certain sulfonamides of the short-, intermediate- and long-acting types (including sulfanilamide) when given to pregnant rats and mice at high oral doses (seven to 25 times the human therapeutic oral dose.)

### **Nursing Mothers**

Sulfanilamide should be avoided in nursing mothers because absorbed sulfonamides will appear in maternal milk and have caused kernicterus in the newborn. Because of the potential for serious adverse reactions in nursing infants from sulfonamides, a decision should be made whether to discontinue nursing or to discontinue the drug.

### **Pediatric Use**

Safety and effectiveness of AVC in pediatric patients have not been established.

## **ADVERSE REACTIONS**

Local sensitivity reactions such as increased discomfort or a burning sensation have occasionally been reported following the use of topical sulfonamides. With the use of AVC Cream, sensitivity reactions (only local) were reported for 0.2% of the investigational patients.

Treatment should be discontinued if either local or systemic manifestations of sulfonamide toxicity or sensitivity occur.

## **DRUG ABUSE AND DEPENDENCE**

Tolerance, abuse, or dependence with AVC have not been reported.

## **OVERDOSAGE**

There have been no reports of accidental overdose with AVC.

The acute oral LD 50 of sulfanilamide is 3700-4200 mg/kg in mice.

The minimum human lethal dose of AVC has not been established.

It is not known if AVC is dialyzable.

## **DOSAGE AND ADMINISTRATION**

One applicatorful (about 6g) intravaginally once or twice daily. Improvements in symptoms should occur within a few days, but treatment should be continued for a period of 30 days.

Douching with a suitable solution before insertion may be recommended for hygienic purposes.

## **HOW SUPPLIED**

### **AVC Cream**

NDC 66663-103-04 4 oz tube with applicator

Store at room temperature, below 86°F.

Protect from cold.

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Product darkens with age. Potency is maintained throughout labeled shelf life when stored as directed.

This leaflet provides a summary of the important information about AVC Cream. You can get more information by calling the toll free number (1-800-890-3098).

Manufactured for:  
Azur Pharma, Inc.  
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Philadelphia, PA 19103, [www.azurpharma.com](http://www.azurpharma.com)

Manufactured by:  
DPT Laboratories, Ltd.  
San Antonio, TX 78215  
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