

Radiation Efficacy Requires Adequate Tumor Margins

BY BRUCE JANCIN
Denver Bureau

DENVER — A margin of 10 mm beyond the gross tumor border of a non-melanoma skin cancer is required to achieve a 95% probability of obtaining clear resection margins, C. Richard Choo, M.D., said at the annual meeting of the American Society for Therapeutic Radiology and Oncology.

In contrast, a 5-mm margin will fully cover the microscopic tumor extent in only 62% of cases, added Dr. Choo, a radiation oncologist at the Mayo Clinic, Rochester, Minn.

This sort of information is critical to the success of radiation therapy, a modality that does not provide resection margins. The radiation therapy volume selected must be sufficient to cover the potential microscopic tumor extent beyond the clinical lesion while avoiding treatment of normal tissue, he explained.

Dr. Choo and his coworkers quantified microscopic tumor extension beyond the clinical gross tumor borders of 71 non-

melanoma skin cancers from 64 consecutive patients. Thirty-eight lesions were sclerosing basal cell carcinomas, 19 were other types of basal cell carcinoma, and 14 were squamous cell carcinomas. Thirty-one were previously treated recurrent malignancies. Sixty were located on the face. The mean tumor size was 2.1 cm.

Preoperatively, the visible border of each lesion was marked with a fine felt-tip pen, and marks were placed at 5-mm intervals in four directions from the outlined borders. A plastic surgeon then excised the gross tumor under local anesthesia, and a dermatopathologist examined frozen tissue sections. A positive resection margin led to further excision using thin slices until clear margins were achieved.

The mean distance of microscopic tumor extension beyond the clinically delineated border was 5.2 mm, with a maximum of 15 mm. The distance correlated positively with the size of the gross tumor, but not with histologic type, location, or history of prior treatment, perhaps due to the limited sample size. ■

Rx ONLY Ovace® (Sodium Sulfacetamide 10%) Cream, Foam, Gel, Wash

FOR DERMATOLOGIC USE ONLY—NOT FOR OPHTHALMIC USE

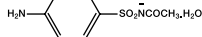
DESCRIPTION:

Each gram of **Ovace® (sodium sulfacetamide 10%) Wash** contains 100 mg of sulfacetamide sodium USP in a vehicle consisting of purified water, sodium laureth sulfate, cocamidopropyl betaine, PEG-150 pentaerythrityl tetraacetate, PEG-6 caprylic/capric glycerides, PEG-60 almond triglycerides, methylparaben, edetate disodium, and sodium thiosulfate.

Each gram of **Ovace® (sodium sulfacetamide 10%) Foam** contains 100 mg of sodium sulfacetamide USP in a vehicle consisting of purified water, PVP/DMAPE acrylates copolymer, povidone, cocamidopropyl betaine, methylparaben, disodium EDTA, sodium thiosulfate, glycerin, quaternium 26/propylene glycol and lactic acid and is dispensed from an aluminum can pressurized with a hydrocarbon propellant (propane/butane).

Each gram of **Ovace® (sodium sulfacetamide 10%) Cream** contains 100 mg of sodium sulfacetamide USP in a vehicle consisting of purified water, glycerin, mineral oil, cetearyl alcohol/ceteareth 20, cetyl alcohol, glyceryl stearate, PEG-100 stearate, phenoxethanol, dimethicone, methylparaben, disodium EDTA, sodium thiosulfate, quaternium-26 and propylene glycol, propylparaben, and lactic acid.

Each gram of **Ovace® (sodium sulfacetamide 10%) Gel** contains 100 mg of sodium sulfacetamide USP in a vehicle consisting of purified water, glycerin, xanthan gum, methylparaben, disodium EDTA, sodium thiosulfate, quaternium-26 and propylene glycol, and lactic acid. Sulfacetamide sodium is $C_8H_9N_2NaO_5S_2H_2O$ with a molecular weight of 254.24. Chemically, it is Acetamidophenylsulfonamide sodium salt, monohydrate, with the following structural formula:



Sulfacetamide sodium is an odorless, white, crystalline powder with a bitter taste. It is freely soluble in water, sparingly soluble in alcohol, while practically insoluble in benzene, in chloroform, and in ether.

CLINICAL PHARMACOLOGY: Sulfacetamide sodium exerts a bacteriostatic effect against sulfonamide sensitive Gram-positive and Gram-negative microorganisms commonly isolated from secondary cutaneous pyogenic infections. It acts by restricting the synthesis of folic acid required by bacteria for growth, by its competition with para-aminobenzoic acid. There are no clinical data available on the degree and rate of systemic absorption of **Ovace®** when applied to the skin or scalp. However, significant absorption of sulfacetamide sodium through the skin has been reported.

The following *in vitro* data are available but their clinical significance is unknown. Organisms which show susceptibility to sulfacetamide sodium are: *Streptococci*, *Staphylococci*, *E. coli*, *Klebsiella pneumoniae*, *Pseudomonas pyocyanea*, *Salmonella*, *Proteus vulgaris*, *Nocardia* and *Actinomyces*.

INDICATIONS AND USAGE: **Ovace®** is intended for topical application in the following scaling dermatoses: seborrheic dermatitis and seborrheic sicca (dandruff). It also is indicated for the treatment of secondary bacterial infections of the skin due to organisms susceptible to sulfonamides.

CONTRAINDICATIONS: **Ovace®** is contraindicated in persons with known or suspected hypersensitivity to sulfonamides or to any of the ingredients of the product.

WARNINGS: Sulfonamides are known to cause Stevens-Johnson syndrome in hypersensitive individuals. Stevens-Johnson syndrome also has been reported following the use of sulfacetamide sodium topically. Cases of drug-induced systemic lupus erythematosus from topical sulfacetamide also have been reported. In one of these cases, there was a fatal outcome.

PRECAUTIONS:

For external use only

General: Nonsusceptible organisms, including fungi, may proliferate with the use of this preparation. Hypersensitivity reactions may recur when a sulfonamide is readministered, irrespective of the route of administration, and cross hypersensitivity between different sulfonamides may occur. If **Ovace®** produces signs of hypersensitivity or other untoward reactions, discontinue use of the preparation. Systemic absorption of topical sulfonamides is greater following application to large, infected, abraded, denuded, or severely burned areas. Under these circumstances, potentially any of the adverse effects produced by the systemic administration of these agents could occur and appropriate observations and laboratory determinations should be performed.

Information For Patients: Patients should discontinue **Ovace®** if the condition becomes worse, or if a rash develops in the area being treated or elsewhere. **Ovace®** also should be discontinued promptly and the physician notified if any arthritis, fever, or sores in the mouth develop.

Drug Interactions: **Ovace®** is incompatible with silver preparations. **Pharmacology:** **Ovace®** has a bacteriostatic effect against Gram-positive and Gram-negative microorganisms commonly isolated from secondary cutaneous pyogenic infections.

Carcinogenesis, Mutagenesis, and Impairment of Fertility: Long-term animal studies for carcinogenic potential have not been performed on **Ovace®** to date. Studies on reproduction and fertility also have not been performed. One author detected chromosomal nondisjunction in the yeast, *Saccharomyces cerevisiae*, following application of sulfacetamide sodium. The significance of this finding to the topical use of sulfacetamide sodium in the human is unknown.

Pregnancy Category C: Animal reproduction studies have not been conducted with **Ovace®**. It also is not known whether **Ovace®** can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. **Ovace®** should be used by a pregnant woman only if clearly needed or when potential benefits outweigh potential hazards to the fetus.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when **Ovace®** is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in children under the age of 12 years have not been established.

ADVERSE REACTIONS: Reports of irritation and hypersensitivity to sulfacetamide sodium are uncommon. The following adverse reactions, reported after administration of sterile ophthalmic sulfacetamide sodium, are noteworthy: instances of Stevens-Johnson syndrome and instances of local hypersensitivity which progressed to a syndrome resembling systemic lupus erythematosus; in one case a fatal outcome has been reported. (See **WARNINGS**)

OVERDOSAGE: The oral LD₅₀ of sulfacetamide in mice is 16.5 g/kg. The LD₅₀ for topical administration of sulfacetamide has not been determined. Oral overdosage may cause nausea and vomiting. Large oral overdosage may cause hematuria, crystalluria, and renal shutdown due to the precipitation of sulfur crystals in the renal tubules and the urinary tract. For treatment, contact local Poison Control Center.

DOSE AND ADMINISTRATION:

Seborrheic dermatitis including seborrhea sicca—

Ovace® Wash: Wash affected areas twice daily (morning and evening), or as directed by your physician. Avoid contact with eyes or mucous membranes. Wet skin and liberally apply to areas to be cleansed, massage gently into skin working into a full lather, rinse thoroughly and pat dry. Rinsing with plain water will remove any excess medication. Repeat application as described for eight to ten days. If skin dryness occurs it may be controlled by rinsing cleanser off sooner or using less frequently. Regular shampooing following **Ovace® Wash** is not necessary, but the hair should be shampooed at least once a week.

Ovace® Foam: For proper dispensing of foam, can must be inverted. Shake well before use. Remove clear cap. Gently break the tiny plastic piece where the back of the nozzle connects to the top. Invert can and dispense small amount of **Ovace® Foam** onto hand. The exact amount needed will vary according to the size of the affected area. Hair should be towel-dried or dry before applying to scalp. With fingers, gently massage **Ovace® Foam** into affected areas of the scalp until foam disappears. Use twice daily or as directed by your physician. Wash your hands after applying the foam. Allow the treated area to air dry. Do not wash the treated area immediately after applying the foam. Hair styling products can be used as usual after the foam has been applied. Repeat application as described for 8-10 days.

Ovace® Cream and Gel: Apply to affected areas twice daily (morning and evening), or as directed by your physician. Avoid contact with eyes or mucous membranes. Repeat application as described for eight to ten days. As the condition subsides, the interval between applications may be lengthened. Applications once or twice weekly or every other week may prevent recurrence. Should the condition recur after stopping therapy, the application of **Ovace®** should be reintitiated as at the beginning of treatment.

Secondary Cutaneous Bacterial Infections— Apply up to four times daily if necessary. See above directions for use.

Occasionally, a slight yellowish discoloration may occur when an excessive amount of the product is used and comes in contact with white fabrics. This discoloration, however, presents no problem, as it is readily removed by ordinary laundering without bleaches.

HOW SUPPLIED:

Ovace® Wash is available in a 6 oz. (170 mL) (NDC 0064-4000-06) and a 12 oz. (340 mL) (NDC 0064-4000-12) bottle.

Ovace® Foam is available in 100 gram (NDC 0064-4101-00) and 50 gram (NDC 0064-4100-50) aluminum cans.

Ovace® Cream is available in 30 gram (NDC 0064-4300-30) and 60 gram (NDC 0064-4300-60) tubes.

Ovace® Gel is available in 30 gram (NDC 0064-4200-30) and 60 gram (NDC 0064-4200-60) tubes.

Store at controlled room temperature 20°-25°C (68°-77°F). Do not freeze.

Ovace® Wash: Protect from freezing and excessive heat. **Ovace® Wash** may tend to darken slightly on storage. Slight discoloration does not impair the efficacy or safety of the product.

Ovace® Foam: WARNING: FLAMMABLE. AVOID FIRE, FLAME OR SMOKING DURING USE. Keep out of reach of children. Contents under pressure. Do not puncture or incinerate container. Do not expose to heat or store at temperatures above 49°C (120°F).

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Ovace® Wash 0064-4000-06 (6 oz. bottle) and 0064-4000-12 (12 oz. bottle)
Ovace® Foam 0064-4101-00 (100 gm can) and 0064-4100-50 (50 gm can)
Ovace® Cream 0064-4300-30 (30 g tube) and 0064-4300-60 (60 g tube)
Ovace® Gel 0064-4200-30 (30 g tube) and 0064-4200-60 (60 g tube)

iPLEDGE Implementation Delayed

Compliance from page 1

task,” said a source at FDA. “We’ve all been having daily meetings on this for months.”

By mid-October, about 15,000 of 55,000 retail pharmacies in the United States had registered with Covance Inc., the company running the iPLEDGE registration system, according to Douglas Hoey, R.Ph., a senior vice president with the National Community Pharmacists Association.

The association was one of several organizations, including the American Academy of Dermatology, that had begun lobbying the FDA for the delay, Mr. Hoey said.

“We wanted to make sure that as many pharmacists as possible were ready to serve patients,” he said.

It is expected that most pharmacies will sign up and that physicians who prescribe isotretinoin will not have trouble finding a dispensing pharmacy in their area, Mr. Hoey said. The snafu was in the timing, getting the word out, and getting pharmacists informed and up to speed, he added.

The delay comes at a time, however, when dermatologists and other physicians are expressing increased irritation about the restrictions being placed on isotretinoin

prescribing (SKIN & ALLERGY NEWS, November 2005, p. 1).

And, sources told this newspaper that physician registration to date in the iPLEDGE program has not been exceptionally brisk.

The number of isotretinoin prescriptions dropped significantly in the year after the implementation of the SMART program.

Alan Shalita, M.D., said he was somewhat relieved to learn of the program implementation delay, adding that he was not worried about being able to prescribe isotretinoin when the time came. He had registered with the iPLEDGE program soon after it came online and by November had still not received his patient materials from the program.

“I think it was an intelligent move to put implementation off,” said Dr. Shalita, chair of dermatology at the State University of New York Downstate Medical Center in Brooklyn.

Dr. Shalita is a consultant for Ranbaxy Pharmaceuticals Inc., a company that manufactures an isotretinoin product. ■

Aggressive Scalp Tumors May Require Bone Resection

ORLANDO — Bone or perineural involvement portends a poorer prognosis when it comes to aggressive and extensive tumors of the scalp, according to a study presented at the annual meeting of the Florida Society of Dermatologic Surgeons.

In the study, 6 of 11 patients with aggressive squamous cell carcinoma of the scalp had bone involvement, said Pearson G. Lang Jr., M.D.

“We don’t think of this—tumors in bony areas such as the scalp.”

The nine men and two women who were diagnosed with aggressive squamous cell carcinoma over a 9-year period all had alopecia or thinning hair. “Their scalps were exposed to chronic actinic damage,” explained Dr. Lang, professor of dermatology, pathology, otolaryngology, and communicative sciences at the Medical University of South Carolina, Charleston.

“You have to strip off the periosteum when these tumors go down to the bone. This may be the source of recurrence, and tumors may progress rapidly,” Dr. Lang said.

Consider a CT scan but be aware, however, that pitting of the bone is helpful as a sign but not always reliable. “To cure, you must resect the bone. Decortication is not recommended—I’ve seen cases over the years where the tumor goes deeper,” he said.

All tumors were moderately or well differentiated. A total of 4 of the 11 pa-

tients had satellite lesions, including 1 patient with a satellite lesion at time of initial treatment. Six patients developed regional or systemic metastases; five of them died.

The study also included four patients with aggressive basal cell carcinoma of the scalp.

“These aggressive basal cell carcinomas all occurred in women with full hair,” Dr. Lang said.

Tumors were 3 cm or bigger in size, up to the entire vertex of the scalp. One case of basal cell carcinoma mimicked recalcitrant seborrheic dermatitis. All of the patients had Mohs surgery along with extensive reconstruction. There were no recurrences or metastases among the patients.

“Remember that a recurrent tumor can look like granulation tissue,” Dr. Lang said at the meeting.

Most squamous cell and basal cell tumors recur within 2-6 years (average, 3 years). “You can get near a 100% cure rate if there is only skin involvement,” Dr. Lang said, but there is less than a 30% cure rate if there is perineural involvement.

Perineural tumors can be asymptomatic for years. Lesions are often small and benign in appearance.

MRI imaging is preferable to CT scans, Dr. Lang said, although only 50% of patients with such tumors will have positive findings.

—Damian McNamara

You have to strip off the periosteum when tumors go down to the bone. This may be the source of recurrence, and tumors may progress quickly.