

FDA warns of rare but serious hypersensitivity reactions with certain over-the-counter topical acne products

Safety Announcement

[6-25-2014] The U.S. Food and Drug Administration (FDA) is warning that certain over-the-counter (OTC) topical acne products can cause rare but serious and potentially life-threatening allergic reactions or severe irritation. Consumers should stop using their topical acne product and seek emergency medical attention immediately if they experience hypersensitivity reactions such as throat tightness; difficulty breathing; feeling faint; or swelling of the eyes, face, lips, or tongue. Consumers should also stop using the product if they develop hives or itching.

These serious hypersensitivity reactions differ from the local skin irritation that may occur at the product application site, such as redness, burning, dryness, itching, peeling, or slight swelling, that are already included in the Drug Facts labels.

Based on the information reported to FDA, we cannot determine if the serious hypersensitivity reactions were triggered by the acne products' active ingredients, benzoyl peroxide or salicylic acid, the inactive ingredients, or by a combination of both. The hypersensitivity reactions may occur within minutes to a day or longer after product use. The OTC topical acne products of concern are marketed under various brand names such as Proactiv, Neutrogena, MaxClarity, Oxy, Ambi, Aveeno, Clean & Clear, and as store brands. They are available as gels, lotions, face washes, solutions, cleansing pads, toners, face scrubs, and other products.

Manufacturers of OTC topical acne drug products have the option to add label directions for sensitivity testing for new users of their products (see [Guidance for Industry](#)). We encourage new users of OTC topical acne drug products to follow these directions. We are also encouraging manufacturers to add these directions to all product labels, to reduce the risk of serious hypersensitivity reactions. According to these directions, before using an OTC topical acne product for the first time, consumers should apply a small amount to one or two small affected areas of the skin for 3 days. If no discomfort occurs, then the product can be used according to the directions on the Drug Facts label. Consumers should avoid using an OTC topical acne product again if they have previously experienced a hypersensitivity reaction with its use.

We are continuing to monitor and evaluate this safety issue, and will work with manufacturers regarding any future label changes that would address the risk of severe hypersensitivity reactions.

Facts about over-the-counter topical acne products

- Some products contain the active ingredients benzoyl peroxide or salicylic acid.
- Sold under various brand names such as Proactiv, Neutrogena, MaxClarity, Oxy, Ambi, Aveeno, Clean & Clear, and as store brands.
- Available as gels, lotions, face washes, solutions, cleansing pads, toners, face scrubs, and other products.

Additional Information for Consumers

- Rare but serious hypersensitivity reactions have been reported with the use of certain over-the-counter (OTC) topical acne products.
- Based on adverse events reported to FDA, it is not possible to determine if these reactions were triggered by the active ingredients benzoyl peroxide or salicylic acid, the inactive ingredients, or a combination of both.
- Stop using the product and seek emergency medical attention immediately if you develop signs and symptoms of a serious hypersensitivity reaction such as:
 - throat tightness
 - difficulty breathing
 - feeling faint
 - swelling of the eyes, face, lips, or tongue
- Also stop using the product if you develop hives or itching of the face or body.
- Do not use an OTC topical acne product again if you have previously experienced a serious hypersensitivity reaction from it.
- Before using an OTC topical acne drug product for the first time, apply a small amount to one or two small affected areas for 3 days to make sure you don't develop any hypersensitivity symptoms. If no discomfort occurs, follow the directions on the Drug Facts label.
- Talk to a health care professional if you have any concerns about using OTC topical acne products. Questions you might ask include:
 - Is an OTC topical acne product right to treat my acne?
 - Are there other products that you can recommend?
- Report side effects from OTC topical acne products to the FDA MedWatch program, using the information in the "Contact FDA" box at the bottom of this page.

Additional Information for Health Care Professionals

- Rare but serious hypersensitivity reactions have been reported with the use of certain over-the-counter (OTC) topical acne products. Based on adverse events reported to FDA, it is not possible to determine if these reactions were triggered

- by the active ingredients benzoyl peroxide or salicylic acid, the inactive ingredients, or a combination of both.
- When recommending OTC topical acne products to consumers, alert them about symptoms of serious hypersensitivity reactions such as skin or mucosal changes and, particularly, about concomitant respiratory or cardiovascular changes such as dyspnea, hypotension, or syncope suggestive of anaphylaxis.
 - Advise consumers to stop using the product if a hypersensitivity reaction occurs and to seek emergency medical attention immediately if they develop symptoms suggestive of anaphylaxis.
 - Advise consumers using an OTC topical acne drug product for the first time to apply a small amount to one or two small affected areas for 3 days to make sure they don't develop any hypersensitivity symptoms. If no discomfort occurs, they can follow the directions on the Drug Facts label.
 - Be aware that some topical prescription acne drug products also contain label warnings about allergy, including anaphylaxis.
 - Report adverse events involving OTC topical acne products to the FDA MedWatch program, using the information in the "Contact FDA" box at the bottom of this page.

Data Summary

A search of the FDA Adverse Event Reporting System (FAERS) database from 1969 through January 28, 2013 identified 131 cases of hypersensitivity reactions with serious outcomes associated with over-the-counter topical acne drug products containing benzoyl peroxide or salicylic acid. The majority of the cases were reported since 2012. Approximately 86 percent (n=113) of the patients were female, and the average patient age was 32 years (range 11-78 years).

The reported adverse reactions ranged from application site reactions (e.g., skin irritation, burning sensation, erythema, and dermatitis) to swelling of the eyes, lips, tongue, or face; throat tightness; and shortness of breath. There were no fatalities; however, 44 percent (n=58) of the cases reported that hospitalization was required. Of the 131 cases, 38 percent (n=50) were categorized as anaphylactic hypersensitivity based on the presence of compromised respiratory or cardiovascular function in addition to skin or mucosal involvement (e.g., facial swelling, hives, angioedema, pruritus, flushing). The other 81 cases were categorized as non-anaphylactic hypersensitivity based on the presence of severe, isolated skin or mucosal involvement without associated respiratory or cardiovascular changes. Approximately 42 percent (n=55) of the 131 hypersensitivity events occurred within minutes to 24 hours of product use. Approximately 43 percent (n=56) of the patients reported discontinuing use of the suspected product. Of the 56 patients who reported discontinuing product use, 73 percent (n=41) experienced some degree of recovery from their symptoms once the drug was discontinued; final outcomes were not provided in the remaining cases. In addition, four patients reported a reappearance of their hypersensitivity reaction once the product was reintroduced.