Contact Dermatitis from Topical Drug Products for Cutaneous Application: Human Safety Assessment

Guidance for Industry

DRAFT GUIDANCE

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For questions regarding this draft document, contact (CDER) Jennifer Harmon at 240-402-4880.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

March 2020
Clinical/Medical

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TABLE OF CONTENTS

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I. INTRODUCTION

The purpose of this guidance is to provide FDA's current thinking about local safety assessment for the risk of contact dermatitis (irritant, allergic, and photoallergic) during development of new drug products[2] intended for topical application to the skin. The recommendations in this guidance are informed in part by the public workshop entitled "Human Dermal (Skin) Safety Testing for Topical Drug Products," which FDA hosted on September 10, 2018.[3]

This guidance does not address local safety assessment for other cutaneous adverse reactions (e.g., hyperpigmentation, atrophy) for topical drug products, local safety assessment for transdermal systems, evaluation of nonprescription drug ingredients to determine whether they are "generally recognized as safe," or development of generic drug products. It also does not address phototoxicity (photoirritation), as this topic has been addressed in the ICH guidance for industry *S10 Photosafety Evaluation of Pharmaceuticals* (January 2015).[4]

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of

[1] This guidance has been prepared by the Division of Dermatology and Dental Products in the Center for Drug Evaluation and Research at the Food and Drug Administration.

[2] For the purposes of this guidance, all references to *drugs* include both human drugs and therapeutic biological products unless otherwise specified.

[3] Check the workshop web page at https://www.fda.gov/drugs/news-events-human-drugs/human-dermal-skin-safety-testing-topical-drug-products-regulatory-utility-and-evaluation-public.

[4] We update guidances periodically. To make sure you have the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

Topical drug products have the potential to induce contact dermatitis because of their route of administration. Information about contact dermatitis, including the etiology (e.g., irritant, allergic, photoallergic), incidence, and severity, is incorporated into labeling to inform treatment decisions and is most clinically relevant when derived from clinical trials that replicate labeled conditions of use.

III. RECOMMENDATIONS

We recommend assessing local skin reactions in clinical studies conducted during topical drug product development:

- Use static (e.g., current state, noncomparative) scales to evaluate cutaneous signs such as erythema, edema, and erosion.
- Use patient-reported outcome measures to assess symptoms such as pruritus or burning.
- Plan the timing and frequency of assessments to identify anticipated reactions.
- Characterize suspected adverse reactions of allergic or photoallergic contact dermatitis using diagnostic patch testing or photopatch testing with the individual ingredients (active and excipient) as well as the product.

We encourage sponsors to obtain information about contact dermatitis from study conditions that reflect proposed labeled use and to meet with FDA to discuss planned safety assessments. Separate studies designed solely to elicit contact dermatitis are not generally needed.

We also recommend that applicants submit information from existing databases regarding known associations of individual ingredients with allergic or photoallergic contact reactions.