

POLICY & PRACTICE

Penalties for Faux-tox

The case involving distribution of counterfeit Botox for use in humans came to a close in a Florida courtroom in January when U.S. District Court Judge James I. Cohn handed down fines and jail sentences. Naturopaths Chad Livdahl and Zarah Karim both pled guilty in November 2005 to charges related to their role in the scheme, which involved purchasing and then selling to other health care providers thousands of vials of botulinum toxin type A and other ingredients designed to mimic Botox. Mr. Livdahl was sentenced to 9

years in jail and Ms. Karim was sentenced to nearly 6 years in prison. Dr. Bach McComb, who pled guilty to one count of misbranding a drug in interstate commerce, was sentenced to 3 years in prison and Dr. Robert Baker, who pled guilty to one count of mail fraud, was sentenced to 180 days of home detention. "Doctors and medical practitioners have a solemn duty to those for whom they care," R. Alexander Acosta, U.S. Attorney for the Southern District of Florida, said in a statement. "These defendants breached that duty and endangered the lives of their patients by selling

deadly toxin packaged in harmless-looking vials." These convictions follow license suspensions or restrictions for at least 10 Florida physicians, including several dermatologists, for their role in purchasing the unapproved drug ("Botulism Disaster Helps Uncover Fake Botox Market: Four physicians indicted on federal charges," SKIN & ALLERGY NEWS, May 2005, p. 1).

Vitamin D Controversy

It's unsafe and unnecessary for people to expose themselves to harmful doses of ultraviolet radiation in an effort to maintain the proper levels of vitamin D, according to a literature review published in the Feb-

ruary issue of the Journal of the American Academy of Dermatology. In the latest chapter in the fight over the importance of sunlight in meeting vitamin D requirements, Dr. Barbara A. Gilchrest and Dr. Deon Wolpowitz of Boston University advise the public to get their vitamin D through fortified foods and nutritional supplements, not unprotected sun exposure. In the article, they noted that incidental, protected sunlight along with foods rich in vitamin D can easily provide young, fair-skinned individuals—who are often targeted by the tanning industry—with the appropriate amount of vitamin D.

Ben Franklin's Psoriasis

Psoriasis Cure Now, a patient advocacy group, has named Benjamin Franklin as its "greatest American with psoriasis" in an effort to raise awareness of the disease and increase federally funded psoriasis research. The group arranged for a Franklin look-alike to distribute psoriasis information to congressional staffers recently on Mr. Franklin's 300th birthday. The group also is developing a pamphlet for children featuring Benjamin Franklin. "His story is striking because many people with psoriasis are suffering as much today as he did so long ago," Psoriasis Cure Now President Michael Paranzino said in a statement. In his writings, Mr. Franklin referred to his psoriasis as a "troublesome disorder" and noted that it had flared up at the time he helped draft the Declaration of Independence and during his years in France where he lobbied for French support of the Revolutionary War. More information is available online at www.ben300.org.

E-Prescribing Pilots

Officials at the Centers for Medicare and Medicaid Services are launching pilots to study new e-prescribing standards that will be implemented in 2008. Under the Medicare Modernization Act, the initial e-prescribing standards must be tested through pilot projects this year, except where there is already adequate industry experience. Three standards were already adopted in a final rule published last November. The pilots will test standards related to formulary and benefit information, the exchange of medication history, prior authorization messages, and clinical drug terminology, among others. CMS also has asked participants in the pilot to consider the impact on quality of care, the impact on physician return on investment, and the possible cost savings. CMS is scheduled to report findings from the pilots to Congress in April 2007. The final standards will be issued no later than April 2008.

'Fair Share' for Health Care

Large employers in the state of Maryland will have to pay a "fair share" for health care under a new state law. Last April, the Maryland General Assembly passed the Fair Share Health Care Fund Act, which requires that employers with more than 10,000 employees must spend at least 8% of wages paid on health insurance, or pay the state the difference between what they do spend and 8%. The law was vetoed by Republican Gov. Robert Ehrlich, but the legislature overrode his veto in January. Currently, WalMart is the only employer in Maryland that is affected by the law.

—Mary Ellen Schneider

METROGEL®

(metronidazole gel), 1%

BRIEF SUMMARY

For topical use only. Not for oral, ophthalmic or intravaginal use.

INDICATIONS AND USAGE

METROGEL® (metronidazole gel), 1% is indicated for the topical treatment of inflammatory lesions of rosacea.

CONTRAINDICATIONS

METROGEL® (metronidazole gel), 1% is contraindicated in those patients with a history of hypersensitivity to metronidazole or to any other ingredient in this formulation.

PRECAUTIONS

General: Topical metronidazole has been reported to cause tearing of the eyes. Therefore, contact with the eyes should be avoided. If a reaction suggesting local skin irritation occurs, patients should be directed to use the medication less often or discontinue use. Metronidazole is a nitroimidazole and should be used with care in patients with evidence of, or history of, blood dyscrasia.

Information for Patients: Patients using METROGEL® (metronidazole gel), 1% should receive the following information and instructions:

1. This medication is to be used as directed.
2. It is for external use only.
3. Avoid contact with the eyes.
4. Cleanse affected area(s) before applying METROGEL® (metronidazole gel), 1%.
5. This medication should not be used for any other condition than that for which it is prescribed.
6. Patients should report any adverse reaction to their physicians.

Drug Interaction: Oral metronidazole has been reported to potentiate the anticoagulant effect of coumarin and warfarin, resulting in a prolongation of prothrombin time. Drug interactions should be kept in mind when METROGEL® (metronidazole gel), 1% is prescribed for patients who are receiving anticoagulant treatment, although they are less likely to occur with topical metronidazole administration because of low absorption.

Carcinogenesis, Mutagenesis and Impairment of Fertility: Metronidazole has shown evidence of carcinogenic activity in a number of studies involving chronic, oral administration in mice and rats, but not in studies involving hamsters.

In several long-term studies in mice, oral doses of approximately 225 mg/m²/day or greater (approximately 37 times the human topical dose on a mg/m² basis) were associated with an increase in pulmonary tumors and lymphomas. Several long-term oral studies in the rat have shown statistically significant increases in mammary and hepatic tumors at doses >885 mg/m²/day (144 times the human dose).

Metronidazole has shown evidence of mutagenic activity in several *in vitro* bacterial assay systems. In addition, a dose-related increase in the frequency of micronuclei was observed in mice after intraperitoneal injections. An increase in chromosomal aberrations in peripheral blood lymphocytes was reported in patients with Crohn's disease who were treated with 200 to 1200 mg/day of metronidazole for 1 to 24 months. However, in another study, no increase in chromosomal aberrations in circulating lymphocytes was observed in patients with Crohn's disease treated with the drug for 8 months.

In one published study, using albino hairless mice, intraperitoneal administration of metronidazole at a dose of 45 mg/m²/day (approximately 7 times the human topical dose on a mg/m² basis) was associated with an increase in ultraviolet radiation-induced skin carcinogenesis. Neither dermal carcinogenicity nor photocarcinogenicity studies have been performed with METROGEL® (metronidazole gel), 1% or any marketed metronidazole formulations.

Pregnancy: Teratogenic Effects: Pregnancy Category B. There are no adequate and well-controlled studies with the use of METROGEL® (metronidazole gel), 1% in pregnant women.

Metronidazole crosses the placental barrier and enters the fetal circulation rapidly. No fetotoxicity was observed after oral administration of metronidazole in rats or mice at 200 and 20 times, respectively, the expected clinical dose. However, oral metronidazole has shown carcinogenic activity in rodents. Because animal reproduction studies are not always predictive of human response, METROGEL® (metronidazole gel), 1% should be used during pregnancy only if clearly needed.

Nursing Mothers: After oral administration, metronidazole is secreted in breast milk in concentrations similar to those found in the plasma. Even though blood levels taken after topical metronidazole application are significantly lower than those achieved after oral metronidazole, 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 and the risk to the infant.

Pediatric Use: Safety and effectiveness in pediatric patients have not been established.

Geriatric Use: While specific clinical trials in the geriatric population have not been conducted, sixty-six patients aged 65 years and older treated with METROGEL® (metronidazole gel), 1% over ten weeks showed comparable safety and efficacy as compared to the general study population.

ADVERSE REACTIONS

In a controlled clinical trial, 557 patients used METROGEL® (metronidazole gel), 1% and 189 patients used the gel vehicle once daily. The following table summarizes adverse reactions that occur at a rate of ≥1% in the clinical trials:

System Organ Class/Preferred Term	Metronidazole Gel, 1% N=557	Gel Vehicle N=189
Patients with at least one AE	186 (33.4)	51 (27.0)
Infections and infestations	76 (13.6)	28 (14.8)
Bronchitis	6 (1.1)	3 (1.6)
Influenza	8 (1.4)	1 (0.5)
Nasopharyngitis	17 (3.1)	8 (4.2)
Sinusitis	8 (1.4)	3 (1.6)
Upper respiratory tract infection	14 (2.5)	4 (2.1)
Urinary tract infection	6 (1.1)	1 (0.5)
Vaginal mycosis	1 (0.2)	2 (1.1)
Musculoskeletal and connective tissue disorders	19 (3.4)	5 (2.6)
Back pain	3 (0.5)	2 (1.1)
Neoplasms	4 (0.7)	2 (1.1)
Basal cell carcinoma	1 (0.2)	2 (1.1)
Nervous system disorders	18 (3.2)	3 (1.6)
Headache	12 (2.2)	1 (0.5)
Respiratory, thoracic and mediastinal disorders	22 (3.9)	5 (2.6)
Nasal congestion	6 (1.1)	3 (1.6)
Skin and subcutaneous tissue disorders	36 (6.5)	12 (6.3)
Contact dermatitis	7 (1.3)	1 (0.5)
Dry skin	6 (1.1)	3 (1.6)
Vascular disorders	8 (1.4)	1 (0.5)
Hypertension	6 (1.1)	1 (0.5)

The following table summarizes the highest scores of local cutaneous signs and symptoms of irritation that were worse than baseline:

	Metronidazole Gel, 1% N= 544	Gel Vehicle N=184
Sign/Symptom	N= 544	N=184
Dryness	138 (25.4)	63 (34.2)
Mild	93 (17.1)	41 (22.3)
Moderate	42 (7.7)	20 (10.9)
Severe	3 (0.6)	2 (1.1)
Scaling	134 (24.6)	60 (32.6)
Mild	88 (16.2)	32 (17.4)
Moderate	43 (7.9)	27 (14.7)
Severe	3 (0.6)	1 (0.5)
Pruritus	86 (15.8)	35 (19.0)
Mild	53 (9.7)	21 (11.4)
Moderate	27 (5.0)	13 (7.1)
Severe	6 (1.1)	1 (0.5)
Stinging/burning	56 (10.3)	28 (15.2)
Mild	39 (7.2)	18 (9.8)
Moderate	7 (1.3)	9 (4.9)
Severe	10 (1.8)	1 (0.5)

The following additional adverse experiences have been reported with the topical use of metronidazole: skin irritation, transient redness, metallic taste, tingling or numbness of extremities, and nausea.

OVERDOSAGE: There are no reported human experiences with overdosage of METROGEL® (metronidazole gel), 1%. Topically applied metronidazole can be absorbed in sufficient amount to produce systemic effects.

HOW SUPPLIED: METROGEL® (metronidazole gel), 1% is available in a 45-gram tube.

DOSE AND ADMINISTRATION: Areas to be treated should be cleansed before application of METROGEL® (metronidazole gel), 1%. Apply and rub in a thin film of METROGEL® (metronidazole gel), 1% once daily to entire affected area(s). Patients may use cosmetics after application of METROGEL® (metronidazole gel), 1%.

Storage Conditions: Store at controlled room temperature: 20° to 25°C (68° to 77°F), excursions permitted between 59° and 86°F (15°-30°C).

Prescribing Information as of June 2005.

Rx Only
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