NDA 21-026
0.25% MICONAZOLE NITRATE AND DIAPER DERMATITIS
MICROBIOLOGY SUMMARY

ETIOLOGY OF DIAPER DERMATITIS

Multifactorial (physical and dermatologic components) with bacteria (*Staphylococcus* spp. and Gram-negatives) and yeast (*C. albicans*) playing a potential role.

MICROBIOLOGIC DIAGNOSIS OF DIAPER DERMATITIS

The literature is ambiguous on diagnosis (clinical and/or laboratory) in a physician's office.

KOH and culture needed in clinical studies to support "Proof of Concept"

TREATMENT OF DIAPER DERMATITIS

The literature suggests that when miconazole nitrate is used it generally is used in a concentration of 1 to 2%. Well-controlled studies are lacking for its use in these concentrations and no studies exist in the literature where a concentration of 0.25% has been used.

SPECTRUM OF ACTIVITY AND MODE OF ACTION OF MICONAZOLE

Miconazole nitrate has been used for a number of years for the treatment of fungal infections primarily yeast infections. It has activity against *Candida albicans* and other *Candida* spp. The majority of *C. albicans* (>90%) are inhibited by 10 μg/mL; 70% are inhibited by concentrations of 0.01 to 1.0 μg/mL. Ninety percent or better of the other clinically predominant species of *Candida* are inhibited by 10 μg/mL.

The fungistatic activity of miconazole is based on the inhibition of ergosterol biosynthesis in the cell membrane of the microorganism. The accumulation of ergosterol precursors and toxic peroxides results in cytolysis. Exposure of yeast cells to a less than inhibitory concentration may alter the amount and composition of sterols in newly formed membranes. Miconazole is active only against yeast cells in the logarithmic phase of growth.

The activity of miconazole is decreased in pH environments above 7.0 and below 6.0.

RESISTANCE TO MICONAZOLE

Resistance to miconazole can occur due to alteration in the drug target, alteration in sterol biosynthesis, efflux, and over expression of the antifungal target. Organisms resistant to miconazole may be resistant to other antifungal azoles (e.g. fluconazole, clotrimazole).

Studies have demonstrated that exposure of *C. albicans* to sub-inhibitory levels of miconazole can lead to resistance to higher concentrations of miconazole. It is

postulated that this resistance is the result of alterations in the cell membrane of *C. albicans*.

Higher incidence of *C. albicans* resistant to miconazole are seen in immunocompromised patients than in immunocompetent patients.