Drugs and Health Products

Regulatory decision summary: MIFEGYMISO

Active ingredient(s)
mifepristone, misoprostol

Therapeutic area
Progesterone Receptor Modulators

What was the purpose of this submission?

A New Drug Submission was filed to seek market authorization for Mifegymiso, a combination drug product of mifepristone and misoprostol, to be used sequentially for the termination of a developing intra-uterine pregnancy up to a gestational age of 49 days.

Why was the decision issued?

The decision to authorize Mifegymiso for the Canadian market was made further to a thorough review of the data package provided by the sponsor that supported the safety, efficacy and quality of the product. The sponsor provided clinical, non-clinical and quality evidence in the form of study data, literature as well as post-approval experience in other countries. It also included proposed risk management measures designed to mitigate the risks known to be associated with this product. During the review process, requests for additional information and clarifications were satisfactorily addressed by the sponsor. Product labelling was revised in order to reflect and communicate the benefits, risks and uncertainties identified in the submission review. Therefore, based on the information in the submission and on the labelling and risk management measures proposed by the sponsor, it was concluded that the evidence provided supports the use of Mifegymiso for the medical termination of a developing intrauterine pregnancy with a gestational age up to 49 days as measured from the first day of the Last Menstrual Period based on a standard 28-day cycle.

The pharmacology evidence provided indicates that Mifegymiso acts to block progesterone effects on the endometrium and myometrium, allows cervical dilatation, and induces contractions of the uterine myometrium that leads to pregnancy termination.

The clinical data to support the authorized indication and dosing regimen were presented in three pivotal clinical trials involving a total of 934 women with a pregnancy with a gestational age of 49 days or less. These data demonstrated that 200 mg oral mifepristone followed by buccal administration of 800 mcg misoprostol 24 to 48 hours later effectively induced the termination of pregnancy in 95.2% to 98.0% of women.

Analysis of the pivotal trials revealed that the average bleeding time was 10.8 days including 2 days of heavy bleeding. The majority of adverse events reported were transient and mild to moderate in severity. The medication causes vaginal bleeding and commonly induced pain and cramping, which required pain medication in some women. The other adverse events more commonly reported were diarrhea, nausea, vomiting, fever/chills, headache, dizziness and weakness. Treatment failure (which was defined as viable pregnancy, non-viable persistent pregnancy, persistent bleeding and abdominal pain that required a surgical termination of pregnancy) was reported in 2% to 4.8% of women.

A small number of patients who took Mifegymiso presented more serious complications, such as pelvic infections (endometritis, salpingitis) and vaginal haemorrhages. Rare cases of fatalities were

reported, therefore access to emergency care which can provide gynaecological surgical procedures, antibiotic intravenous therapy and blood transfusion in the rare cases where complications occur, is recommended in the labelling to ensure patient's safety.

The data provided to support this indication included data for women less than 18 years of age. The efficacy of Mifegymiso in these patients was similar to that seen in adults, however nausea and pain were reported more frequently in these patients. There were insufficient data to comment on the safety and efficacy in patients less than 15 years of age.

The mifepristone formulation proposed for the Canadian market was tested in one trial and was shown bioequivalent to the formulation used in the two other trials. Bridging of misoprostol was considered sufficiently robust for regulatory approval based on chemistry, clinical and regulatory criteria. In addition, efficacy and safety of the proposed mifepristone and misoprostol combination were further supported in 5356 patients that have used Mifegymiso (200 mg oral mifepristone and 800 mcg buccal misoprostol) for the indication of medical termination of pregnancy as reported in an additional post market study.

To support the safe and effective use of Mifegymiso, Linepharma International Ltd. agreed to implement risk management activities including physician only dispensing, development of an education and registration program for prescribers and a post-approval observational safety study. Additional risk management measures include a 24 hour patient support line, a patient consent form and distribution of Patient Medication Information to be provided to each patient.

Decision issued

Approved; issued Notice of Compliance in accordance with the *Food and Drug Regulations*.

Date of decision

2015-07-29

For more information on Health Canada's decision, please view the Summary Basis of Decision.

Additional information

Manufacturer
Linepharma International Limited

Drug Identification Numbers (DIN) issued
DIN 02444038

Prescription status
Mifegymiso is available by prescription only.

Type of submission
New Drug Submission (New Active Substance)

Date filed
2012-11-14

Control number
160063

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