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RESEARCH**

APPLICATION NUMBER:

020687Orig1s020

CHEMISTRY REVIEW(S)

(b) (6)

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Chemistry Review of Efficacy Supplement with PLR label conversion

For Clinical Division:

(b) (6)

REVIEW #2:

Mifeprex

20-687/ S-020

Efficacy Supplement with Labeling/PLR Conversion

Letter date: 28-May-2015

Stamp date: 29-May-2015

Final label submitted: 17-Mar-2016

Review Date: 21-Mar-2016

Chemistry Reviewer: (b) (6)

Chemistry Review #2

Chemistry review #2 evaluates the DOSAGE FORMS AND ADMINISTRATION and HOW SUPPLIED sections updated in the Final Label submitted on 17-Mar-2016. These sections reflect that the drug product will be provided as one tablet per blister card.

All other evaluation of the label and supplement 20 is provided in chemistry review #1 by [REDACTED]^{(b) (6)}, dated January 2016.

Highlights of Prescribing Information:

The dosage forms and strengths section is the following:

-----**DOSAGE FORMS AND STRENGTHS**-----
Tablets containing 200 mg of mifepristone each, supplied as 1 tablet on one blister card

Evaluation: Acceptable

PRESCRIBING INFORMATION

The dosage forms and strengths section is the following:

3 DOSAGE FORMS AND STRENGTHS

Tablets containing 200 mg of mifepristone each, supplied as 1 tablet on one blister card. MIFEPREX tablets are light yellow, cylindrical, and bi-convex tablets, approximately 11 mm in diameter and imprinted on one side with "MF."

Evaluation: Acceptable.

Section 16

16 HOW SUPPLIED/STORAGE AND HANDLING

MIFEPREX is only available through a restricted program called the MIFEPREX REMS Program [see *Warnings and Precautions* (5.3)].

MIFEPREX is supplied as light yellow, cylindrical, and bi-convex tablets imprinted on one side with "MF." Each tablet contains 200 mg of mifepristone. One tablet is individually blistered on one blister card that is packaged in an individual package (National Drug Code 64875-001-01).

Store at 25°C (77°F); excursions permitted to 15 to 30°C (59 to 86°F) [see USP Controlled Room Temperature].

Evaluation: Acceptable.

ELECTRONIC SIGNATURES

(b) (6), chemistry reviewer, (b) (6) / (b) (6) (b) (6)

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Chemistry Review of Efficacy Supplement with PLR label conversion

For Clinical Division:

(b) (6)

REVIEW OF:

Mifeprex

20-687/ S-020

Efficacy Supplement with Labeling/PLR Conversion

Letter date: 28-May-2015

Stamp date: 29-May-2015

Review Date: 11-Jan-2016

Chemistry Reviewer: (b) (6)

Chemistry Review

Mifeprex NDA 20-687/ S020, received 28-May-2015, from Danco Laboratories, LLC, is an efficacy supplement that provides for the following changes to the approved indication and dosing regimen for Mifeprex:

1. Decrease mifepristone dose from 600 to 200 mg
2. May administration misoprostol at home
3. Administration of misoprostol at 24-48 hours instead of 48 hours
4. Follow up needed, but not necessarily in clinic at 14 days
5. Buccal administration of misoprostol and increase in gestational age from 49 days (b) (4)
6. Change in the labeled time for expulsion from 4-24 hours to 2-24 hours post misoprostol administration
7. Add that a repeat dose of misoprostol may be used if needed
8. Changes to the label adverse event profile
9. Change "licensed physician" to "(b) (4)" in the label and Risk Evaluation and Mitigation Strategies (REMS) document
10. Change indication to add misoprostol: "Mifeprex is indicated, in a regimen with misoprostol, for the medical termination of pregnancy (b) (4)."
11. Remove references to "under Federal law" from the Prescriber's Agreement
12. Addressing the Pediatric Research Equity Act (PREA) requirement for pediatric studies

In the currently approved dosing, three 200 mg tablets are administered. In the proposed supplement, one 200 mg tablet will be administered.

Chemistry Evaluation of Efficacy Supplement

Acceptable

No changes have been made in the approved chemistry, manufacturing and controls. The approved 200 mg tablet will be used.

This review evaluates the PLR conversion of the labeling. Sections 3, 11, and 16 of the PLR labeling, and the Highlights of Prescribing Information, have been evaluated from a chemistry perspective.

Overall Evaluation: Acceptable. The labeling provided in Section 3, Section 11, and Section 16, and the Highlights of Prescribing Information, is identical in content to the approved information. The PLR conversion labeling, therefore, is

acceptable from a chemistry perspective. The PLR label also corresponds to the content and format required in 21 CFR 201.57.

Highlights of Prescribing Information:

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use MIFEPREX safely and effectively. See full prescribing information for MIFEPREX.

MIFEPREX® (mifepristone) tablets, for oral use
Initial U.S. Approval: 2000

- Instruct the patient what to do if significant adverse reactions occur. (2.3)
- Follow-up is needed to confirm complete termination of pregnancy. (2.4)

DOSAGE FORMS AND STRENGTHS

Tablets containing 200 mg of mifepristone each, supplied as (b) (4) on one blister card (3)

CONTRAINDICATIONS

- Confirmed/suspected ectopic pregnancy or undiagnosed adnexal mass (4)
- Chronic adrenal failure (4)

This section contains the proprietary and established name along with the approved route or administration.

Evaluation: Acceptable

Section 3

3 DOSAGE FORMS AND STRENGTHS

Tablets containing 200 mg of mifepristone each, supplied as (b) (4) on one blister card. Mifeprex tablets are light yellow, cylindrical, and bi-convex tablets, approximately 11 mm in diameter and imprinted on one side with "MF."

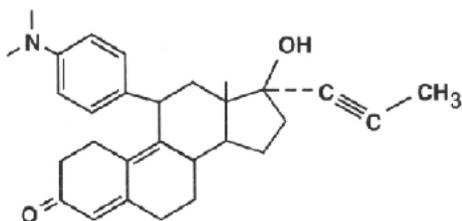
Evaluation: Acceptable. The information is the approved information.

Section 11

11 DESCRIPTION

Mifeprex tablets each contain 200 mg of mifepristone, a synthetic steroid with antiprogesterational effects. The tablets are light yellow in color, cylindrical, and bi-convex, and are intended for oral administration only. The tablets include the inactive ingredients colloidal silica anhydrous, corn starch, povidone, microcrystalline cellulose, and magnesium stearate.

Mifepristone is a substituted 19-nor steroid compound chemically designated as 11β-[p-(Dimethylamino)phenyl]-17β-hydroxy-17-(1-propynyl)estra-4,9-dien-3-one. Its empirical formula is C₂₉H₃₅NO₂. Its structural formula is:



The compound is a yellow powder with a molecular weight of 429.6 and a melting point of 192-196°C. It is very soluble in methanol, chloroform and acetone and poorly soluble in water, hexane and isopropyl ether.

Evaluation: Acceptable. The information is the approved information.

Section 16

16 HOW SUPPLIED/STORAGE AND HANDLING

(b) (4)

Mifeprex is supplied as light yellow, cylindrical, and bi-convex tablets imprinted on one side with "MF." Each tablet contains 200 mg of mifepristone. (b) (4) individually blistered on one blister card that is packaged in an individual package (National Drug Code 64875-001-03).

Store at 25°C (77°F); excursions permitted to 15 to 30°C (59 to 86°F) [see USP Controlled Room Temperature].

Evaluation: Acceptable. The information is the approved information.

ELECTRONIC SIGNATURES

(b) (6) chemistry reviewer, (b) (6) (b) (6) (b) (6)

(b) (6) signing for (b) (6), (b) (6) / (b) (6)

(b) (6)