1 ABSTRACT

Post-Authorisation Surveillance Study of the Efficacy and Safety of Medabon (Mifepristone/Misoprostol) for Early Pregnancy Termination

Keywords

Medabon, outcome, Pregnancy termination, adverse events

Rationale and background

The combination regimen of Mifepristone and a prostaglandin analogue is well established for termination of early intrauterine pregnancy. The effective dose of Mifepristone has been demonstrated to be 200 mg, followed by 800 µg of vaginal Misoprostol (≤ 63 days of gestation). In addition, there is an approved alternative posology with 200 mg of Mifepristone for pregnancies up to 63 days of amenorrhea, provided the subsequent prostaglandin is vaginal gemeprost as reflected in the EU Summary of Product Characteristics (SPC) of Mifegyne.

There are no conclusive data showing that the increased exposure to Misoprostol with the Medabon formulation causes no additional undesirable effects compared to the same dose of Cytotec following vaginal administration. Therefore, this post-authorisation study was conducted to allow a direct and robust assessment of the safety and efficacy of Medabon in clinical practice, in comparison with historical data for the regimen of Mifepristone and Misoprostol.

Research question and objectives Study design

The present study assessed outcomes and safety associated with the use of Medabon (Mifepristone/Misoprostol) in subjects undergoing medical termination of developing intrauterine pregnancy of up to 63 days of amenorrhea. Data collected in this study further characterized the emergency evacuation rate, continuing pregnancy rate and requirement for surgical intervention for subjects receiving Medabon compared to the historical rates for this combination treatment using the regimen of Mifepristone (Mifegyne, Exelgyn Laboratories) and Misoprostol (Cytotec, Pfizer). Subjects were to be treated with Medabon per institutional practice and according to the European SPC, and followed for at least 10 to 14 days for treatment outcome, adverse events (AEs), and the requirement for other subsequent interventional treatment. If standard institutional ethical practice allowed, data from routine contact with the subject at 30 days were also collected in the Electronic Case Report Form (eCRF).

Setting

This was an open-label, non-interventional, prospective, observational, post-authorisation study of the outcomes and safety associated with the use of Medabon for the medical termination of developing intra-uterine pregnancy of up to 63 days of amenorrhoea conducted in 3 centres across Europe. This study was designed to obtain descriptive information on the safety and efficacy of Medabon in women undergoing termination of early pregnancy, and to evaluate and compare the emergency evacuation rate, continuing pregnancy rate and

requirement for surgical intervention to the historical rates for this combination treatment. Subjects requesting medical abortion were to be treated with Medabon per institutional practice in accordance with European SPC. This was followed by assessment of treatment outcome, AEs, and the requirement for other subsequent interventional treatment for at least 14 days.

Subjects and study size, including dropouts

There were 499 screened subjects, of which 498 were eligible (the subject 01/47 was not following the inclusion criteria 01 [Is she in good general health?] and 05 [The pregnancy is intrauterine]), 486 were in safety population and 482 in ITT population. Of 486 subjects (safety population), 345 subjects had completed the study. Of 482 subjects (ITT population), 344 subjects had completed the study.

Variables and data sources

Data from study centres were collected in electronic form via electronic data capture and data managed using SAS based clinical data management system (CDMS). The rate of incomplete abortion and continuing pregnancy at the time of the follow-up visit; (10 to 14 days after the administration of Mifepristone), requirement for subsequent surgical evacuation, the emergency evacuation rate (because of haemorrhage or other reason) were analyzed. Incidence of AEs related to Medabon treatment and necessity for additional medical treatment related to the termination of early pregnancy, such as the use of antibiotics to treat genital infections were captured.

Results

Of those subjects, who completed study, 98.3% of subject with complete abortion were on study drug. In addition, 10 (2.1%) and 9 (2.6%) subjects required manual vacuum aspiration (MVA) or electric vacuum aspiration (EVA) or surgical evacuation in ITT population and those who completed study, respectively. The percentage of complete abortion in subjects treated with Medabon were found to be higher when compared with historical data in subjects with $\leq$ 57 days of amenorrhea category (p value 0.0056). The rate of continuing pregnancy was 0.2% at the end of study for ITT population and 0.3% for subjects who completed the study. Adverse events were observed in 9.7% subjects in present study with severity in less than one percent subjects. Hospitalization was required for 0.8% subjects and medications were needed in 4.9% subjects for recovery.

Discussion

The drug was found to be safe and effective in subjects for medical termination of pregnancy. The percentage of incomplete abortion was lower in present study as compared to previous WHO (2003) study (1.9 % Vs 3.0 to 4.0% [intent to treat percentage in oral

Misoprostol, vaginal Misoprostol and oral Misoprostol and vaginal only Misoprostol, 3.5%, 3% and 4.2%; respectively]).