ABORTIONS IN THE U.S.
INTERNET WEB SITES FOR FURTHER INFORMATION

The Henry J. Kaiser Family Foundation at www.kff.org

The Alan Guttmacher Institute at www.agi-usa.org

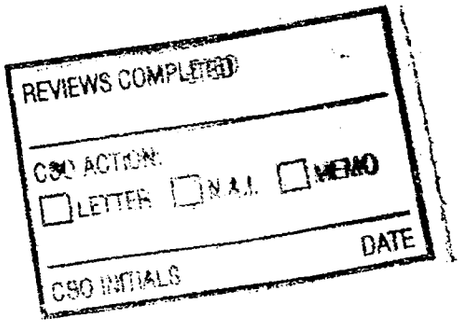
ORIGINAL

ORIG AMENDMENT

B2

NDA 20-687
Mifepristone Tablets, 200 mg

International Product Labeling with English Translations



Population Council
New York, New York 10017

Table of Contents

International Product Labeling with English Translations
NDA 20-687
Mifepristone Tablets, 200 mg

Introduction

Copies of approved currently available international product labeling with English translations are provided in response to the Approvable Letter of February 18, 2000 received by the Population Council from the Food and Drug Administration. The attached product labeling was provided by Exelgyn, the European marketer of mifepristone.

A European market authorization (MA) for mifepristone was obtained on July 6, 1999 for a selected number of countries through the mutual recognition procedure (MRP) where France acted as a Reference Member State (RMS). These countries are Austria, Belgium, Denmark, Finland, Germany, Greece, Netherlands and Spain. The product labeling for each of these nine (9) countries including France corresponds to the English translation of the European Summary of Product Characteristics (SPC) included in Appendix 1. Each country had the English version of the European SPC translated into their native language.

Appendix 2 includes a copy of the English version of the European Patient's Information Leaflet. The Patient's Information Leaflets have been modified to conform with local/national requests and regulations and therefore the texts in the local language do not correspond exactly to this English version. However, the contents of the Patient's Information Leaflets are essentially the same as the English version. A Patient Information Leaflet is not required in Denmark or Finland.

Copies of the product labeling for Austria, Belgium, Denmark, Finland, Germany, Greece, Netherlands, Spain and France are included in Appendices 3-11, respectively.

Also included are copies of product labeling for Sweden (Appendix 12), Israel (Appendix 13) and Russia (Appendix 14). The labeling for Russia has not been translated into English.

Copies of product labeling from the United Kingdom and Switzerland were included in our submission dated September 30, 1999 to NDA 20-687.

are awaiting final approved labeling.

Appendix 1

European Summary of Product Characteristics (SPC) Approved July 6, 1999

This is the English translation for the product labeling for Austria, Belgium, Denmark, Finland, France, Germany, Greece, the Netherlands and Spain. Each country had this English version of the European SPC translated into their native language.

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

MIFEGYNE® 200 mg tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 200-mg mifepristone.

3. PHARMACEUTICAL FORM

Tablet.
Light yellow, cylindrical, biconvex tablets marked "167 B" on one side.

4. CLINICAL PARTICULARS

For termination of pregnancy, MIFEGYNE® and the prostaglandin can only be prescribed and administered in accordance with the countries laws and regulations.

As a consequence, they can only be prescribed by a medical doctor and in public or private hospital or centre (having approval to undertake termination of pregnancy). The product will be administered in the presence of the medical practitioner or of a delegated health professional.

If required by the afore mentioned laws and regulations, the patient should sign a letter of informed consent to certify that she has been fully informed about the method and its risks.

This timing of the first visit should take into account the requirement of some countries for a period of reflection prior to the abortion procedure.

4.1 Therapeutic indications

1- **Medical termination of developing intra-uterine pregnancy.**

In sequential use with a prostaglandin analogue, up to 49 days of amenorrhea.

2- **Softening and dilatation of the cervix uteri prior to surgical termination of pregnancy during the first trimester.**

3- **Preparation for the action of prostaglandin analogues in the termination of pregnancy for medical reasons *(beyond the first trimester).***

4- **Labour induction in foetal death in utero.**

In patients where prostaglandin or oxytocin cannot be used.

127
3

4.2 Posology and Method of Administration

1- Medical termination of developing intra-uterine pregnancy

The method of administration will be as follows:

600 mg of mifepristone (i.e. 3 tablets of 200 mg each) is taken in a single oral dose, followed by 36 to 48 hours later, the administration of a prostaglandin analogue; misoprostol 400 µg orally, or gemeprost 1 mg per vaginum.

2- Softening and dilatation of the cervix uteri prior to surgical termination of pregnancy during the first trimester

200 mg of mifepristone (one tablet), followed 36 to 48 hours later (but not beyond) by surgical termination of pregnancy.

3- Preparation for the action of prostaglandin analogues in the termination of pregnancy for medical reasons

600 mg of mifepristone (i.e. 3 tablets of 200 mg each) taken in a single oral dose, 36 to 48 hours prior to scheduled prostaglandin administration which will be repeated as often as indicated.

4- Labour induction in foetal death in utero

600 mg of mifepristone (e.g. 3 tablets of 200 mg each) in a single oral daily dose, for two consecutive days.

Labour should be induced by the usual methods if it has not started within 72 hours following the first administration of mifepristone.

4.3 Contra-indications

This product SHOULD NEVER be prescribed in the following situations.

<u>In all indications</u>

- chronic adrenal failure
- known allergy to mifepristone or to any component of the product
- severe asthma uncontrolled by therapy

<u>In the indication: medical termination of developing intra-uterine pregnancy</u>

- pregnancy not confirmed by ultrasound scan or biological tests
- pregnancy of 50 days' amenorrhea and beyond
- suspected extra-uterine pregnancy
- contra-indication to the prostaglandin analogue selected

128

4

In the indication: softening and dilatation of the cervix uteri prior to surgical termination of pregnancy:

- pregnancy not confirmed by ultrasound scan or biological test
- pregnancy of 84 days of amenorrhea and beyond (according to legal requirements)
- suspected extra-uterine pregnancy

Preparation for the action of prostaglandin analogues in the termination of pregnancy for medical reasons *(beyond the first trimester)*

- contra-indications to the prostaglandin analogue selected

Labour induction in foetal death in utero

Should prostaglandin combination be required, refer to contra-indications to the prostaglandin analogue selected.

4.4 Special warnings and special precautions for use

Warnings

In the absence of specific studies, MIFEGYNE® is not recommended in patients with:

- ***Renal failure***
- ***Hepatic failure***
- ***Malnutrition***

1- Medical termination of developing intra-uterine pregnancy

This method requires an active involvement of the woman who should be informed of the method's requirements:

- the necessity to combine treatment with prostaglandin to be administered at a second visit,
- the need for a control visit (3rd visit) within 10 to 14 days after MIFEGYNE's intake in order to check for complete expulsion,
- The possible failure of the method, leading to a pregnancy termination by another method.

In the case of a pregnancy occurring with an intra-uterine device in situ, this device must be removed before administration of MIFEGYNE®.

The expulsion may take place before prostaglandin administration (in about 3% of cases). This does not preclude the control visit in order to check for the complete expulsion and the uterine vacuity.

- Risks related to the method

  - Failures

    The non-negligible risk of failure, which occurs in 1.3 to 7.5 % of the cases, makes the control visit mandatory in order to check that the expulsion is completed.

  - Bleeding

    The patient must be informed of the occurrence of prolonged vaginal bleeding (up to 12 days after MIFEGYNE® intake) which may be heavy. Bleeding occurs in almost all cases and is not in anyway a proof of complete expulsion.

    The patient should be informed not to travel far away from the prescribing centre as long as complete expulsion has not been recorded. She will receive precise instructions as to whom she should contact and where to go, in the event of any problems emerging, particularly in the case of very heavy vaginal bleeding.

A follow-up visit must take place within a period of 10 to 14 days after administration of MIFEGYNE® to verify by the appropriate means (clinical examination, ultrasound scan, and Beta-HCG measurement) that expulsion has been completed and that vaginal bleeding has stopped. In case of persistent bleeding (even light) beyond the control visit, its disappearance should be checked within a few days.

If an ongoing pregnancy is suspected, a further ultrasound scan may be required to evaluate its viability.

Persistence of vaginal bleeding at this point could signify incomplete abortion, or an unnoticed extra-uterine pregnancy, and appropriate treatment should be considered.

In the event of an ongoing pregnancy diagnosed after the control visit, termination by another method will be proposed to the woman.

Since heavy bleeding requiring hemostatic curettage occurs in 0 to 1.4% of the cases during the medical method of pregnancy termination, special care should be given to patients with hemostatic disorders with hypocoagulability, or with anemia. The decision to use the medical or the surgical method should be decided with specialised consultants according to the type of hemostatic disorder and the level of anaemia.

130
6