

San Francisco to Consider Circumcision Ban

BY MARY ELLEN SCHNEIDER

This November, voters in San Francisco will decide whether to ban circumcision in boys younger than age 18 years, and to make the practice a crime.

Opponents of circumcision gathered more than 7,000 signatures from city residents in order to place the referendum on the Nov. 8 ballot.

If approved, circumcision of boys younger than age 18 would be prohibited unless it was medically necessary. The referendum does not allow for exceptions based on religious beliefs. Anyone who violates the policy would face misdemeanor charges, with a possible fine of up to \$1,000, up to a year in the county jail, or both.

The effort to pass the referendum is being led by Lloyd Schofield, an activist against circumcision.

In the "notice of intent" to circulate the petition, which was filed with the

city's Department of Elections, Mr. Schofield wrote that "genital mutilation constitutes a major health risk, violates human rights, and has lifelong physical and psychological effects." Complications from the procedure can include hemorrhage, infection, nerve damage, sexual dysfunction, and decreased sexual sensitivity, he wrote.

In its official policy on male circumcision, the American Academy of

Pediatrics states that existing scientific evidence shows potential medical benefits for newborn male circumcision. But that evidence is not enough to recommend routine neonatal circumcision, according to the AAP's policy statement, which was published in 1999 and reaffirmed in 2005.

The AAP leaves the decision to parents, saying they should determine what is in the "best interest of the

child" based on "accurate and unbiased information."

San Francisco's ballot measure on circumcision is sure to face opposition and possible legal challenges if it is approved.

The Anti-Defamation League is heading up a coalition of groups to defeat the proposal, saying it threatens religious freedom, privacy, and parental rights. ■

New Autism and Pregnancy Survey Launches

The Interactive Autism Network (IAN) Project is launching a new research survey that will explore the possible association between pregnancy- and birth-related factors and autism spectrum disorder. The research initiative will explore the use of fertility treatments; pregnancy complications; illness or infection during pregnancy; medications taken during pregnancy; number of ultrasounds; and induction of labor and birth complications.

The IAN Project needs information on pregnancies and births of both children with autism spectrum disorder and their siblings. To enroll in the IAN Project, survey participants must be U.S. residents and the birth mother of a child with an autism spectrum disorder who is between the ages of 0 and 17 years. To register, visit www.ianresearch.org. ■

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BRIEF SUMMARY

VELTIN™ (clindamycin phosphate and tretinoin) Gel 1.2%/0.025%

The following is a brief summary only; see full prescribing information for complete product information.

INDICATIONS AND USAGE

VELTIN Gel is indicated for the topical treatment of acne vulgaris in patients 12 years or older.

CONTRAINDICATIONS

VELTIN Gel is contraindicated in patients with regional enteritis, ulcerative colitis, or history of antibiotic-associated colitis.

WARNINGS AND PRECAUTIONS

Colitis

Systemic absorption of clindamycin has been demonstrated following topical use. Diarrhea, bloody diarrhea, and colitis (including pseudomembranous colitis) have been reported with the use of topical clindamycin. If significant diarrhea occurs, VELTIN Gel should be discontinued.

Severe colitis has occurred following oral or parenteral administration of clindamycin with an onset of up to several weeks following cessation of therapy. Antiperistaltic agents such as opiates and diphenoxylate with atropine may prolong and/or worsen severe colitis. Severe colitis may result in death.

Studies indicate a toxin(s) produced by clostridia is one primary cause of antibiotic-associated colitis.

Ultraviolet Light and Environmental Exposure

Exposure to sunlight, including sunlamps, should be avoided during the use of VELTIN Gel, and patients with sunburn should be advised not to use the product until fully recovered because of heightened susceptibility to sunlight as a result of the use of tretinoin. Patients who may be required to have considerable sun exposure due to occupation and those with inherent sensitivity to the sun should exercise particular caution. Daily use of sunscreen products and protective apparel (e.g., a hat) are recommended. Weather extremes, such as wind or cold, also may be irritating to patients under treatment with VELTIN Gel.

ADVERSE REACTIONS

Adverse Reactions in Clinical Studies

The safety data reflect exposure to VELTIN Gel in 1,104 patients with acne vulgaris. Patients were 12 years or older and were treated once daily in the evening for 12 weeks. Observed local treatment-related adverse reactions ($\geq 1\%$) in clinical studies with VELTIN Gel were application site reactions, including dryness (6%), irritation (5%), exfoliation (5%), erythema (4%), pruritus (2%), and dermatitis (1%). Sunburn (1%) was also reported. Incidence of skin reactions peaked at week 2 and then gradually decreased.

Local skin reactions were actively assessed at baseline and at the end of 12 weeks of treatment in patients exposed to VELTIN Gel. At baseline (N=476), local skin reactions included erythema (24%), scaling (8%), dryness (11%), burning (8%), and itching (17%). At 12 weeks of treatment (N=409), local skin reactions included erythema (21%), scaling (19%), dryness (22%), burning (13%), and itching (15%). During the 12 weeks of treatment, each local skin reaction peaked at week 2 and gradually reduced thereafter.

DRUG INTERACTIONS

Erythromycin

VELTIN Gel should not be used in combination with erythromycin-containing products due to possible antagonism to the clindamycin component. *In vitro* studies have shown antagonism between these 2 antimicrobials. The clinical significance of this *in vitro* antagonism is not known.

Neuromuscular Blocking Agents

Clindamycin has been shown to have neuromuscular blocking properties that may enhance the action of other neuromuscular blocking agents. Therefore, VELTIN Gel should be used with caution in patients receiving such agents.

USE IN SPECIFIC POPULATIONS

Pregnancy

Pregnancy Category C. There are no well-controlled studies in pregnant women treated with VELTIN Gel. VELTIN Gel should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. A limit teratology study performed in Sprague Dawley rats treated topically with VELTIN Gel or 0.025% tretinoin gel at a dose of 2 mL/kg during gestation days 6 to 15 did not result in teratogenic effects. Although no systemic levels of tretinoin were detected, craniofacial and heart abnormalities were described in drug-treated groups. These abnormalities are consistent with retinoid effects and occurred at 16 times the recommended clinical dose assuming 100% absorption and based on body surface area comparison. For purposes of comparison of the animal exposure to human exposure, the recommended clinical dose is defined as 1 g of VELTIN Gel applied daily to a 50 kg person.

Tretinoin: Oral tretinoin has been shown to be teratogenic in mice, rats, hamsters, rabbits, and primates. It was teratogenic and fetotoxic in Wistar rats when given orally at doses greater than 1 mg/kg/day (32 times the recommended clinical dose based on body surface area comparison). However, variations in teratogenic doses among various strains of rats have been reported. In the cynomolgous monkey, a species in which tretinoin metabolism is closer to humans than in other species examined, fetal malformations were reported at oral doses of 10 mg/kg/day or greater, but none were observed at 5 mg/kg/day (324 times the recommended clinical dose based on body surface area comparison), although increased skeletal variations were observed at all doses. Dose-related teratogenic effects and increased abortion rates were reported in pigtail macaques.

With widespread use of any drug, a small number of birth defect reports associated temporally with the administration of the drug would be expected by chance alone. Thirty cases of temporally associated congenital malformations have been reported during two decades of clinical use of another formulation of topical tretinoin. Although no definite pattern of teratogenicity and no causal association have been established from these cases, 5 of the reports describe the rare birth defect category, holoprosencephaly (defects associated with incomplete midline development of the forebrain). The significance of these spontaneous reports in terms of risk to fetus is not known.

Nursing Mothers

It is not known whether clindamycin is excreted in human milk following use of VELTIN Gel. However, orally and parenterally administered clindamycin has been reported to appear in breast milk. Because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. It is not known whether tretinoin is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when VELTIN Gel is administered to a nursing woman.

Pediatric Use

Safety and effectiveness of VELTIN Gel in pediatric patients below the age of 12 years have not been established. Clinical trials of VELTIN Gel included 2,086 patients 12-17 years of age with acne vulgaris. [See *Clinical Studies (14)* of full prescribing information.]

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term animal studies have not been performed to evaluate the carcinogenic potential of VELTIN Gel or the effect of VELTIN Gel on fertility. VELTIN Gel was negative for mutagenic potential when evaluated in an *in vitro* Ames *Salmonella* reversion assay. VELTIN Gel was equivocal for clastogenic potential in the absence of metabolic activation when tested in an *in vitro* chromosomal aberration assay.

Clindamycin: Once daily dermal administration of 1% clindamycin as clindamycin phosphate in the VELTIN Gel vehicle (32 mg/kg/day, 13 times the recommended clinical dose based on body surface area comparison) to mice for up to 2 years did not produce evidence of tumorigenicity.

Tretinoin: In two independent mouse studies where tretinoin was administered topically (0.025% or 0.1%) three times per week for up to two years no carcinogenicity was observed, with maximum effects of dermal amyloidosis. However, in a dermal carcinogenicity study in mice, tretinoin applied at a dose of 5.1 μ g (1.4 times the recommended clinical dose based on body surface area comparison) three times per week for 20 weeks acted as a weak promoter of skin tumor formation following a single application of dimethylbenz[α]anthracene (DMBA).

In a study in female SENCAR mice, papillomas were induced by topical exposure to DMBA followed by promotion with 12-O-tetradecanoyl-phorbol 13-acetate or mezerein for up to 20 weeks. Topical application of tretinoin prior to each application of promoting agent resulted in a reduction in the number of papillomas per mouse. However, papillomas resistant to topical tretinoin suppression were at higher risk for pre-malignant progression.

Tretinoin has been shown to enhance photo-carcinogenicity in properly performed specific studies, employing concurrent or intercurrent exposure to tretinoin and UV radiation. The photo-carcinogenic potential of the clindamycin tretinoin combination is unknown. Although the significance of these studies to humans is not clear, patients should avoid exposure to sun.

PATIENT COUNSELING INFORMATION

[See FDA-approved Patient Labeling in full prescribing information.]

Instructions for Use

- At bedtime, the face should be gently washed with a mild soap and water. After patting the skin dry, apply VELTIN Gel as a thin layer over the entire affected area (excluding the eyes and lips).
- Patients should be advised not to use more than a pea sized amount to cover the face and not to apply more often than once daily (at bedtime) as this will not make for faster results and may increase irritation.
- A sunscreen should be applied every morning and reapplied over the course of the day as needed. Patients should be advised to avoid exposure to sunlight, sunlamp, ultraviolet light, and other medicines that may increase sensitivity to sunlight.
- Other topical products with a strong drying effect, such as abrasive soaps or cleansers, may cause an increase in skin irritation with VELTIN Gel.

Skin Irritation

VELTIN Gel may cause irritation such as erythema, scaling, itching, burning, or stinging.

Colitis

In the event a patient treated with VELTIN Gel experiences severe diarrhea or gastrointestinal discomfort, VELTIN Gel should be discontinued and a physician should be contacted.

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