Atopic Dermatitis: Timing of Pediatric Studies During Development of Systemic Drugs
Guidance for Industry

DRAFT GUIDANCE

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For questions regarding this draft document, contact (CDER) CDR Dawn Williams at 301-796-5376, or (CBER) the Office of Communication, Outreach, and Development at 800-835-4709 or 240-402-8010.

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

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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

I. INTRODUCTION AND BACKGROUND

This guidance addresses FDA's current thinking about the relevant age groups to study and how early in a drug's development pediatric patients should be incorporated during development of systemic drugs for atopic dermatitis (AD). The recommendations in this guidance are based on input received from the March 9, 2015, Dermatologic and Ophthalmic Drug Advisory Committee (DODAC) meeting on this topic and review of medical literature and relevant statutes and regulations. This guidance does not address the technical aspects of drug development for pediatric patients with AD, which will be addressed in a future guidance.[2]

AD is a chronic pruritic inflammatory skin disease that primarily affects pediatric patients but also occurs in adults. AD is associated with substantial morbidity, including sleep disruption, decreased neurocognitive function, and impaired quality of life for patients and their families. AD is also associated with numerous comorbidities, including cutaneous infections, extracutaneous infections, asthma, rhinitis, food allergies, obesity, and hypertension.

Historically, FDA recommended that applicants provide data on the use of topical drug products in pediatric patients for treatment of AD before initial drug approval. In contrast, FDA did not recommend initiation of pediatric studies for systemic drugs under development for treatment of AD until after approval for adult use. At its March 9, 2015, meeting, the DODAC recommended

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

[2] Currently available is the draft guidance for industry *General Clinical Pharmacology Considerations for Pediatric Studies for Drugs and Biological Products*. When final, this guidance will represent the FDA's current thinking on this topic. For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

that, for systemic drugs for AD, pediatric studies generally should be initiated earlier during development.[3]

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

II. TIMING OF PEDIATRIC STUDIES OF SYSTEMIC DRUGS FOR AD

Applicants should consider the following recommendations concerning the timing of pediatric studies of systemic drugs for AD, the relevant age groups to study, and the inclusion of pediatric use information in labeling at the time of initial approval:

- Applicants should provide as much information as possible in labeling regarding use in relevant pediatric populations at the time of initial approval to facilitate an understanding of how to use the drug safely and effectively in pediatric patients.

- Studies of systemic treatments in pediatric patients with AD should be initiated early in development, typically after obtaining initial evidence of efficacy and safety from early phase studies in adults. Applicants are encouraged to discuss the specifics of pediatric programs as early as is feasible with the division because sponsors are required to submit pediatric study plans under section 505B of the Federal Food, Drug, and Cosmetic Act no later than 60 days after an end-of-phase 2 meeting.[4]

- A juvenile animal toxicity study that incorporates appropriate endpoints should be considered before enrollment of pediatric patients with AD in clinical studies.

- Some major safety questions, such as the risk for long-latency or low-frequency adverse reactions, may not be resolved before initiation of studies in pediatric patients with AD. Considering the effect on the pediatric population of disease-related morbidity, the risk of disease-related progression (e.g., atopic march), and the relative risk-benefit calculus with off-label use of immunosuppressive therapies,[5] it is not generally necessary to have an extensive safety database in adults before initiation of pediatric studies.

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[3] See the 2015 DODAC meeting materials available at https://wayback.archive-it.org/7993/20170111202321/http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/DermatologicandOphthalmicDrugsAdvisoryCommittee/ucm431514.htm.

[4] See the draft guidance for industry *Pediatric Study Plans: Content of and Process for Submitting Initial Pediatric Study Plans and Amended Initial Pediatric Study Plans*. When final, this guidance will represent the FDA's current thinking on this topic.

[5] Sidbury R, Davis DM, Cohen DE, Cordoro KM, Berger TG, Bergman JN et al., 2014, Guidelines of Care for the Management of Atopic Dermatitis: Section 3. Management and Treatment With Phototherapy and Systemic Agents, J Am Acad Dermatol, Aug,71(2):327–349.

- It is important to study all relevant age groups, including children younger than 2 years of age. A sequential approach (i.e., studying older pediatric subpopulations before younger subpopulations) may not be needed unless:

  – Specific information from the older subpopulation (e.g., pharmacokinetic information) is needed to inform the study design for the younger subpopulation;

  – An age-related technical issue (e.g., development of an age-appropriate dosage form or measurement instrument) needs to be addressed before study of the younger subpopulation; or

  – A safety concern is expected to arise in a younger subpopulation (e.g., because of immaturity of metabolic pathways), even if it was not observed in an older subpopulation.