

FDA to Allow Radio Frequency Tags in Drug Labels

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Contributing Writer

ROCKVILLE, MD. — The Food and Drug Administration has reassured pharmaceutical companies that they can use radio frequency identification technology in product packaging without running afoul of agency rules, at least through 2007.

“Today’s actions were designed with one goal in mind: to increase the safety of medications consumers receive by creating the capacity to track a drug from the manufacturer all the way to the pharmacy,” acting FDA Commissioner Lester M. Crawford, D.V.M., Ph.D., said in a press briefing sponsored by the FDA.

At the same time, Purdue Pharma LP, Pfizer, and GlaxoSmithKline all said they

The move was designed to increase drug safety by creating the capacity to track a drug from the manufacturer all the way to the pharmacy.

soon would begin using radio frequency identification (RFID) technology in packaging for some of their products.

RFID is slowly being adopted by retailers to track inventory. Tags that contain information about the product can

be embedded into pallets or labels and then read by wireless scanners.

The new FDA policy should convince drug makers that they can safely use RFID tags, said Paul Rudolf, M.D., FDA senior adviser for medical and health policy. Between now and 2007, companies can experiment with RFID without fear of sanctions, he said.

FDA officials said that until now pharmaceutical manufacturers have hesitated to incorporate the tags into their products out of concern that the agency—which by law must approve everything about a drug’s label—might then consider a drug mislabeled.

The agency believes RFID technology could also deter counterfeiting. A tag could be embedded into a large pill bottle or block of packages at the factory, with information on the drug’s potency, its destination, and other important data. Using special scanners and software, the distributor and the pharmacy will then be able to read the tag. RFID will help create an “electronic pedigree,” allowing manufacturers, distributors, and pharmacists to verify the drug’s legitimacy, according to the FDA.

“The entire chain of custody can be followed,” Dr. Rudolf said.

“The threat [of counterfeiting] is real and needs to be addressed in a real and strong way,” said William Hubbard, FDA’s associate commissioner for policy and planning, who added that the “drug supply in this country is very safe now.”

There have been some instances, however, when impurities have been discovered in counterfeit pharmaceuticals, and in one case, where an injectable drug was filled with “nothing more than tap water,” explained Thomas McGinnis,

Pharm.D., FDA’s director of pharmacy affairs.

At press time, Purdue Pharma, which has weathered difficulties with theft and diversion of its pain killer OxyContin (oxycodone), said it would begin sending RFID-tagged 100-tablet bottles to Wal-Mart and H.D. Smith Wholesale Drug Co. The company is also donating 100 handheld scanners to law enforcement groups around the country and using special color-shifting ink on the label that will let pharmacists

know that the bottle came from Purdue.

GlaxoSmithKline said it would start using RFID tags on at least one of its products deemed to be susceptible to counterfeiting in the next year-and-a-half. Those products include Retrovir (zidovudine), Combivir (lamivudine/zidovudine), Epivir (lamivudine), Trizivir (abacavir, lamivudine, and zidovudine), Ziagen (abacavir), and Zofran (ondansetron), according to the company.

Pfizer said that it expected to have RFID

tags for Viagra (sildenafil) by the end of next year.

Dr. Rudolf added that he did not expect the cost of anticounterfeiting technology to be passed on to consumers, as it would save money by curbing counterfeiting.

A report by the Healthcare Distribution Management Association’s Healthcare Foundation seems to back up that assertion: The report estimated that \$200 million to \$400 million could be saved each year by decreasing drug counterfeiting. ■

Topicort® (Desoximetasone)

LP Cream 0.05%, Gel 0.05%, and Cream and Ointment 0.25%

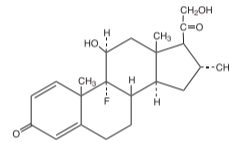
For topical use only. Not for ophthalmic use.

Rx only

DESCRIPTION

Topicort® LP (desoximetasone) Cream 0.05%; Topicort® (desoximetasone) Cream 0.25%; Topicort® (desoximetasone) Gel 0.05%; and Topicort® (desoximetasone) Ointment 0.25% contain the active synthetic corticosteroid desoximetasone. The topical corticosteroids constitute a class of primarily synthetic steroids used as anti-inflammatory and antipruritic agents. Each gram of TOPICORT LP Cream 0.05% contains 0.5 mg of desoximetasone in an emollient cream base consisting of white petrolatum, purified water, isopropyl myristate, lanolin alcohols, mineral oil, cetostearyl alcohol, and edetate disodium. Each gram of TOPICORT Cream 0.25% contains 2.5 mg of desoximetasone in an emollient cream base consisting of white petrolatum, purified water, isopropyl myristate, lanolin alcohols, mineral oil, and cetostearyl alcohol. Each gram of TOPICORT Gel 0.05% contains 0.5 mg of desoximetasone in a gel base consisting of purified water, docusate sodium, edetate disodium, isopropyl myristate, carbomer 940, trolamine, and SDAG-1B 95% alcohol. Each gram of TOPICORT Ointment 0.25% contains 2.5 mg of desoximetasone in an ointment base consisting of white petrolatum and fractionated coconut oil. The chemical name of desoximetasone is Pregna-1, 4-diene-3, 20-dione, 9-fluoro-11, 21-dihydroxy-16-methyl-, (11β,16α)-. Desoximetasone has the molecular formula C₂₂H₃₂O₄ and a molecular weight of 376.47. The CAS Registry Number is 382-67-2.

The structural formula is:



CLINICAL PHARMACOLOGY

Topical corticosteroids share anti-inflammatory, antipruritic and vasoconstrictive actions. The mechanism of anti-inflammatory activity of the 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.

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.

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.

Pharmacokinetic studies in men with Topicort® (desoximetasone) Cream 0.25% with tagged desoximetasone showed a total of 5.2% ± 2.9% excretion in urine (4.1% ± 2.3%) and feces (1.1% ± 0.8%) and no detectable level (limit of sensitivity: 0.005 µg/mL) in the blood when it was applied topically on the back followed by occlusion for 24 hours. Seven days after application, no further radioactivity was detected in urine or feces. The half-life of the material was 15 ± 2 hours (for urine) and 17 ± 2 hours (for feces) between the third and fifth trial day.

Pharmacokinetic studies in men with Topicort® (desoximetasone) Ointment 0.25% with tagged desoximetasone showed no detectable level (limit of sensitivity: 0.003 µg/mL) in 1 subject and 0.004 and 0.006 µg/mL in the remaining 2 subjects in the blood when it was applied topically on the back followed by occlusion for 24 hours. The extent of absorption for the ointment was 7% based on radioactivity recovered from urine and feces. Seven days after application, no further radioactivity was detected in urine or feces. Studies with other similarly structured steroids have shown that predominant metabolite reaction occurs through conjugation to form the glucuronide and sulfate ester.

INDICATIONS AND USAGE

Topicort® LP (desoximetasone) Cream 0.05%; Topicort® (desoximetasone) Cream 0.25%; Topicort® (desoximetasone) Gel 0.05%; and Topicort® (desoximetasone) Ointment 0.25% 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.

WARNINGS

Topicort® LP (desoximetasone) Cream 0.05%; Topicort® (desoximetasone) Cream 0.25%; Topicort® (desoximetasone) Gel 0.05%; and Topicort® (desoximetasone) Ointment 0.25% are not for ophthalmic use.

Keep out of reach of children.

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 or 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.

Pediatric patients 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:

- This medication is to be used as directed by the physician. It is for external use only. Avoid contact with the eyes.
- Patients should be advised not to use this medication for any disorder other than for which it was prescribed.
- The treated skin area should not be bandaged or otherwise covered or wrapped as to be occlusive unless directed by the physician.
- Patients should report any signs of local adverse reactions, especially under occlusive dressings.
- 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 hypothalamic-pituitary-adrenal (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. Desoximetasone did not show potential for mutagenic activity in vitro in the Ames microbial mutagen test with or without metabolic activation.

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. Desoximetasone has been shown to be teratogenic and embryotoxic in mice, rats, and rabbits when given by subcutaneous or dermal routes of administration in doses 3 to 30 times the human dose of Topicort® (desoximetasone) Cream 0.25% or Topicort® (desoximetasone) Ointment 0.25% and 15 to 150 times the human dose of Topicort® LP (desoximetasone) Cream 0.05% or Topicort® (desoximetasone) Gel 0.05%. There are no adequate and well-controlled studies in pregnant women on teratogenic effects from topically applied corticosteroids. Therefore, TOPICORT LP Cream 0.05%, TOPICORT Cream 0.25%, TOPICORT Gel 0.05%, and TOPICORT Ointment 0.25% 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 quantities 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.

HPA axis suppression, Cushing’s syndrome, and intracranial hypertension have been reported in pediatric patients receiving topical corticosteroids. Manifestations of adrenal suppression in pediatric patients 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 pediatric patients should be limited to the least amount compatible with an effective therapeutic regimen. Chronic corticosteroid therapy may interfere with the growth and development of pediatric patients. Safety and effectiveness of TOPICORT Ointment in pediatric patients below the age of 10 have not been established.

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	Milia

In controlled clinical studies the incidence of adverse reactions was low (0.8% for Topicort® (desoximetasone) Cream 0.25% and included burning, folliculitis, and folliculo-pustular lesions. The incidence of adverse reactions was also 0.8% for Topicort® LP (desoximetasone) Cream 0.05% and included pruritus, erythema, vesiculation, and burning sensation. The incidence of adverse reactions was low (0.3% for Topicort® (desoximetasone) Ointment 0.25% and consisted of development of comedones at the site of application.

OVERDOSAGE

Topically applied corticosteroids can be absorbed in sufficient amounts to produce systemic effects (see **PRECAUTIONS**).

DOSE AND ADMINISTRATION

Apply a thin film of Topicort® LP (desoximetasone) Cream 0.05%, Topicort® (desoximetasone) Cream 0.25%, Topicort® (desoximetasone) Gel 0.05%, and Topicort® (desoximetasone) Ointment 0.25% to the affected skin areas twice daily. Rub in gently.

HOW SUPPLIED

Topicort® LP (desoximetasone) Cream 0.05% is supplied in 5 gram tubes for physician samples, 15 gram and 60 gram tubes.

Topicort® (desoximetasone) Cream 0.25% is supplied in 5 gram tubes for physician samples, 15 gram and 60 gram tubes.

Topicort® (desoximetasone) Gel 0.05% is supplied in 5 gram tubes for physician samples, 15 gram and 60 gram tubes.

Topicort® (desoximetasone) Ointment 0.25% is supplied in 5 gram tubes for physician samples, 15 gram and 60 gram tubes.

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

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