
Male Breast Cancer: Developing Drugs for Treatment Guidance for Industry

**U.S. Department of Health and Human Services
Food and Drug Administration
Oncology Center of Excellence (OCE)
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)**

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Contains Nonbinding Recommendations

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This guidance represents 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

This guidance provides recommendations to sponsors regarding the development and labeling of cancer drugs, including biological products,² regulated by CDER and CBER for the treatment of male patients with breast cancer.

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. BACKGROUND

Breast cancer is rare in males, with less than one percent of all breast cancer cases occurring in male patients. In addition, males are more likely to be diagnosed at an older age, with a more advanced stage of disease, and are more likely to have lymph node involvement compared to females with breast cancer.

Males have historically been excluded from clinical trials of breast cancer drugs because breast cancer in males is rare. This exclusion has resulted in limited FDA-approved treatment options for males with breast cancer. Treatment strategies for males with breast cancer are not based on data from prospective, randomized clinical trials. Rather, clinical management of male breast cancer is generally based on clinical experience with breast cancer in females and data from studies conducted in females with breast cancer.

¹ This guidance has been prepared by the Oncology Center of Excellence, the Center for Drug Evaluation and Research (CDER), and the Center for Biologics Evaluation and Research (CBER) at the Food and Drug Administration.

² For the purposes of this guidance, references to *drugs* include drugs approved under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) and biological products licensed under section 351 of the Public Health Service Act (42 U.S.C. 262).

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III. RECOMMENDATIONS

FDA encourages sponsors to discuss their breast cancer drug development plan early in development with CDER or CBER, as applicable. These discussions may include expectations related to the number of male patients and data in male patients for specific development programs. FDA recommends the following:

- Eligibility criteria for clinical trials of breast cancer drugs should allow for inclusion of both males and females
 - Scientific rationale should be included in the protocol when proposing to exclude males from breast cancer trials. FDA does not intend to consider low expected accrual rates of male patients with breast cancer to be a sufficient scientific rationale for excluding them from a clinical trial.
- When males have not been included or when inclusion of males is very limited in clinical trials for a specific breast cancer drug:
 - It may be possible to extrapolate findings to include male patients in the FDA-approved indication for the drug where no difference in efficacy or safety is anticipated between males and females based on the mechanism of action of a drug. The use of extrapolation should be supported by, for example, data from earlier stages of development (e.g., nonclinical testing), literature, or both.
 - Further clinical data may be necessary to support extrapolation of findings to support an FDA-approved indication for male patients with breast cancer where there is a concern for differential efficacy or safety between males and females. In breast cancer, this may be relevant when a drug results in or relies upon manipulation of the hormonal axis, as with endocrine therapy. The additional data to support efficacy and safety for male patients with breast cancer can be generated through a variety of trial designs using different data sources, including small single-arm trials and studies using real-world data sources.
- In general, when males are included in clinical trials evaluating breast cancer drugs, sponsors should conduct nonclinical general toxicology studies in male and female animals.^{3, 4}

³ For nonclinical data needed to support clinical trial design and marketing applications, refer to ICH guidance for industry *S9 Nonclinical Evaluation for Anticancer Pharmaceuticals* (March 2010), ICH guidance for industry *S9 Nonclinical Evaluation for Anticancer Pharmaceuticals Questions and Answers* (June 2018), and guidance for industry *Oncology Pharmaceuticals: Reproductive Toxicity Testing and Labeling Recommendations* (May 2019). We update guidances periodically. For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/regulatory-information/search-fda-guidance-documents>.

⁴ The Agency supports the principles of the 3Rs to reduce, refine, and replace animal use in testing when feasible. Sponsors can consult with the Agency if they wish to use other testing methods or strategies. The Agency will consider whether such an alternative method or strategy could be used instead of an animal study.