

POLICY & PRACTICE

Prempro Damages Reduced

A Nevada District Court judge has significantly reduced compensatory and punitive damages awarded to three women who alleged that the hormone therapy drugs Premarin and Prempro caused their breast cancer. Last month, Washoe County District Judge Robert Perry reduced the original damages against the drug maker Wyeth from \$134.3 million to \$57.8 million. The bulk of the reduction came from the punitive damages, which were lowered from \$99 million to \$35 million. Despite the reduction in the damage award, Wyeth

still is planning to appeal the findings to the state supreme court. "While it's encouraging that the district court acknowledged the excessiveness of the award to some extent, it doesn't change the fact that the verdict was irreparably flawed and fraught with error," Wyeth spokesman Doug Petkus said in a statement.

ACOG Tightens Industry-Gifts Advice

Ob.gyns. should keep in mind that even gifts of nominal value offered by pharmaceutical and device companies are intended to influence behavior, the Ameri-

can College of Obstetricians and Gynecologists wrote in an updated opinion on relationships with industry. ACOG advises that cash gifts should not be accepted and that if physicians choose to take any other gifts, they should benefit the patient primarily. For example, textbooks and study aids could be considered acceptable gifts if they have a legitimate educational value, states the opinion produced by the ACOG Committee on Ethics, which updates an opinion issued in 2004. The statement includes recommendations on product promotion to individual physicians; support of educational activities and awards; donations, parties, and opportu-

nities for investment; industry sponsorship of research; and speakers bureaus and consulting. The ACOG committee opinion was published in the March issue of *Obstetrics and Gynecology*.

Don't Blame Technology for Costs

Medical devices and in vitro diagnostics account for a relatively small 6% (\$112 billion) of the nation's overall health expenditures and should not be blamed for rising health costs, said officials from the device industry's lobby, AdvaMed, at a briefing in February. The group released what it called one of the first-ever studies to examine device cost trends. The study—paid for by AdvaMed—was conducted by Roland Guy King, a former chief actuary for the Medicare and Medicaid programs. Devices and diagnostics accounted for a steady 6% of expenses from 1989 to 2004. Prices grew more slowly—1.2% annually—than the medical consumer price index, which is about 5% a year, or the consumer price index, which is about 2.8% annually, according to the study. "The highly competitive medical device marketplace is working and delivering tremendous value both in patient care and in economic terms," said Stephen J. Ubl, AdvaMed president and CEO.

FDA Would Expand Promotion

The Food and Drug Administration last month proposed draft guidance that would allow drug and medical device makers to distribute medical or scientific journal articles and reference publications that involve unapproved uses of FDA-approved drugs and medical devices. Drug and device makers had been allowed to disseminate such materials under guidelines set by the FDA, but that authority expired in September 2006. The FDA's new "Good Reprint Practices" draft guidance states that the article or reference should be published by an organization that has an editorial board and fully discloses conflicts of interest. In addition, articles should be peer reviewed, and manufacturers should not distribute special supplements, publications funded by product manufacturers, or articles not supported by credible medical evidence. Rep. Henry Waxman (D-Calif.), chairman of the House Committee on Oversight and Government Reform, blasted the FDA for its proposal.

Medicare Launches EHR Demo

Small- and medium-size physician practices in a dozen health markets across the country will be eligible to receive Medicare incentive payments for using certified electronic health records under a new demonstration being launched by officials at the Department of Health and Human Services. Financial incentives will be awarded to up to 1,200 practices that use certified EHRs to meet certain quality measures. Physicians who participate in the demonstration also would be eligible to receive bonus payments, based on the number of EHR functionalities physicians incorporate into their practices. Over the course of the 5-year project, individual physicians can earn up to \$58,000 and \$290,000 per practice. HHS will accept applications from officials in communities interested in participating in the demonstration through mid-May.

—Mary Ellen Schneider

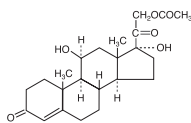
Item # 69341
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Analpram HC®

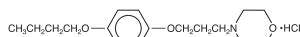
hydrocortisone acetate 2.5%
pramoxine HCl 1% Cream 2.5%

DESCRIPTION: Analpram HC® Cream 2.5% is a topical preparation containing hydrocortisone acetate 2.5% w/w and pramoxine hydrochloride 1% w/w in a Hydrolipid™ base containing cetostearyl alcohol, ceteth 20, mineral oil, white petrolatum, propylparaben, triethanolamine lauryl sulfate, citric acid, sodium citrate, and purified water.

Topical corticosteroids are anti-inflammatory and anti-pruritic agents. The structural formula, the chemical name, molecular formula and molecular weight for active ingredients are presented below.



hydrocortisone acetate
Pregn-4-ene-3,20-dione, 21-(acetoxy)-11,
17-dihydroxy-, (11-beta)-
C₂₃H₃₂O₆; mol. wt. 404.50



pramoxine hydrochloride
4-(3-(p-butoxyphenoxy)propyl)morpholine
hydrochloride
C₁₇H₂₇NO₃·HCl; mol. wt. 329.87

CLINICAL PHARMACOLOGY: Topical corticosteroids share anti-inflammatory, anti-pruritic and vasoconstrictive actions.

The mechanism of anti-inflammatory activity of topical corticosteroids is unclear. Various laboratory methods, including vasoconstrictor assays, are used to compare and predict potencies and/or clinical efficacies of the topical corticosteroids. There is some evidence to suggest that a recognizable correlation exists between vasoconstrictor potency and therapeutic efficacy in man.

Pramoxine hydrochloride is a topical anesthetic agent which provides temporary relief from itching and pain. It acts by stabilizing the neuronal membrane of nerve endings with which it comes into contact.

Pharmacokinetics: The extent of percutaneous absorption of topical corticosteroids is determined by many factors including the vehicle, the integrity of the epidermal barrier, and the use of occlusive dressings.

Topical corticosteroids can be absorbed from normal intact skin. Inflammation and/or other disease processes in the skin increase percutaneous absorption. Occlusive dressings substantially increase the percutaneous absorption of topical corticosteroids. Thus, occlusive dressings may be a valuable therapeutic adjunct for treatment of resistant dermatoses. (See DOSAGE AND ADMINISTRATION.)

Once absorbed through the skin, topical corticosteroids are handled through pharmacokinetic pathways similar to systemically administered corticosteroids. Corticosteroids are bound to plasma proteins in varying degrees. Corticosteroids are metabolized primarily in the liver and are then excreted by the kidneys. Some of the topical corticosteroids and their metabolites are also excreted into the bile.

INDICATIONS AND USAGE: Topical corticosteroids are indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.

CONTRAINDICATIONS: Topical corticosteroids are contraindicated in those patients with a history of hypersensitivity to any of the components of the preparation.

PRECAUTIONS: General: Systemic absorption of topical corticosteroids has produced reversible hypothalamic-pituitary-adrenal (HPA) axis suppression, manifestations of Cushing's syndrome, hyperglycemia, and glucosuria in some patients. Conditions which augment systemic absorption include the application of the more potent steroids, use over large surface areas, prolonged use, and the addition of occlusive dressings.

Therefore, patients receiving a large dose of a potent topical steroid applied to a large surface area and under an occlusive dressing should be evaluated periodically for evidence of HPA axis suppression by using the urinary free cortisol and ACTH stimulation tests. If HPA axis suppression is noted, an attempt should be made to withdraw the drug, to reduce the frequency of application, or to substitute a less potent steroid.

Recovery of HPA axis function is generally prompt and complete upon discontinuation of the drug. Infrequently, signs and symptoms of steroid withdrawal may occur, requiring supplemental systemic corticosteroids. Children may absorb proportionally larger amounts of topical corticosteroids and thus be more susceptible to systemic toxicity. (See Precautions-Pediatric Use.)

If irritation develops, topical corticosteroids should be discontinued and appropriate therapy instituted.

In the presence of dermatological infections, the use of an appropriate antifungal or antibacterial agent should be instituted. If a favorable response does not occur promptly the corticosteroid should be discontinued until the infection has been adequately controlled.

Information for the Patient: Patients using topical corticosteroids should receive the following information and instructions:

1. This medication is to be used as directed by the physician. It is for external use only. Avoid contact with the eyes.
2. Patients should be advised not to use this medication for any disorder other than for which it was prescribed.
3. The treated skin area should not be bandaged or otherwise covered or wrapped as to be occlusive unless directed by the physician.
4. Patients should report any signs of local adverse reactions especially under occlusive dressings.
5. Parents of pediatric patients should be advised not to use tight-fitting diapers or plastic pants on a child being treated in the diaper area, as these garments may constitute occlusive dressings.

Laboratory Tests: The following tests may be helpful in evaluating the HPA axis suppression: Urinary free cortisol test
ACTH stimulation test

Carcinogenesis, Mutagenesis, and Impairment of Fertility: Long-term animal studies have not been performed to evaluate the carcinogenic potential or the effect on fertility of topical corticosteroids. Studies to determine mutagenicity with prednisolone and hydrocortisone have revealed negative results.

Pregnancy: Teratogenic Effects: Pregnancy Category C: Corticosteroids are generally teratogenic in laboratory animals when administered systemically at relatively low dosage levels. The more potent corticosteroids have been shown to be teratogenic after dermal application in laboratory animals. There are no adequate and well-controlled studies in pregnant women on teratogenic effects from topically applied corticosteroids. Therefore, topical corticosteroids should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Drugs of this class should not be used extensively on pregnant patients, in large amounts, or for prolonged periods of time.

Nursing Mothers: It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable amounts in breast milk. Systemically administered corticosteroids are secreted into breast milk in quantities NOT likely to have a deleterious effect on the infant. Nevertheless, caution should be exercised when topical corticosteroids are administered to a nursing woman.

Pediatric Use: Pediatric patients may demonstrate greater susceptibility to topical corticosteroid induced HPA axis suppression and Cushing's syndrome than mature patients because of a larger skin surface area to body weight ratio.

Hypothalamic-pituitary-adrenal (HPA) axis suppression, Cushing's syndrome, and intracranial hypertension have been reported in children receiving topical corticosteroids. Manifestations of adrenal suppression in children include linear growth retardation, delayed weight gain, low plasma cortisol levels, and absence of response to ACTH stimulation. Manifestations of intracranial hypertension include bulging fontanelles, headaches, and bilateral papilledema.

Administration of topical corticosteroids to children should be limited to the least amount compatible with an effective therapeutic regimen. Chronic corticosteroid therapy may interfere with the growth and development of children.

ADVERSE REACTIONS: The following local adverse reactions are reported infrequently with topical corticosteroids, but may occur more frequently with the use of occlusive dressings. These reactions are listed in an approximate decreasing order of occurrence:

Burning	Hypertrichosis	Maceration of the skin
Itching	Acneiform eruptions	Secondary infection
Irritation	Hypopigmentation	Skin atrophy
Dryness	Perioral dermatitis	Striae
Folliculitis	Allergic contact dermatitis	Miliaria

OVERDOSAGE: Topically applied corticosteroids can be absorbed in sufficient amounts to produce systemic effects. (See PRECAUTIONS.)

DOSAGE AND ADMINISTRATION: Topical corticosteroids are generally applied to the affected area as a thin film three to four times daily depending on the severity of the condition. Occlusive dressings may be used for the management of psoriasis or recalcitrant conditions. If an infection develops, the use of occlusive dressings should be discontinued and appropriate antimicrobial therapy instituted.

HOW SUPPLIED:

Analpram HC® Cream 2.5%	1 oz tube	(NDC 0496-0800-04)
	4 gram tube	(NDC 0496-0800-74)
	12 x 4 gram tubes	(NDC 0496-0800-65)
	30 x 4 gram tubes	(NDC 0496-0800-64)

Storage Conditions: Store at controlled room temperature 59° - 86°F (15° - 30°C).

Rx Only.



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