

**Patient Leaflet in accordance to Pharmacist's Regulations (Medications) 1986**

The medicine is marketed by prescription only

This medicine is approved for use only in a hospital or recognized clinic setting, for the termination of pregnancy, and only under a doctor's supervision.

Read this leaflet in its entirety before you use the medication. This leaflet summarizes information about the medication.

If you have any additional questions please contact your physician or your nurse.

Afterwards, you must sign an informed consent form.

This medication has been prescribed for you. Do not give it to others, as it may cause them harm, even if it seems that their medical condition is similar to yours.

## Mifegyne

### Oral Tablets

**Active ingredient: Mifepristone 200 mg**

For a list of excipients see section 6 at the end of this leaflet.

### 1. WHAT THIS MEDICINE INTENDED FOR

**Mifegyne** is recommended to be used:

1. For the medical termination of a pregnancy:
  - no later than 63 days after the first day of your last menstrual cycle (until period is 35 days (5 weeks) late in a woman with regular menstrual cycles).
  - in combination with a second medicine, a prostaglandin (a substance that triggers contraction of the womb and softens the cervix), which you take 36 to 48 hours after taking Mifegyne.
2. Softening and dilatation of the cervix before surgical termination of pregnancy within the first trimester (up to 84 days from the start of the last period).
3. Termination of pregnancy after the first trimester (for medical reasons) as pre-treatment before giving prostaglandins (which cause uterine contractions).
4. To induce labor in cases where the fetus has died in the womb and where it is not possible to use other medical treatments (prostaglandin or oxytocin).

### Therapeutic Group:

**Mifegyne** oral tablets include the active ingredient Mifepristone which is anti-hormone, a synthetic steroid that works by blocking the action of the hormone progesterone (a hormone which is needed for pregnancy to continue). Therefore, **Mifegyne** can cause termination of pregnancy. It can also be used to soften and open the cervix.

The efficacy of the method is not perfect and in isolated cases curettage (a regular surgical abortion) may be necessary in order to complete the termination of pregnancy or to stop severe bleeding.

### Mechanism of Action:

1. Medical termination of a pregnancy up to 63 days includes taking two types of tablets: 3 tablets of **Mifegyne** (mifepristone 200 mg x 3) and after about two days, treatment with a prostaglandin analogue. **Mifegyne** tablets work by blocking the action of the hormone progesterone which supports and maintains the pregnancy. The prostaglandin causes uterine contractions, relaxation and dilatation of the cervix.
2. Prior to a surgical abortion, **Mifegyne** causes softening and dilatation of the cervix, thus aiding performance of the curettage.
3. In termination of pregnancy after the first trimester, **Mifegyne** is given in combination with prostaglandins which cause uterine contractions and expulsion of the pregnancy.

## **2. BEFORE USING THE MEDICINE**

### **Do not take Mifegyne if:**

- **In all cases (as mentioned in section 1)**
  - if you are allergic to mifepristone or any of the other ingredients of this medicine (listed in section 6),
  - if you suffer from adrenal failure,
  - if you suffer from severe asthma, which cannot be adequately treated with medication,
  - if you have hereditary porphyria.
- **In addition, do not take Mifegyne:**
  - **For termination of pregnancy up to 63 days after your last menstrual cycle:**
    - if your pregnancy has not been confirmed by a biological test or an ultrasound scan,
    - if the first day of your last menstrual cycle was more than 63 days ago,
    - if your doctor suspects an ectopic pregnancy (the egg is implanted outside the womb),
    - if you cannot take the selected prostaglandin analogue.
  - **For softening and opening the cervix before surgical termination of pregnancy:**
    - if the pregnancy has not been confirmed by a biological test or ultrasound scan,
    - if your doctor suspects an ectopic pregnancy,
    - if the first day of your last menstrual cycle was 84 days ago or more.
  - **For termination of pregnancy beyond 3 months pregnancy (for medical reasons):**
    - if you cannot take the selected prostaglandin analogue

**Inform the doctor if you suffer or have suffered in the past from any sort of disease or if you are breast-feeding.**

### **Special warnings regarding the use of the medicine:**

#### **Talk to your doctor before taking Mifegyne:**

- if you have liver or kidney disease,
- if you suffer from anaemia or malnutrition,
- if you have cardiovascular disease (heart or circulatory disease),
- if you are at increased risk of cardiovascular disease. Risk factors include being aged over 35 years and a cigarette smoker or having high blood pressure, high blood cholesterol levels or diabetes,
- if you have an illness that affects the clotting of your blood,
- if you suffer from asthma.

If you use a contraceptive coil, it must be removed before you take **Mifegyne**.

Before taking **Mifegyne** your blood will be tested for Rhesus factor. If you are Rhesus negative your doctor will advise you of the routine treatment required.

**If you are taking another drug concomitantly, including non-prescription medicines and food supplements, or if you have just finished treatment with another medicine, inform the attending doctor.** In particular if you are taking the following:

- corticosteroids (used in the treatment of asthma or other inflammation treatments)
- ketoconazole, itraconazole (used in antifungal treatment)
- erythromycin, rifampicin (antibiotics)
- ST John's Wort -Hypericum plant extract (natural remedy used in the treatment of mild depression)
- phenytoin, phenobarbital, carbamazepine (used in the treatment seizures; epilepsy)
- non-steroidal anti-inflammatory drugs (NSAIDs) such as acetyl salicylic acid (aspirin) or diclofenac (voltaren).

#### **Mifegyne with food and drink**

Do not drink grapefruit juice while being treated with **Mifegyne**.

#### **Pregnancy and breast feeding**

##### Pregnancy

Failure of pregnancy termination (continuing pregnancy) after taking **Mifegyne** alone or in combination with prostaglandin has been associated with birth defects. This risk of failure in pregnancy termination increases:

- if the prostaglandin is not administered according to the medication prescribing information
- with the duration of the pregnancy
- with the number of pregnancies you have had before

If termination of pregnancy fails after taking **Mifegyne** or combination of medicines, the pregnancy must be terminated by another procedure, since using **Mifegyne** with prostaglandin may cause fetal defects. Your doctor will advise you about the other methods for completing the termination of the pregnancy.

##### Breastfeeding

If you are breastfeeding, talk to your doctor before using this medicine. Do not breastfeed while taking **Mifegyne** as this medicine is passed into breast milk.

##### Fertility

This medicine does not affect fertility. You can become pregnant again as soon as your termination completed. You should start contraception immediately after the termination of the pregnancy is confirmed by your doctor.

#### **Driving and using machines**

Dizziness can occur as side effect related to the abortion process. Take special care when driving or using machines after taking this medicine until you know how **Mifegyne** affects you.

### 3. HOW TO TAKE MIFEGYNE

**Always take Mifegyne exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.**

#### Duration of treatment, its effects and your reactions:

#### First Stage: Meeting with the doctor after approval of the pregnancy termination by the committee:

- You will receive an explanation about using drugs for terminating a pregnancy (or before surgical termination of a pregnancy), and you can ask about any subjects that are unclear to you.
- The doctor will ascertain that there is indeed an intra-uterine pregnancy and determine the age of the pregnancy (by ultrasound). The doctor will make sure that there are no medical limitations for performing the pregnancy termination using drugs, will check blood type and whether there is need for an anti-D injection. In the event that there is an intrauterine device, the doctor will remove it before treatment begins.
- At this stage you will have to sign a consent form for the termination of pregnancy using **Mifegyne** tablets.

#### **1) Medical termination of a developing intra-uterine pregnancy (MToP)**

##### Termination of pregnancy up to **49** days after your last menstrual cycle:

Dosage in adults:

- 3 tablets to be taken orally

Taking the tablets:

- swallow the tablets whole with a glass of water in the presence of a doctor or a member of his/her medical staff and remain under medical supervision for two hours.
- It is recommended that you obtain analgesics already at this stage: paracetamol (e.g. Acamol, Dexamol) or dipyrrone (e.g. Optalgin, Phanalgin), for the pain that results from uterine contractions. Do not use aspirin or other anti-inflammatory medicines.
- During the first hours, you may feel weakness, nausea and/or vomiting, headache, loss of appetite and even light vaginal bleeding and pains similar to menstrual pains.
- If you vomit within 45 minutes after taking the mifepristone tablets, talk to your doctor immediately. You will need to take the tablets again.
- If you are meant to receive an anti-D injection, it is advisable to receive it at this stage (although you can also receive it on the second appointment).
- Ask for a telephone number that you can call, if necessary, during the next two days and make an appointment for 36-48 hours later for continuation of treatment.
- Take the prostaglandin analogue, 36-48 hours after **Mifegyne**. The prostaglandin is given either orally as tablets which should be swallowed with water (misoprostol 400 micrograms) or as a vaginal pessary (gemeprost 1 mg).

##### Termination of pregnancy **50-63** days after your last menstrual cycle

Dosage in adults:

- 3 tablets to be taken orally. Your doctor may recommend a dose of only one tablet.

Taking the tablet:

- swallow the tablets whole with a glass of water in the presence of a doctor or a member of his/her medical staff and remain under medical supervision for two hours.
  - It is recommended that you obtain analgesics already at this stage: paracetamol (e.g. Acamol, Dexamol) or dipyrrone (e.g. Optalgin, Phanalgin), for the pain that results from uterine contractions.
- Do not use aspirin or other anti-inflammatory medicines.
- During the first hours, you may feel weakness, nausea and/or vomiting, headache, loss of appetite and even light vaginal bleeding and pains similar to menstrual pains.
  - Take the prostaglandin analogue, 36-48 hours after **Mifegyne**. The prostaglandin is given as a vaginal pessary (gemeprost 1 mg).
  - If you vomit within 45 minutes after taking the mifepristone tablets, talk to your doctor immediately. You will need to take the tablets again.
  - If you are meant to receive an anti-D injection, it is advisable to receive it at this stage (although you can also receive it on the second appointment).

This method involves your active participation and you should therefore be aware that:

- You should take the second medicament (which contains prostaglandin) to ensure the treatment is effective.
- You need to attend a check-up consultation (3<sup>rd</sup> consultation) within 14-21 days of taking **Mifegyne** in order to check that your pregnancy has been completely expelled and you are well.

The schedule for the medical termination of pregnancy will be as follows:

1. At the prescribing center you will be given **Mifegyne**, which must be taken orally.
2. 36-48 hours after this the prostaglandin analogue will be administered. You should stay at rest for 3 hours after having the prostaglandin analogue.
3. The embryo may be expelled within a few hours of taking the prostaglandin analogue or during the next few days. You will have vaginal bleeding which will last for an average of 12 days after taking **Mifegyne**, and the flow will become lighter as time continues.
4. You must return to the center within 14-21 days of taking **Mifegyne**, for a follow up consultation to make sure the expulsion is completed.

Contact your prescribing center immediately:

- if you have vaginal bleeding for longer than 12 days and/or if it is very heavy (e.g. you need more than 2 sanitary pads per hour for 2 hours)
- if you have severe abdominal pain
- if you have fever or if you are feeling cold and shivering.

**Other important points to remember:**

- Vaginal bleeding does not mean the expulsion has been completed. Uterine bleeding usually starts 1 to 2 days after taking **Mifegyne**.
- In rare cases, an expulsion can occur before you take the prostaglandin. It is essential that you are checked to confirm that a complete evacuation has occurred and you must return to the centre for this.

- Ask for a telephone number that you can call, if necessary, during the next two days and make an appointment for 36-48 hours later for continuation of treatment.

If pregnancy continues or expulsion is incomplete, your doctor will advise you of the options for completion of the pregnancy termination.

It is recommended that you do not travel too far away from your prescribing centre until the follow-up consultation is done.

In case of emergency or if you have any questions, telephone or visit your prescribing centre. You do not have to wait for your follow-up appointment.

**2) For softening and opening the cervix before surgical termination of pregnancy within the first trimester (up to 84 days from the start of the last period):**

- One tablet to be taken orally.

Taking the tablet:

- swallow the tablet whole with a glass of water.
- if you vomit within 45 minutes after taking the mifepristone tablet, talk to your doctor immediately. You will need to take another tablet.
- If you are meant to receive an anti-D injection, it is advisable to receive it at this stage (although you can also receive it on the second appointment).

The schedule for the medical termination of pregnancy will be as follows:

1. At the prescribing centre you will be given **Mifegyne**, which must be taken orally.
2. 36 to 48 hours after this you will come back to the prescribing centre for the surgical procedure.

Your doctor will explain the procedure to you. It is possible that you will experience bleeding after taking **Mifegyne**, before the surgery.

In rare cases, expulsion can also occur before surgery. It is essential that you return to the centre to confirm that a complete evacuation has occurred.

You must return to the centre selected for the surgery.

In case of emergency or if you have any questions, telephone or visit your prescribing centre. You do not have to wait for your follow-up appointment.

**3) For termination of pregnancy beyond the first trimester for medical reasons:**

Dosage in adults:

- 3 tablets to be taken orally

Taking the tablets:

- Swallow the tablets whole with a glass of water
- 36-48 hours after **Mifegyne** take the prostaglandin analogue, which may be repeated several times at regular intervals until the termination is complete.
- If you vomit within 45 minutes after taking the mifepristone tablets, talk to your doctor immediately. You will need to take the tablets again.
- If you are meant to receive an anti-D injection, it is advisable to receive it at this stage (although you can also receive it on the second appointment).

**4) To induce labor in cases where the fetus has died in the womb and where it is not possible to use other medical treatments (prostaglandin or oxytocin)..**

Dosage in adults

- 3 tablets to be taken orally each day for two days.

Taking the tablets:

- Swallow the tablets whole with a glass of water
- If you vomit within 45 minutes after taking the mifepristone tablets, talk to your doctor immediately. You will need to take the tablets again.
- If you are meant to receive an anti-D injection, it is advisable to receive it at this stage (although you can also receive it on the second appointment).

**Use in adolescents:**

Only limited data is available on the use of **Mifegyne** in adolescents.

General instructions:

- Pain relievers: paracetamol (such as Acamol, Dexamol) or Dipyron (such as Optalgin, phenylgin) should be used. For the pain of uterine contractions, do not use aspirin or other anti-inflammatory drugs.
- During the first few hours of taking **Mifegyne**, you may experience weakness, nausea and / or vomiting, headaches, loss of appetite, and even light bleeding from the vagina and pains similar to menstrual pain.
- Take a telephone number to call if necessary for the next two days, and make an appointment for 36-48 hours later for continuation of treatment.
- After about 12 hours, about half of the women have pain and bleeding similar to a strong cycle (in the second trimester, the bleeding may not begin until prostaglandins are given).
- Be prepared to use sanitary towel or pads, do not use tampons.
- Use pain medication (mentioned earlier) as needed. If the pain is very strong and you have an extreme reaction to the drug, do not hesitate to call your doctor.
- Pregnant for up to 63 days - in some cases pregnancy termination occurs at this stage (48 hours after taking mifegine). If this happens, a piece of tissue resembling a large blood clot will emerge with the bleeding. You may not feel it at all. It is very important that in any case you return to a follow-up consultation.

**Second Stage: Continuation of treatment (second appointment):**

36–48 hours after taking the **Mifegyne** tablets, you must return to the clinic/hospital to receive the prostaglandin (except in the case of surgical abortion) and to remain under medical supervision:

1. For a pregnancy termination within 63 days of pregnancy: for 3 hours.
2. For a surgical pregnancy termination within the first trimester: hospitalization in accordance with the doctor's instructions.
3. For a pregnancy termination within the second trimester: hospitalization in accordance with the doctor's instructions.

- It is recommended to eat a full meal before taking the tablets.
- In the event that you need an anti-D injection, and you have not yet received it, now is the time to receive it.

- A short time after taking the pills, you will feel pain that results from uterine contractions and there will be vaginal bleeding.
- At the beginning, the pains will be similar to menstrual pains and towards the end of the abortion they will become stronger, and it is possible that you will need analgesics.

In a pregnancy of up to 63 days – for most women the peak of pain and the end of the abortion occur within the 3 hours after taking the misoprostol tablets.

In a second trimester pregnancy the process might take longer.

There may be other effects such as: dizziness, nausea and/or vomiting, weakness and an overall unwell feeling. The nurse will instruct you how to collect the pads and the detritus of the pregnancy and will check whether the pregnancy terminated during your stay at the clinic/ hospital.

Attention! In termination of a pregnancy of up to 63 days - there are cases where pregnancy does not terminate within the 3 hours after treatment with prostaglandin analogue (the time that you are in the hospital/clinic) but during the subsequent days. In this case, a piece of tissue the size of a large blood clot will be expelled with the bleeding. It is possible that you will not even be aware of it.

Make sure that you have a sufficient amount of the analgesics mentioned above. Use sanitary towels/pads. Do not use tampons. Vaginal bleeding can continue until your next period. Usually the bleeding lessens after a few days. If the bleeding is intense and does not lessen, consult a doctor.

It is recommended not to have intercourse until the bleeding stops and in any case, you must take immediate contraceptive measures in order to prevent another unwanted pregnancy.

### **Third Stage: Follow-up examination**

It is very important to come for a follow-up examination at the time determined by your doctor. In the follow-up examination, the doctor will ascertain, using an acceptable method (ultrasound, blood test or a physical examination), that the pregnancy has indeed been terminated.

In case the pregnancy continues, it must be terminated by another method since the treatment with **Mifegyne** and prostaglandin can cause birth defects in the fetus. Your doctor will advise you about the other methods for completing the termination of the pregnancy.

### **4. POSSIBLE SIDE EFFECTS**

As with any drug, the use of **Mifegyne** may cause side effects. Do not be alarmed from the list of the side effects. You may not suffer from any of them.

If you suffer from any side effects, talk to your doctor or pharmacist. This includes any side effects not listed in this leaflet.

*Serious side effects:* allergic reaction, skin rash, localized swelling of face and/or larynx which can be with urticaria

*Other serious side effects:* cases of serious or fatal toxic or septic shock. Fever with aching muscles, rapid heart rate, dizziness, diarrhea, vomiting or feeling weak. This side effect may occur if you do not take the second medicine, the selected prostaglandin analogue.



If you experience any of these side effects contact your doctor immediately or go to your nearest hospital casualty department.

#### Other side effects

*Very common* (may affect more than 1 in 10 people):

- uterine contractions or cramping
- diarrhea
- feeling sick (nausea), or being sick (vomiting)

*Common* (may affect up to 1-10 in 100 people):

- heavy bleeding,
- gastro intestinal cramping light or moderate
- infection of the uterus (endometritis and pelvic inflammatory disease)

*Uncommon* (may affect 1-10 in 1000 people):

- blood pressure fall

*Rare* (may affect 1-10 in 10000 people):

- fever
- headaches
- generally feeling unwell or tired
- vagal symptoms (hot flushes, dizziness, chills)
- hives and skin disorders which can be serious
- Uterine rupture following prostaglandin administration within the second and third trimester of pregnancy, particularly in multiparous women or in women with a caesarean section scar

#### Reporting of side effects

Side effects can be reported to the Ministry of Health by clicking on the link "Reporting adverse events due to drug treatment" found on the homepage of the Ministry of Health website ([www.health.gov.il](http://www.health.gov.il)), which refers to the online form for reporting adverse events, or by entering the link:

<https://sideeffects.health.gov>.

#### 5. HOW TO STORE THE MEDICINE

- Prevent poisoning! This medicine and any other medicine should be kept in a safe place out of the reach of children and / or infants and thereby prevent poisoning. Do not induce vomiting without explicit instructions from your doctor.
- Do not use this medicine after the expiration date (exp. Date) that appears on the packaging. The expiry date refers to the last day of that month.
- Storage conditions: Store the medicine at temperatures below 25 ° C. Store in the original packaging in order to protect from light.
- Do not use **Mifegyne** if the box or blisters show signs of damage.
- Do not throw away any medicines via wastewater. Talk to your pharmacist about how to get rid of drugs you do not use. This will help to protect the environment.

#### 6. ADDITIONAL INFORMATION

- In addition to the active ingredient the medicine includes also: Maize starch, Povidone, Microcrystalline cellulose, Magnesium stearate and Silica colloidal anhydrous.
- What **Mifegyne** looks like and contents of the pack:  
**Mifegyne** is available as yellow biconvex tablet, with a diameter of 11 mm with a code engraved on one side. Every blister contains 3 tablets.

- License Holder: A.Lapidot Pharmaceuticals Ltd., 8 Hashita Street, Industrial Park, Caesarea, 3088900.
- Manufacturer: Macors Laboratories, Auxerre, France for Exelgyn Laboratories, Paris, France
- License number of the drug: 115522964100
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