

CMS Backs Coverage for Diet, Lifestyle Changes

BY JOYCE FRIEDEN

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BALTIMORE — There might not have been thunderous applause at the meeting of the Medicare Coverage Advisory Committee, but the quiet approval was quite enough for Dean Ornish, M.D.

The committee, which advises Medicare on coverage issues, voted to recommend that Medicare cover the use of physician-supervised intensive diet and lifestyle change programs for preventing and reversing heart disease—programs such as the one developed by Dr. Ornish.

“I’m pleased by the opportunity to have all the evidence considered,” he said after the panel approved the recommendation, adding that he hoped that the evidence was compelling enough for Medicare to make this type of lifestyle intervention a part of its benefits package. Medicare is not obligated to accept the recommendation of its advisory committee.

Dr. Ornish, president of the Preventive Medicine Research Institute, Sausalito, Calif., outlined his program, which consists of putting patients on a very low-fat diet (about 10% fat), getting them on a moderate exercise program, teaching them stress management techniques such as stretching and meditation, and enrolling them in support groups.

In a 1-year study of 28 patients who took part in the program and 20 controls, he found that the average percentage diameter stenosis regressed from 40% to 37.8% in the experimental group, compared with an average progression from 42.7% to 46.1% in the control group. In addition, there was a 91% reduction in angina in the intervention group, compared with a 165% increase in the control group.

Dr. Ornish also investigated whether other providers could be trained to implement his program, so he set up demonstration projects in other sites with more than 2,000 patients.

In the first project, funded by Mutual of Omaha, the researchers studied 194 patients with angiographically documented coronary artery disease and compared them with 139 controls. Although no patients in the intervention group had had a recent cardiac event, 55% had had a prior myocardial infarction, compared with 28% of controls.

The researchers found that after 3 years, 77% of intervention patients who met insurance company criteria to undergo bypass or angioplasty were able to avoid it, saving Mutual of Omaha \$30,000 per patient, Dr. Ornish reported.

He admitted that his program requires a lot of commitment. For the first few months, participants attend two 4-hour sessions, each consisting of exercise, meditation or other stress reduction, a support group meeting, and a lunch/lecture. Later, they decrease to once-weekly sessions, but continue for 9 months.

In a payment demonstration project for Medicare, Dr. Ornish found that patients’ body weight decreased both at 12 weeks and at 1 year. “Just on weight loss alone, I think a program like this could be beneficial.” He said that the primary determinant

of how much patients improved on the program was adherence. “The more people changed, the better they got,” he noted.

Advisory committee members expressed several concerns about Dr. Ornish’s results.

Clifford Goodman, Ph.D., a senior scientist with the Lewin Group, a Falls Church, Va. consulting firm, noted that some of the improvements in the patient groups started to reverse slightly after a year, and speculated that many patients

may be self-selecting for the program at a time when their weight and other negative indicators are at their peak. “How much of the effect we’re observing is simply regression to the mean?” he asked.

Dr. Ornish admitted that there was some regression but added, “there is a direct correlation between degree of adherence and outcomes at 1 year.”

Adherence was a concern for several panel members who wondered whether patients could really keep up with strict

regimens such as that of Dr. Ornish.

But Dr. Ornish said he was merely asking for these types of programs to be treated the same way as other interventions.

“We will pay for bypass surgery and angioplasty, but diet and lifestyle interventions, Medicare generally doesn’t pay for it,” he said, adding that many insurers pay for cholesterol-lowering statin drugs even though studies have shown that patients go off the drugs after a few months because they don’t like the side effects.

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.

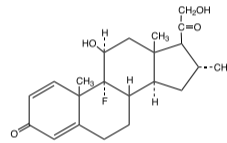
Each gram of TOPICORT Gel 0.05% contains 0.5 mg of desoximetasone in a gel base consisting of purified water, docusate sodium, edetate disodium, isopropyl myristate, carbomer 940, trolamine, and SDAG-1B 95% alcohol.

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-, (11 β ,16 α).

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% ± 0.6%) 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).

DOSEAGE 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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Also testifying were spokesmen from two Blue Cross Blue Shield plans—Mountain State in West Virginia and Highmark in Pennsylvania—that pay patients to enroll in the Ornish program. Both said their plans were happy with the clinical outcomes and the cost savings.

David Lambert, vice president of health services for Mountain State Blue Cross Blue Shield, said his plan began covering the Ornish program for heart disease prevention in 2002.

More than 400 patients, average age 56, have participated, with a 90% completion rate, Mr. Lambert said. “They collectively reduced their risk of a cardiac event by

50% as measured by the ATP Framingham risk tool, and lowered their LDL by 21%.”

He noted that the average cost of the behavioral management program was \$5,700, compared with the cost of heart surgery, which ranges from \$57,000 to \$67,000. “By avoiding one procedure, it pays for 10 members to complete the program.”

The committee also heard from Alex Clark, Ph.D., of the University of Alberta’s Centre for Health Evidence in Edmonton. The Centers for Medicare and Medicaid Services contracted with Dr. Clark’s center to review outcomes studies for patients with symptomatic coronary artery disease undergoing one of three types of therapy:

cardiac rehabilitation (group education and counseling only), comprehensive cardiac rehabilitation (such as Dr. Ornish’s program, which includes exercise in addition to group education and counseling), and individual counseling. All studies had to have outcomes for at least 50 patients to be included in the review.

The reviewers found that all three types of programs had some long-term benefits, including reductions in mortality and hospitalization, and improved quality of life, Dr. Clark said. “The foundation for change is happening at 12 months.”

Information on program costs was sketchier, he noted. Only 6 out of 41 stud-

ies mentioned costs, and three of those “reported or implied” cost savings without giving any relevant data. Most of the studies were heavy on male participants, with seven studies having no women at all.

In the end, panel members generally agreed that the Ornish program and similar interventions improved patients’ long-term survival rates and quality of life, but they were less certain that other providers would be able to successfully implement the program and that it could be easily translated to Medicare patients, many of whom have multiple chronic illnesses.

“This is a spectacular example of personalized health care,” said William F. Owen Jr., M.D., a professor of medicine at Duke University, Durham, N.C. “I believe this works in a certain patient segment that’s cared for by very passionate providers, but I’m uncomfortable about extrapolating it.”

Now that the advisory committee has made its recommendation, CMS must decide whether to take up the issue of a national coverage determination, and what scope that potential coverage might have. An agency spokesman said there is no timetable for making the decision. ■

There’s a lot of Flexibility in *Topicort*[®] (Desoximetasone)



Topicort[®] provides you with a choice of multiple potencies^{1,2} and vehicles, giving you remarkable flexibility to treat a broad range of dermatoses. And when it comes to treating corticosteroid-responsive dermatoses, *Topicort*[®] gives you flexibility you can trust... with established efficacy and safety through decades of clinical use.



In corticosteroid-responsive dermatoses prescribe...

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

Multiple Choices, One Solution

The most common adverse reactions include burning, itching, irritation, dryness, folliculitis, hypertrichosis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, maceration of the skin, secondary infection, skin atrophy, striae and miliaria. When used in large areas or under occlusive dressing, patients should be evaluated for HPA axis suppression. Before prescribing, please see complete prescribing information.

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2. Gilman AG, Hardman JG, Limbird LE. *Goodman & Gilman's The Pharmacological Basis of Therapeutics*. 10th ed. McGraw-Hill, 2001, pg. 1799.
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INDEX OF ADVERTISERS

3M Pharmaceuticals	
Aldara	54-55
Allergan, Inc.	
Tazarac	28a-28d, 29
Ameripath	
Dermpath Diagnostics	21
Centocor, Inc.	
Corporate	10
Connetics Corporation	
Evoclin	32-34
Coria Laboratories, Ltd.	
Cloderm	7-8
Ovace	17-18
Salex Lotion	23-24
Salex Cream	35-36
CosMedical Technologies, Inc.	
Retinol Drops	6
Doak Dermatologics	
Selseb	26-28
Fujisawa Healthcare, Inc.	
Protopic	43-44
Galderma Laboratories, L.P.	
Clobex	36a-36b
Cetaphil	45
Genentech, Inc.	
Raptiva	46-48
INTENDIS Inc.	
Finacea	14-16
MediNotes Corporation	
Charting Software	25
Merz Pharmaceuticals	
Naftin	41-42
OrthoNeutrogena	
Ertaczo	3-4
T/Gel	13
Centany	51-52
Retin-A Micro	63-64
PharmaDerm	
ApexiCon	39-40
Physician's Choice of Arizona, Inc.	
Skin Care Products	53
Stiefel Laboratories, Inc.	
Sarna	11
ZNP Bar	19
Zeosorb	31
Rosac	49-50
Taro Pharmaceuticals U.S.A., Inc.	
Lustra AF	9
Topicort	60-61
Travel Tech Mohs Services, Inc.	
Corporate	22