

Baby Boomers Are the Biggest Users of Botox

BY DOUG BRUNK

LAS VEGAS — Dr. Alastair Carruthers remembers a time when the public perceived repeated injections of Botox as an experimental treatment reserved exclusively for the well-heeled crowd.

Today, the people most often requesting Botox treatment for dermatologic conditions are baby boomers who

are accustomed to the concept of maintenance and are less concerned about vanity issues, compared with previous generations, he said at the annual meeting of the American Society of Cosmetic Dermatology and Aesthetic Surgery.

“They go to the gym regularly. They look after their diets. Having these same principles applied to their appearance is no great change for them,” he said.

Baby boomers also are busy. “They don’t have any down time,” said Dr. Carruthers, who with his wife, Dr. Jean D.A. Carruthers, pioneered the cosmetic use of Botox.

“They’re stressed, but they don’t want to look it, and they have increased disposable income,” he said.

Worldwide, Botox has 85% of the neurotoxin market while Dysport has much of the remainder, he said.

Despite its popularity and proven safety record over 2 decades of clinical studies, he finds so-called Botox parties a troubling development.

He described such parties as media events, pointing out that “you can’t get proper consent because you don’t have the individual in an informed consent situation. There’s peer pressure, and [the drinking of] alcohol may be involved.”

He showed a newspaper clipping of a Canadian dermatologist who applied the product at a Botox party without wearing latex gloves. “Need I say more?” commented Dr. Carruthers, who practices dermatology in Vancouver, B.C.

He went on to note that, while it’s hard to imagine new uses for Botox, “I

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:

Sign/Symptom	Metronidazole Gel, 1% N= 544	Gel Vehicle 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.

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%.

HOW SUPPLIED: METROGEL® (metronidazole gel), 1% is supplied as follows:

60 gram tube – NDC 0299-3820-60

60 gram tube with complimentary 4 oz Cetaphil® Gentle Skin Cleanser – NDC 0299-3820-04

Keep out of the reach of children.

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 February 2007.

Rx Only

US Patent No. 6,881,726

Manufactured by:

Galderma Production Canada Inc.
Baie d’Urfé, QC, H9X 3S4 Canada
Made in Canada.

Marketed by:

Galderma Laboratories, L.P.
Fort Worth, Texas 76177 USA
P50742-1 0207

References: 1. Wolters Kluwer, PHasT Database, January 2008. 2. Data on file. A multi-center clinical study of metronidazole 1% compared to vehicle for 10 weeks (n=552). 3. Data on file. HSA-3. Galderma Laboratories, L.P. 4. Odom RB. The subtypes of rosacea: implications for treatment. *Cutis*. 2004;73:9-14.

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“Wouldn’t it be great to have a short-acting Botox [to use] when you throw your back out?”

DR. CARRUTHERS

think we’ll get better with it. I don’t see expanding its cosmetic use. I think the lower face is still a challenge, even for expert injectors.”

Dr. Carruthers does not anticipate a dermal filler on par with Botox being developed in the future, but he noted that “there is certainly going to be increasing competition. Will the product itself be changed? There may be changes to increase purity; they may reduce the human serum albumin that’s in there, but I don’t see changes to the actual molecule.”

He added that short-acting toxins such as BTX-E and BTX-F may be of value postsurgically or after trauma.

“Wouldn’t it be great,” he asked, “to have a short-acting Botox [to use] when you throw your back out, or if you have spasms in your back and you can’t move around? Or you’ve had surgery and you need to rest an area in the face or elsewhere?”

Dr. Carruthers disclosed that he is a consultant and performs research for Allergan Inc., Merz GmbH & Co., and Bi-form Medical Inc.

VERBATIM

“Microbes have had 3.5 billion years to learn how to adapt. Given sufficient time and drug use, resistance will develop; there are no antibiotics to which resistance has never developed.”

Dr. Theodore Rosen, p. 41

