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International press release

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New French Good Practice Guidelines for Medical Abortion:

A big step towards safety and compliance for healthcare professionals and patients…

The HAS published new 2011 guidelines for Best Medical Practice for Medical Abortion Management. It confirmed that the protocol for MToP up to 49 DA with the higher risk/benefit ratio is 600 mg mifepristone associated with 400 µg misoprostol by the oral route 36 to 48 hours later. They also emphasized that patient choice is crucial: Every woman should be able to choose her abortion method whenever possible, both when deciding on the surgical vs. a medical method and when choosing whether or not to have a medical abortion at home.

New recommendations regarding Medical Termination of Pregnancy were recently published by the French Health Authority, the HAS (*Haute Autorité de Santé*).

Today, many countries offer both surgical and medical methods for terminating pregnancies to their female citizens. Access to these methods, delays and procedures vary according to national legislation.

Throughout its 25 years of experience in the field of Medical Termination of Pregnancy, Exelgyn has always dealt with wide diversity in terms of guidelines and practices. Many actions have been implemented in order to improve harmonization**. In 2007, after a global review of the literature and expert opinions**, **and following safety and efficacy concerns regarding the protocols used, the European Medicines Agency concluded that the available data support the effectiveness of a 600 mg dose of mifepristone** up to 63 days of amenorrhea. It confirmed that the risk/benefit profile of **mifepristone 600 mg in combination with oral misoprostol 400 µg** for pregnancies up to 49 days of amenorrhea is favorable.

Following this European arbitration, the Health Authorities of some countries decided to review their national guidelines.

Background

In France, medical abortion has been available for all women since Mifegyne® was launched in 1989. French practitioners have long used of Mifegyne in association with a prostaglandin analogue. Thanks to this method, women who want to terminate their pregnancy have an alternative to surgery.

The HAS reviewed and updated its 2001 recommendations on Medical Termination of Pregnancy management in order **to optimize and secure practices**.

In France, Clinical Practice Guidelines are defined as "proposals developed according to an explicit method in order to help healthcare professionals and patients to seek the most suitable care for a given clinical situation".

The HAS created a multidisciplinary, multi-professional working group composed of healthcare professionals in public or private practice, from various geographical areas or schools of thought. Their conclusion is based on the critical analysis and review of the available scientific literature as well as on the opinion of the multidisciplinary group of professionals involved in the subject. Indeed, peer reviewers were consulted to give their opinion on the content, structure of evidence and acceptability of the guidelines.

These guidelines concern women who wish to undergo a medical abortion and are intended for medical gynaecologists, obstetricians, general practitioners, midwives and any other health care professionals working in the public or private sector who may participate in medical Termination of Pregnancies.

These new recommendations, published in April 2011**,** are the result of a long and heavy investment leading to the following conclusions:

Choice: A woman's right

First, the HAS reiterates that, in all cases, whenever possible, **women should have the choice to select their method, medical or surgical, for terminating their pregnancy**. Moreover, they should receive detailed information to be able to make an enlightened choice. Indeed, practices reveal that in some countries where both methods are available**,** women still not have really the choice. This choice is a woman's right and needs to be strongly supported by abortion stakeholders.

Choice and receiving detailed information increase post-abortion satisfaction in women. According to the HAS, women who choose the medical method rather than the surgical one do so mainly to avoid surgery or general anesthesia and to have more control over the abortion process.

Medication strategy

The efficacy of the medical method is evaluated according to two criteria:

- the success rate, whereas success is defined as achieving complete abortion without needing a subsequent surgical procedure, regardless of the indication
- the rate of ongoing pregnancy.

❖ Medical Termination of Pregnancy up to 49 days of amenorrhea (DA)

The HAS recommends the therapeutic regimen mentioned in the Mifegyne® Marketing Authorization:

600 mg oral mifepristone followed 36 to 48 hours later by 400 µg misoprostol by the oral route

Oral mifepristone at a dose of 200 mg may be used when followed 36 to 48 hours later by 1 mg of gemeprost by the vaginal route. However, it should be noted that gemeprost, which is only administered vaginally and only used in hospitals, is very infrequently used in France due to the intense pain with which it is associated and its storage constraints.

By using approved and recommended regimens, the ongoing pregnancy rate is approximately 1%. Using a non-authorized protocol would lead to an increasing rate of ongoing pregnancies (up to 2.6%), and then to a number of additional unplanned pregnancies and which could be at risk..

They mention that the follow-up visit should allow detecting those on-going pregnancies but remind that this follow-up is not always performed. This could lead in country as France to up to 400 additional unplanned pregnancies.

Thus, the HAS has stated that the **risk/benefit ratio is less favorable with a 200 mg mifepristone regimen**. **Using a protocol with low dose mifepristone and higher dose misoprostol will further render the risk/benefit ratio unfavorable**, especially since it is acknowledged that **the higher the dose of prostaglandin used, the more adverse events there are.**

❖ Medical Termination of Pregnancy from 50 to 63 DA

For a pregnancy of 7 to 9 weeks of amenorrhea, French Authority does not really give a clear recommendation.

Mifegyne®'s Marketing Authorization (200 mg Mifegyne® + gemeprost) is mentioned in the HAS and they specify that 600 mg of mifepristone does not improve success rates and ongoing pregnancies rates when combined with gemeprost.

However, concerning the off-label combination with misoprostol, there is a **specific warning on the risk of using misoprostol vaginally: "more efficacious but more painful".** In addition to these pain issues, the HAS warned about the **risk of fatal septic shock when using misoprostol vaginally**. Recent fatal *Clostridium Sordellii* infection cases reported in Europe after the use of misoprostol vaginally have increased awareness about this administration route. Although the causal link between the vaginal administration of misoprostol and *Clostridium Sordellii* infection has not been established, **clinicians should consider this risk and respect the rules of good medication use.**

To sum up, after the EMA's arbitration, **the HAS once again confirmed the efficacy and tolerance of the Marketing Authorization regimens**. Moreover some strong arguments were clearly identified to support the approved dosages and administration routes.

Procedures for Medical Termination of Pregnancy management

Procedures for Medical Termination of Pregnancy management are country-dependent. The HAS reiterated the entire French procedure and highlighted two topics:

- **Give women the choice to take the misoprostol at home up to 49 DA**

The working group discussed the possibility of taking the misoprostol at home. Some healthcare professionals already perform this procedure, but these new recommendations further discuss this option.

In France, up to 7 weeks of amenorrhea, medical Termination of Pregnancy can be performed either in a health establishment (public or private) with or without post-misoprostol hospitalisation or in a private office.

According to clinical studies with the 600 mg mifepristone + 400 μg oral misoprostol protocol, 30 to 70 % of women expelled the products of conception within the first 3 hours, which is the standard duration of hospitalisation, and 75% to 85% of women expelled within the first 24 hours. Therefore, **there is a risk of expulsion during the woman's trip home even after a monitoring period of 3 hours.**

The frequency of home Termination of Pregnancy complications (like severe haemorrhage) is low and comparable to the frequency seen in TOPs performed in hospital settings. Therefore **there is no real medical reason for post-misoprostol monitoring**. Due to this, the second consultation becomes more and more virtual because women choose to take the misoprostol comfortably at home.

Some studies seem to demonstrate that administering misoprostol at home is considered acceptable by women. HAS recommends certain precautions, such as limiting the distance between a patient's home and the referent hospital (less than one hour), providing the patient with full information on adverse events and suitable painkillers and a 24/7 phone access.

According to studies, over 90% of women consider home misoprostol administration acceptable and almost 90% would choose this method again if they were faced with the same situation.

Finally, when possible, women who want to terminate their pregnancy by medical method should have the choice of being monitored in a medical institution or undergoing this procedure at home in a more private environment.

- **Increase awareness on the importance of the follow up visit**

These new French recommendations reiterate the importance of the follow-up visit. By checking the method's success with a clinical exam and a β-HCG test or an ultrasound, **this visit is a key step in medical termination of pregnancy management.**

During this visit, **appropriate birth control methods** need to be discussed with patients. This is also the appropriate time to offer psychological support.

French experts reiterate that this crucial step should be scheduled between the 14th and the 21st day post-mifepristone intake.

About Mifegyne®

Mifegyne® (mifepristone) is the first anti-progesterone molecule authorised for use in obstetrics and gynaecology.

In 1988, the first MA was obtained in France for medical termination of pregnancy up to 49 days of amenorrhea in combination with prostaglandin analogues.

Today, Mifegyne® is marketed in 25 European and non-European countries.

Mifegyne is an orally active antiprogestogen that acts by competing with endogenous progesterone for receptor binding sites. Therefore, administration of mifepristone during pregnancy has been shown to cause:

1. Detachment of the embryo, decrease of β-HCG and secondary luteolysis
2. Increase in myometrial activity
3. Opening and ripening of cervix

These effects elicit the following actions:

- Expulsion of the embryo in early pregnancy
- Easier mechanical cervical dilatation prior to vacuum aspiration
- A shorter induction/abortion interval in prostaglandin-induced termination of second trimester pregnancy and consequent reduced prostaglandin dose
- Induction of labour for foetal death *in utero* in the late second and third trimesters.

Now, Mifegyne® is registered in 4 indications in most countries:

- Medical termination of developing intra-uterine pregnancy in association with prostaglandin up to 63 Days of amenorrhea
- Softening and dilatation of the *cervix uteri* prior to surgical termination of pregnancy during the first trimester.
- Preparation for the action of prostaglandin analogues in the termination of pregnancy for medical reasons (beyond the first trimester).
- Labour induction in foetal death *in utero*.

Used in over 2 million procedures in more than 20 countries, Mifegyne® is recognized as a safe, effective and well-tolerated product by healthcare professionals who perform abortions.

About Exelgyn

Exelgyn was established in 1997 to be devoted to Mifegyne®, which is registered on the WHO's list of essential medicines. By offering this essential medicine to patients, Exelgyn has earned a reputation as a company that is active in promoting women's rights.

Exelgyn has taken the necessary risks to change the life of women for the discernible better. Our mission is to provide women with freedom of choice regarding their decision to terminate a pregnancy and access to the best medical method available to do so.

The company is known as a pioneer in medical termination of pregnancy in Europe and abroad. Exelgyn joined the Nordic Group in 2010 in their ongoing drive for excellence. Exelgyn priorities are patient safety, quality and customers' services. Synergies between the Nordic Group and Exelgyn enable us to strengthen our expertise and experience in gynecology medicines and the hospital market.

Exelgyn is proud to be focused and results driven. Intelligent communication to ensure that the right patients and physicians have the information they need to make appropriate choices about abortion methods is one of Exelgyn priorities.

If you have any questions, please feel free to contact:

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We would greatly appreciate receiving a copy of articles published based on this press release.