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APPLICATION NUMBER:

210326Orig1s000

CLINICAL REVIEW(S)

CLINICAL REVIEW

Application Type	Commercial
Application Number(s)	210326
Priority or Standard	Standard
Submit Date(s)	03/20/2019
Received Date(s)	
PDUFA Goal Date	05/20/2019
Division / Office	DOP1/OHOP
Reviewer Name(s)	Tara Berman, MD
Review Completion Date	5/15/19
Established Name	Fulvestrant Injection
Therapeutic Class	Hormone antagonist
Applicant	Fresenius Kabi USA, LLC
Formulation(s)	Injection
Dosing Regimen	250 mg per 5 mL syringe for intramuscular injection
Indication(s)	Monotherapy Fulvestrant Injection is indicated for the treatment of: • Hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced breast cancer in postmenopausal women not previously treated with endocrine therapy, or • HR-positive advanced breast cancer in postmenopausal women with disease progression following endocrine therapy. Combination Therapy Fulvestrant Injection is indicated for the treatment of: • HR-positive, HER2-negative advanced or metastatic breast cancer in postmenopausal women in combination with ribociclib as initial endocrine based therapy or following disease progression on endocrine therapy. • HR-positive, HER2-negative advanced or metastatic breast cancer in combination with palbociclib or abemaciclib in women with disease progression after endocrine therapy.

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1 Recommendations/Risk Benefit Assessment

1.1 Recommendation on Regulatory Action

This NDA is for fulvestrant injection, in accordance with section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, was submitted to request approval of therapeutic equivalence and alternative formulation of the proposed product to the Listed Drug (LD) Faslodex® injection under NDA 201326. For approval, this application intends to rely on FDA's finding of safety and effectiveness of the LD that led to approval on April 25, 2002 for the treatment of hormone receptor positive metastatic breast cancer in postmenopausal women with disease progression following antiestrogen therapy. In 2017, two additional indications were added: 1) for the treatment of HR-positive, HER2-negative advanced breast cancer in postmenopausal women not previously treated with endocrine therapy; and 2) for the treatment of HR-positive, HER2-negative advanced or metastatic breast cancer in combination with abemaciclib in women with disease progression after endocrine therapy. This is a resubmission for this product, submitted March 20, 2019.

Based on the review of the CMC, nonclinical and bioequivalence studies, as well as the submitted documentation, this 505(b)(2) application is recommended for approval for all indications for which Faslodex® has been approved. This application has been cleared for regular approval by the Office of Regulatory Policy, OND/CDER, following an analysis of the consent judgement issued January 22, 2018.

1.2 Risk Benefit Assessment

Please refer to the clinical review for the initial submission for NDA 210326, dated May 30, 2018, for the Risk/Benefit Assessment, as well as other pertinent details of the application.

2 Introduction and Regulatory Background

2.1 Product Information

Established name: Fulvestrant injection, for intravenous use

Proprietary name: Fulvestrant Injection

Applicant name: Fresenius Kabi USA, LLC

Drug Class: Steroidal estrogen receptor antagonist

Proposed Indications:

Monotherapy
Fulvestrant Injection is indicated for the treatment of:

- Hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced breast cancer in postmenopausal women not previously treated with endocrine therapy, or
- HR-positive advanced breast cancer in postmenopausal women with disease progression following endocrine therapy.

Combination Therapy
Fulvestrant Injection is indicated for the treatment of:

- HR-positive, HER2-negative advanced or metastatic breast cancer in postmenopausal women in combination with ribociclib as initial endocrine based therapy or following disease progression on endocrine therapy.
- HR-positive, HER2-negative advanced or metastatic breast cancer in combination with palbociclib or abemaciclib in women with disease progression after endocrine therapy.

2.2 Summary of Presubmission Regulatory Activity Related to Submission

This is a class one resubmission for this product, initially granted tentative approval in 2018.

Other pre-IND activities in the past have included written responses provided to the sponsor by FDA on 06/30/14, 09/22/2014, 01/28/2015, 03/23/2016, and 04/26/2016.

2.3 Pediatric Waiver

Waiver for pediatric studies was requested on 08/31/2017.

2.4 Other Relevant Background

Refer to the CDTL review for NDA 210326 dated May 30, 2018.

3 Significant Efficacy/Safety Issues Related to Other Review Disciplines

Please refer to NDA 210326 CMC, Nonclinical, and Clinical Pharmacology reviews.

4 Sources of Clinical Data

Refer to the CDTL review for NDA 210326 dated May 30, 2018.

5 Review of Efficacy

Refer to the CDTL review for NDA 210326 dated May 30, 2018.

6 Review of Safety

Refer to the CDTL review for NDA 210326 dated May 30, 2018.

7 Appendices

7.1 Literature Review/ References

Refer to the CDTL review for NDA 210326 dated May 30, 2018. 7.2 Labeling Recommendations

See final label.

7.3 Advisory Committee Meeting

None

APPEARS THIS WAY ON ORIGINAL

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

SANJEEVE BALASUBRAMANIAM on behalf of TARA A BERMAN
05/20/2019 12:55:17 PM

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