

WHO-PQ RECOMMENDED PATIENT INFORMATION LEAFLET

*This patient information leaflet focuses on uses of the medicine covered by WHO's Prequalification Team - Medicines. The recommendations for use are based on WHO guidelines and on information from stringent regulatory authorities.**

The medicine may be authorised for additional or different uses by national medicines regulatory authorities.

* https://extranet.who.int/pqweb/sites/default/files/documents/75%20SRA%20clarification_Feb2017_newtempl.pdf

Information for the patient

[RH089 trade name][†]

Mifepristone + misoprostol

The warnings and instructions in this leaflet are intended for the person taking the medicine. If you are a parent or carer responsible for giving the medicine to someone else such as a child, you will need to apply the instructions accordingly.

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have questions about the medicine, ask your health care provider.
- This medicine is for you only. Do not pass it on to others. It may harm them, even if their illness seems to be the same as yours..
- If you are concerned about any side effects, talk to your health care provider. This includes unwanted effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What [RH089 trade name] is and what it is used for
2. What you need to know before you take [RH089 trade name]
3. How to take [RH089 trade name]
4. Possible side effects
5. How to store [RH089 trade name]
6. Contents of the pack and other information

1. What [RH089 trade name] is and what it is used for

[RH089 trade name] contains two types of medicines that are used together to induce abortion (termination of pregnancy). They may also be used to help remove the fetus if it has died in the womb and cannot be expelled naturally.

The medicines in [RH089 trade name] are:

- Mifepristone (1 tablet)
- Misoprostol (4 tablets)

Mifepristone and misoprostol work in different ways to produce abortion. Mifepristone is given first, and blocks the effects of the hormone progesterone, which is needed for the pregnancy to continue. It also helps to soften the cervix (the opening to the womb).

Once mifepristone has acted, misoprostol can be given. It is a version of a natural substance called prostaglandin E1 which acts on the womb to produce contractions, and helps the cervix (the opening of the womb) to relax and widen so that the contents can be expelled.

2. What you need to know before you take [RH089 trade name]

Do not take [RH089 trade name] if:

- you are allergic to mifepristone or misoprostol or any of the other ingredients of the tablets (listed in section 6)
- you have had a previous allergic reaction to prostaglandin medicines

† Trade names are not prequalified by WHO. This is the national medicines regulatory agency's responsibility.

- your pregnancy has not been properly confirmed (by an examination by a health care provider, an ultrasound scan or biological tests)
- you have, or are suspected to have, a pregnancy growing outside the womb (ectopic pregnancy)
- your adrenal gland does not work properly (adrenal failure)
- you have severe asthma that cannot be adequately treated with medication
- have inherited porphyria (a rare metabolic disorder)

Warnings and precautions

Talk to your health care provider before taking [RH089 trade name] if:

- you have had genital cutting or circumcision
- you have had a previous baby delivered by caesarean section, or have had surgery on your womb
- you have heart disease, or you are at risk of heart disease because of, for example, high blood pressure, high cholesterol, smoking or diabetes
- you have liver disease; if you have severe liver disease you should not use this medicine and your health care provider will recommend another procedure
- you are malnourished
- you have anaemia (low red blood cell count), or an illness that affects the clotting of your blood (which makes you bleed easily)
- you have been using corticosteroid medication.

If any of these apply, your health care provider will discuss with you whether [RH089 trade name] is suitable for you.

Before you receive [RH089 trade name] you will normally need to be checked by a health care provider to see how far along your pregnancy is. This might include an ultrasound scan.

If you have an intrauterine contraceptive device (coil) in place, this must be removed before treatment.

Speak to your health care provider if you have any infection in your genital area, as this should be treated before you receive [RH089 trade name]. Also speak to your health care provider at once if you think you have an infection after you have been treated with [RH089 trade name].

Before taking [RH089 trade name] your blood may be tested for Rhesus factor. If you are Rhesus negative your health care provider will advise you of the routine treatment required.

If you are taking [RH089 trade name] to terminate an ongoing pregnancy, your health care provider should explain the procedure to you, including how to take the medicines in [RH089 trade name]. They will also give you information about possible bleeding after the procedure and how long it may last, how to look after yourself and look out for complications that may occur, and how and where to get help if you need it.

Children and adolescents

There is not much information on the use of this medicine in patients under 18 years.

[RH089 trade name] should not be used in children who have not reached puberty.

Other medicines and [RH089 trade name]

Tell your health care provider if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Medicines containing the following active substances may interfere with the action of mifepristone or increase the risk of side effects:

- corticosteroids (used in the treatment of asthma or other conditions where there is inflammation)
- ketoconazole, itraconazole (medicines used for fungus infections)
- erythromycin, rifampicin (antibiotics)
- St John's wort (natural remedy used in the treatment of mild depression)

- phenytoin, phenobarbital, carbamazepine (used in the treatment of epilepsy and seizures (fits))
Mifepristone tablets may interfere with the action of some other medicines, such as:
- cyclosporine, tacrolimus, sirolimus, everolimus (used after organ transplantation)
- ergotamine, dihydroergotamine (used for migraine headache)
- fentanyl (morphine-like medicine used to treat severe pain)
- quinidine (heart medicine)
- some medicines used in general anaesthesia.

Taking mifepristone with food and drink

Do not drink grapefruit juice when you are treated with mifepristone tablets.

Pregnancy, breast-feeding and fertility

Pregnancy

This medicine should not be used during pregnancy if you wish to go on and have the baby, unless it is used when the baby is ready to be born.

It is important that you take the tablets in [RH089 trade name] as instructed by your health care provider. If you take [RH089 trade name] to terminate a pregnancy and the medicine does not work, your baby may be at risk of birth defects. It is not known how big the risk is.

If the medicine does not work and you still want to terminate your pregnancy another procedure will be used. Your health care provider will talk to you about the options.

If you decide to continue with the pregnancy, careful pre-natal monitoring and repeated ultrasound scans must be carried out in a specialised clinic. Your health care provider will talk to you about this.

You should avoid getting pregnant again before your next period after taking this medicine. To avoid becoming pregnant, you should start contraception (birth control) immediately after your health care provider tells you that the termination of the pregnancy is successful.

Breastfeeding

If you are breastfeeding, talk to your health care provider before using [RH089 trade name]. Mifepristone passes into breast milk and you should not breastfeed for one week after taking the mifepristone tablet in [RH089 trade name].

Fertility

[RH089 trade name] does not affect fertility. You can become pregnant again as soon as your termination is completed. You should start contraception immediately after the termination of the pregnancy is confirmed.

Driving and using machines

Both active ingredients in [RH089 trade name] can cause headache and dizziness. If you get these symptoms you should avoid potentially hazardous tasks such as driving or operating machinery.

3. How to take [RH089 trade name]

[RH089 trade name] consists of 2 different types of tablet, mifepristone 200 mg and misoprostol 200 micrograms. Your health care provider will explain how to take these medicines, which may vary depending on why you are taking the medicine and for how long the pregnancy has gone on.

Always take [RH089 trade name] exactly as your health care provider has told you. Check with your health care provider if you are not sure.

The tablets must not be crushed, broken or chewed.

Induction of abortion (termination of pregnancy)

Termination of pregnancy at less than 12 weeks of gestation:

- The mifepristone 200-mg tablet should first be swallowed with some water. If you vomit (throw up) shortly after taking the tablet, tell your health care provider as soon as you can.

- Then *after 24 to 48 hours* you should take 4 tablets of misoprostol 200 micrograms (800 micrograms of misoprostol). You can take the misoprostol tablets in different ways. The tablets may be:
 - inserted as high as possible into your vagina, after which you should stay lying down for 30 minutes, *or*
 - placed under your tongue for 30 minutes and anything left swallowed, *or* ○ held between your cheek and gums for 20 to 30 minutes and anything left swallowed. Your health care provider will discuss with you how you can take the tablets.
- Your health care provider may ask you to take some further doses of misoprostol to complete the procedure.

Termination of pregnancy at more than 12 weeks of gestation:

- The mifepristone 200-mg tablet should first be swallowed with some water. If you vomit (throw up) shortly after taking the tablet, tell your health care provider as soon as you can.
- Then *after 24 to 48 hours* you should take 2 tablets of misoprostol 200 micrograms (400 micrograms of misoprostol). You can take the misoprostol in different ways. The tablets may be:
 - inserted as high as possible into your vagina, after which you should stay lying down for 30 minutes, *or*
 - placed under your tongue for 30 minutes and anything left swallowed, *or* ○ held between your cheek and gums for 20 to 30 minutes and anything left swallowed. Your health care provider will discuss with you how you can take the tablets.
- *Three hours later*, you should take 2 more tablets of misoprostol 200 micrograms (400 micrograms of misoprostol) in the same way.
- Your health care provider may ask you to take some further doses of misoprostol every 3 hours to complete the procedure.

Your health care provider may also schedule a follow-up visit within 7 to 14 days after taking [RH089 trade name] to confirm the procedure has worked and that you are well.

After treatment you should be aware that:

- The pregnancy may be expelled within a few hours or during the next few days after misoprostol treatment. In rare cases, the pregnancy may be expelled before you take misoprostol tablets.
- After taking the first (mifepristone 200 mg) tablet, you will have some bleeding from your womb. Bleeding usually starts 1 to 2 days after taking the mifepristone tablet. The bleeding may last 2 or 3 weeks (on average 9 to 13 days). Your health care provider will explain how to manage the bleeding. If the bleeding is heavy and prolonged, contact your health care provider immediately for an earlier appointment.
- Bleeding does not mean the treatment has already worked. You must continue to take the tablets as instructed by your health care provider.
- If pregnancy continues or expulsion is incomplete, another procedure may be needed. Your health care provider will advise you of the options.

Missed abortion at less than 14 weeks of gestation

If your pregnancy has stopped developing early on, and is not expelled naturally from the womb (missed abortion), then you may be given:

- a dose of mifepristone (200 mg) by mouth, *followed after at least 24 hours by*
- 4 tablets of misoprostol 200 micrograms (800 micrograms of misoprostol). The tablets may be: ○ inserted as high as possible into your vagina, after which you should stay lying down for 30 minutes, *or*
 - placed under your tongue for 30 minutes and anything left swallowed, *or* ○ held between your cheek and gums for 20 to 30 minutes and anything left swallowed.

Your health care provider will discuss with you how you can take the tablets.

Death of the baby in the womb (intrauterine fetal death) at 14 to 28 weeks of gestation

If your baby dies in the womb, and is not expelled naturally from the womb (stillbirth), then you may be given:

- a dose of mifepristone (200 mg) by mouth, *followed after 24 hours to 48 hours by*
- 4 tablets of misoprostol 200 micrograms (800 micrograms of misoprostol). The tablets may be:
 - inserted as high as possible into your vagina, after which you should stay lying down for 30 minutes, *or*
 - placed under your tongue for 30 minutes and anything left swallowed, *or* ◦ held between your cheek and gums for 20 to 30 minutes and anything left swallowed. Your health care provider will discuss with you how you can take the tablets.

If you take more mifepristone 200 mg tablets than you should

As [RH089 trade name] only contains one tablet of mifepristone, it is unlikely that you will take more mifepristone 200 mg tablets than you should. In you do take too many tablets, tell your health care provider as soon as you can.

If you take more misoprostol 200 micrograms tablets than you should

If you have taken too much misoprostol you may get effects such as: fever, changes in blood pressure or effects on the heart, feeling sick (nausea), diarrhoea, belly ache (abdominal pain) and shaking (tremors).

If you have accidentally taken too many tablets, contact your health care provider as soon as you can.

If you forget to take [RH089 trade name]

If you forget to take the tablets in [RH089 trade name] as advised by your health care provider, the procedure may not work properly. Talk to your health care provider if you forget to take any of your tablets.

If you have any further questions on the use of this medicine, ask your health care provider.

4. Possible side effects

Like all medicines, [RH089 trade name] can cause side effects, although not everybody gets them.

If you notice any of the following symptoms or side effects, **tell your health care provider immediately**:

- sudden severe pain in your belly that may indicate a tear or rupture of the womb, especially if you have had a previous caesarean section or other operation on the womb
- persistent heavy bleeding, for example soaking two sanitary pads per hour, for more than two hours
- signs of infection of the womb such as persistent fever with a temperature of 38°C or higher for more than 4 hours, or an unpleasant smelling discharge
- persistent pain unrelieved by medication

Other side effects (contact your health care provider if any of these get serious or if you are worried):

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

- uterine contractions or cramping in the hours following use of misoprostol
- feeling sick (nausea)
- being sick (vomiting)
- shivering
- fever (including temperature above 40°C)

Common side effects (may affect up to 1 in 10 people):

- cramping in the gut (gastrointestinal cramping)
- headache
- dizziness/fainting
- chills

Uncommon side effects (may affect up to 1 in 100 people):

- low blood pressure
- rash
- tiredness

Rare side effects (may affect up to 1 in 1,000 people):

- nettle rash, serious skin rashes with redness or blistering (erythroderma, epidermal necrolysis and erythema nodosum)
- hot flushes
- feeling generally unwell

Very rare side effects (may affect up to 1 in 10,000 people):

- Swelling under the skin of the face and throat, sometimes with rash (angioedema)
- effects on the heart or circulation, including heart attack (myocardial infarction), spasm of the arteries supplying the heart, severe low blood pressure
- serious or fatal toxic shock syndrome caused by infection of the womb by certain bacteria, which may occur without fever or other obvious symptoms of infection Side effects whose **frequency has not been determined**:
- allergic reaction, potentially severe (anaphylaxis)
- back pain **Pregnancy**

If the pregnancy continues despite taking [RH089 trade name] and you decide to keep it, the medicine can cause abnormalities (malformation) in the baby. Discuss this with your health care provider, as careful prenatal monitoring may need to be arranged.

Reporting of side effects

If you get a side effect, talk to your health care provider. This includes side effects not listed in this leaflet. You may also be able to report such effects directly to your national reporting system if one is available. By reporting side effects, you can help to improve the available information on this medicine.

5. How to store [RH089 trade name]

Do not store above 30°C. Protect from light. Store in the original package.

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date stated on the label. The expiry date refers to the last day of that month.

Do not throw away any medicines in wastewater or household waste. Ask your health care provider how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What [RH089 trade name] contains

The co-blistered combination comprises the following active substances:

mifepristone 200 mg as tablets
misoprostol 0.2 mg as tablets

The other ingredients of [RH089 trade name] are:

Mifepristone tablet

Colloidal silicon dioxide
Corn starch
Povidone
Magnesium stearate
Microcrystalline cellulose

Misoprostol tablet

Microcrystalline cellulose
Sodium starch glycolate
Hydrogenated castor oil
Hypromellose (HPMC)

What [RH089 trade name] looks like and contents of the pack

Mifepristone 200 mg tablets

Yellowish, biconvex round tablets debossed with M1 on one side. The other side is plain.

Misoprostol 0.2 ml tablets

Hexagonal white tablets, debossed with M and 3 at each side of a score line on the flat side, the other side is slightly convex.

The score line is not intended for breaking the tablet. The tablet should not be divided.

Supplier and manufacturer

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Detailed information on this medicine is available on the World Health Organization (WHO) website:
<https://extranet.who.int/pqweb/medicines>