What You Need to Know About The Off-Label Use of Pharmaceuticals

There's no need to be afraid to use these products.

By: Barry H. Block, DPM, JD

Dr. Block is editor of Podiatry Management and PM-News. He is a healthcare attorney admitted to both the New York State and the Federal Bars.

The off-label use of pharmaceuticals is neither new nor novel, yet many podiatrists are reluctant to incorporate these products into their treatment regimens. When questioned on this point many will respond, "I'm worried about the legal implications" or "I don't want to be bothered with additional paperwork." In truth, as this article will illustrate, there are very few potential legal implications and very little paperwork involved.

What is Off-Label Use?

- **1) It is the use of an existing FDA-Approved pharmaceutical to treat a condition for which the FDA has not yet approved the medication AND;**

- **2) There is evidence that the use by others of this pharmaceutical for this condition has been successful.**

How Does Off-Label Use Begin

Generally, off-label use begins when it is discovered that an FDA-approved drug has beneficial side-effects. Consider Rogaine (minoxidil). Today, we associate this medication for use in the growth or maintenance of hair in balding individuals. Minoxidil, however, was initially FDA-approved as oral medication for the treatment of hypertension.

Doctors prescribing minoxidil began reporting that their patients had thicker eyebrows or were growing new hair. Dermatologists then began experimenting with the topical application of minoxidil on patients' scalps. This early experimentation was the investigational stage of the off-label process. Eventually, studies were conducted and research papers were published demonstrating the hair-growing capability of minoxidil. At that point, the use of this medication was considered off-label.

Only when the FDA approved minoxidil as a hair-growing treatment did the use of this medication move from off-label to being a formulary-type drug.

Responsibilities of an Off-Use Prescriber

Podiatrists may also have opportunities to use off-label medications. For example, Many DPM's use Tagemet for the treatment of verruca. More recently, some podiatrists have begun using Solaraze Gel®, 3% (diclofenac sodium), a topical

NSAID/cox2 inhibitor indicated for the treatment of actinic keratosis, to treat of foot and ankle pain.

In order to use any medication on an off-label use basis, the following four criteria must be met:

1) You have a responsibility to be well-informed about the product. This requirement doesn't differ from that of any pharmaceutical that you prescribe. It simply means that you are aware of the dosage, adverse effects, counter-indications, and drug interactions associated with this product. These are found in the package inserts of the drug or in the Physician's Desk Reference and other similar sources.

2) You must base its use on firm scientific rationale and on sound medical evidence. This standard differentiates off-label use from the more stringent classification of investigational use. Scientific rationale means that there is a basis for the use of your product. For example, diclofenic is a non-steroidal anti-inflammatory, thus it would be anticipated that it would have an analgesic effect when used topically.

Sound medical evidence means that some research has been conducted on the off-label use of a product and that there is an availability of at least one published paper showing some efficacy of the product. Articles on off-label usage can be downloaded from Medline. If you are using any medicine on an off-label, you should keep such articles in your files.

3) You must maintain records of the product's use and effects. This requirement merely mirrors the same standard required for all prescription medications. The most effective way of doing this is to use no-carbon-required (NCR) prescription pads, although simply notating your prescriptions in the patient's chart is quite acceptable. You should note any adverse reactions to such medicine, just as you would with any prescribed medication.

4) You must inform your patient that you are using a medication for an indication which has not yet been approved by the FDA. This is a lesser standard than the "informed consent" which we utilize for surgical procedures. The easiest and most effective method of meeting this standard is to hand the patient a pre-printed form when you apply, inject, or prescribe the medication (see sample off-label information form). You should note in you records that the patient was given an information sheet on the prescribed product. For an added level of security, you can have patient sign a copy of the information sheet.

Incidentally, it's a good idea to have handouts for most of the medicines you prescribe, particularly if they are topicals, because such sheets tend to increase patient compliance.

It is important to note that off-label use of pharmaceuticals does not require the submission of an Investigational New Drug Application (IND), Investigational Device Exemption (IDE) or review by an Institutional Review Board (IRB). These complicated forms are essentially reserved for the use non-FDA-approved drugs.

Conclusion

The use of off-label pharmaceuticals is not limited to pioneers or researchers. By following the above-referenced guidelines, you can add these additional options to your treatment regimen.

==========

Information Form For the Off-Label Use of Solaraze Gel™, 3%

This is to inform you that the medicine being prescribed to you by John Doe, D.P.M.,
is not currently FDA-Approved for the condition for which it is being prescribed.

Solaraze Gel™, 3% is currently FDA-approved for the treatment of actinic keratosis, a skin condition.

You are being prescribed this medicine because there is a firm scientific rational for its use in treatment of foot and ankle pain. There is also published research supporting this rationale.

CONTRAINDICATIONS
Solaraze™ (diclofenac sodium) Gel is contraindicated in patients with a known hypersensitivity to diclofenac, benzyl alcohol, polyethylene glycol monomethyl ether 350 and/or hyaluronate sodium.
WARNINGS
As with other NSAID's, anaphylactoid reactions may occur in patients without prior exposure to diclofenac.
Diclofenac sodium should be given with caution to patients with the aspirin triad. The triad typically occurs in asthmatic patients who experience rhinitis with or without nasal polyps, or who exhibit severe, potentially fatal bronchospasm after taking aspirin or other NSAID's.
PRECAUTIONS
Solaraze™ (diclofenac sodium) Gel should be used with caution in patients with active gastrointestinal ulceration or bleeding and severe renal or hepatic impairments. Solarazę should not be applied to open skin wounds, infections, or exfoliative dermatitis. It should not be allowed to come in contact with the eyes. The safety of the concomitant use of sunscreens, cosmetics or other topical medications and Solarazę is unknown.
Information For Patients
In clinical studies, localized dermal side effects such as contact dermatitis, exfoliation, dry skin, and rash were found in patients treated with Solaraze at a higher incidence than in those with placebo.
Patients should understand the importance of monitoring and follow-up evaluation, the signs and symptoms of dermal adverse reactions, and the possibility of irritant or allergic contact dermatitis. If severe dermal reactions occur, treatment with

Solarazę may be interrupted until the condition subsides. Exposure to sunlight and the use of sunlamps should be avoided. Safety and efficacy of the use of Solarazętogether with other dermal products, including cosmetics, sunscreens, and other topical medications on the area being treated have not been studied.

Drug Interactions

Although the systemic absorption of Solarazę is low, concomitant oral administration of other NSAID's, such as aspirin at anti-inflammatory/analgesic doses should be minimized.

==========

Chart 1 Comparison of Off-Label Vs. Investigational Use