Topogyne® 400 microgram tablets
Misoprostol

PACKAGE LEAFLET: INFORMATION FOR THE USER

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 any further questions, ask your doctor.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects talk to your doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Topogyne® is and what it is used for

Topogyne® tablets contain misoprostol, which is similar to a chemical substance called 'prostaglandin' that your body produces naturally. Misoprostol triggers contractions of the womb and softens the cervix.
For medical termination of pregnancy:
Topogyne® is used after taking another medicine called mifepristone. It should be taken no later than 49 days after the first day of your last menstrual period.
For surgical termination of pregnancy:
Topogyne® is taken on its own prior to surgical termination of pregnancy during the first trimester of pregnancy (within 12 weeks after the first day of your menstruation).

2. What you need to know before you take Topogyne®

Do not take Topogyne®
- if you are allergic to misoprostol, any other prostaglandin or any of the other ingredients of this medicine (listed in section 6).
- if the pregnancy has not been confirmed by ultrasound scan or biological tests.
- if your doctor suspects an ectopic pregnancy (the egg is implanted outside the womb).
- if you cannot take mifepristone (when mifepristone is used in combination with Topogyne®).
- for medical termination of pregnancy, if the first day of your last period was more than 49 days (7 weeks) ago.

Warnings and precautions
Talk to your doctor before taking Topogyne®
- 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 have had a previous caesarean section or surgery of the womb.

Health care professionals should ensure that due to the risk of the failure of the method and the birth defects observed in these ongoing pregnancies, patients are being informed about the risk of teratogenicity and that a follow-up visit must be scheduled in order to check that the expulsion is completed (see section Pregnancy, breast-feeding and fertility).

Before taking mifepristone and Topogyne® your blood will be tested for Rhesus factor. If you are Rhesus negative your doctor will advise you of the routine treatment required.

For medical termination of pregnancy:
If you use a contraceptive coil, it must be removed before you take the first medicine, mifepristone.

For surgical termination of pregnancy:
- As no data are available on cervical preparation with misoprostol prior to surgical termination of pregnancy beyond the first trimester, Topogyne® is not taken beyond 12 weeks after the first day of your menstruation.
- Due to possible occurrence of vaginal bleeding after taking this medicine, you should preferably take Topogyne® at the treatment centre before the surgical procedure.

Other medicines and Topogyne®
Tell your doctor if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription.

In particular tell your doctor if you are taking any of the following:
- Non-steroidal anti-inflammatory drugs (NSAIDs) such as acetylsalicylic acid or diclofenac
- Antacid medicines or an antacid medicine containing magnesium (used to treat heartburn and acid indigestion)

Pregnancy, breast-feeding and fertility
Pregnancy
Failure of pregnancy termination (continuing pregnancy) after taking Topogyne® has been associated with a 3-fold increased risk of birth defects, in particular facial paralysis, head and limb malformations. Defects in newborns have also been seen when this medicine is taken on its own. For medical termination of pregnancy, you **must** take the other medicine, mifepristone, 36 – 48 hours before taking Topogyne®.
The risk of failure of Topogyne® increases:
- If it is not taken orally
- With the duration of the pregnancy
- With the number of pregnancies you have had before.
- For medical termination of pregnancy, if it is taken later than 49 days after the first day of your last menstrual period.

If termination of the pregnancy fails after taking this medicine there is an unknown risk to the foetus. If you decide to continue with the pregnancy, careful pre-natal monitoring and repeated ultrasound examinations, with a special attention to the limbs and head, in a specialised clinic must be carried out. Your doctor will advise further.

If you decide to continue with the termination of the pregnancy a new procedure will be used. Your doctor will advise you of the options.
You should avoid getting pregnant again before your next period after taking this medicine. You should start contraception immediately after the termination of the pregnancy is confirmed by the doctor.

Breast-feeding
If you are breast-feeding, ask your doctor for advice before taking this medicine. Do not breast-feed 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 is completed. You should start contraception immediately after the termination of the pregnancy is confirmed.

Driving and using machines
This medicine can cause dizziness. Take special care when driving or using machines after taking this medicine until you know how Topogyne® affects you.

3. How to take Topogyne®

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

Dosage in Adults
- One tablet to be taken orally.

Taking the Tablet
- **In all instances**
  - Swallow the tablet whole with a glass of water.
  - If you vomit within 30 minutes of taking the tablet, talk to your doctor immediately. You will need to take another tablet.

Contact your prescribing centre immediately after the termination of pregnancy procedure (medical or surgical):
- **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 a fever or if you are feeling cold and shivering.**

- **For medical termination of pregnancy**

The schedule for taking Topogyne® for a medical termination of pregnancy will be as follows.
1) At the prescribing centre you will be given the first drug mifepristone, which must be taken orally.
2) 36 – 48 hours after this, you will take Topogyne® orally. You must rest for at least 3 hours after taking this medicine.
3) The embryo may be expelled within a few hours of taking Topogyne® or during the next few days. You will have vaginal bleeding which will last for an average of 12 days after taking the first drug, mifepristone, and the flow will become lighter as time continues.
4) **You must return to the centre within 14 - 21 days of taking the first medicine, mifepristone, for a check-up consultation to make sure the expulsion is complete.**

Important things to remember when taking this medicine:

This tablet must be taken orally
For medical termination of pregnancy, Topogyne® must be taken 36 – 48 hours after taking 600 mg of mifepristone

If you do not follow these instructions the risks associated with this medicine will increase

- **For surgical termination of pregnancy**

The tablet is to be taken 3 to 4 hours before the surgical procedure of termination of pregnancy.

The schedule for taking Topogyne® for a surgical termination of pregnancy will be as follows.
1) Take Topogyne® orally
2) Surgical procedure will be conducted 3 to 4 hours after this intake

You will have vaginal bleeding which will last for an average of 12 days after the surgical procedure, and the flow will become lighter as time continues.
3) **You must return to the centre within 14 - 21 days after this surgical procedure, for a check-up consultation.**

Other important points to remember:
- In all instances
  - Do not take this medicine if the blister foil is damaged or if the tablet has been stored outside the packaging.

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

- For medical termination of pregnancy
  - Vaginal bleeding does not mean the expulsion has been completed after a termination of pregnancy.
  - The risk of side effects increases if you do take this medicine later than 49 days after the first day of your last menstrual period or if you do not take it orally.

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

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

- For surgical termination of pregnancy
  - After taking Topogyne®, there is a risk of abortion before surgical procedure has started even though this risk is low.
  - The risk of side effects increases if you take it later than 12 weeks after the first day of your last menstrual period (first trimester of pregnancy).

Use in children and adolescents
Only limited data is available on the use of misoprostol in adolescents.

If you take more Topogyne® than you should
If you take too many tablets, contact your doctor immediately or go to the nearest hospital casualty department.

The doctor will give you the exact amount of Topogyne®; it is therefore unlikely that you will take too many tablets. Taking too many tablets may cause symptoms such as drowsiness, shaking, fits, difficulty in breathing, abdominal pain, diarrhoea, fever, chest pain, low blood pressure and a slow heartbeat that can be fatal.

If you forget to take Topogyne®
If you forget to take mifepristone or Topogyne® it is likely that the termination will not be fully effective. Talk to your doctor or the prescribing centre if you forget to take Topogyne®.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

The following side effects may occur:

Serious Side Effects
The risk of serious side effects increases if you take this medicine later than:
- 49 days after the first day of your last menstrual period for a medical termination of pregnancy.

Or
- 12 weeks after the first day of your last menstrual period for a surgical termination of pregnancy.

Serious side effects include:
- allergic reaction. Severe skin rashes such as itchy red spots, blisters or lesions.

Other serious side effects include:
- cardiovascular accidents. Chest pain, difficulty breathing, confusion, or an irregular heartbeat.
- cases of serious or fatal toxic or septic shock. Fever with aching muscles, rapid heart rate, dizziness, diarrhoea, vomiting or feeling weak.

These side effects may occur if you do not take this medicine orally or if you take it later than 49 days after the first day of your last menstrual period for a medical termination of pregnancy.

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
- diarrhoea
- feeling sick (nausea) or being sick (vomiting)
- uterine bleeding

Common (may affect up to 1 in 10 people):
- heavy vaginal bleeding
- abdominal pain
- gastro-intestinal cramping light or moderate
- infection of the uterus (endometritis and pelvic inflammatory disease)
- birth defects (foetal malformations)

Rare (may affect up to 1 in 1,000 people):
- fever
- foetal death
- headache, dizziness and generally feeling unwell or tired
- hives and skin disorders which can be serious
- tearing of the womb (uterine rupture): tearing of the womb after administration of prostaglandins in the second or third trimester of pregnancy, mainly in women with previous deliveries of a child or with a scar of a caesarian section

Very rare (may affect up to 1 in 10,000 people)
- localised swelling of face and/or larynx which can be with urticaria

Other side effects include
- feeling cold, shivering
- back pain

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via: United Kingdom Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Topogyne®

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

Do not use this medicine after the expiry date, which is stated on the carton after "EXP". The expiry date refers to the last day of that month.

Store below 25°C.

Do not use this medicine if you notice that the box or the blister packs show signs of damage.

Do not use if the tablet has been stored outside the blister pack.

Do not throw away any medicines via wastewater.

Ask your pharmacist 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 Topogyne® contains
The active substance is misoprostol.
One tablet of Topogyne® contains 400 microgram misoprostol.
The other ingredients are microcrystalline cellulose, hypromellose, sodium starch glycolate (type A), hydrogenated castor oil.

What Topogyne® looks like and contents of the pack
White, round, flat tablet with a diameter of 11 mm and thickness of 4.5 mm, with a break line on each side and double "M" engraved on one side. The tablet can be divided into equal doses.
Topogyne® is available in pack sizes of 1, 4, 16 or 40 tablets in perforated unit dose PVC-PCTFE/Alu or Alu/Alu blisters.

Marketing Authorisation Holder and Manufacturer

Marketing authorisation holder
EXELGYN
216 boulevard Saint-Germain
75007 Paris
France

Manufacturer
Nordic Pharma B.V.
Siriusdreef 41
2132 WT Hoofddorp
The Netherlands

Delpharm Lille SAS
Z.I. de Roubaix Est, Rue de Toufflers,
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89000 Auxerre, France

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Topogyne® 400 microgram tablets Misoprostol

MATERIAL FOR PATIENTS

Information on Medical Termination of Pregnancy

You have chosen the medical termination of pregnancy [ToP] method (also called the medical abortion method). This leaflet will provide you with some information that you should be aware of before taking the medicine including the steps involved in your treatment and what to do if you experience any problems. It is important that you read and consider this information carefully.

Before taking this medicine for the ToP:

- Please read the mifepristone and misoprostol patient leaflets (PIL)
- Inform your doctor about the following:
  - 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 have had a previous caesarean section or surgery of the womb

If you feel uncomfortable or are worried about the ToP or if you have further questions, don't hesitate to contact your doctor. A safety card is available for you below. Your doctor should have noted all relevant contact details and where to go should you experience any problems or require more advice.

This ToP is carried out in 3 steps:

1. At this stage, you have taken the 600 mg oral dose Mifegyne® (3 tablets) 36 to 48h ago.
2. You are now about to have the 400 mcg oral dose Topogyne®: **one tablet to be taken.**
3. **2 to 3 weeks after the first drug (Mifegyne®) is taken, a follow-up visit is required (this is compulsory)**.
   This visit is important because your doctor will verify that the abortion is successful and make sure that everything is all right.

What will you experience during the ToP:

- Medical ToP induces womb contractions. You may experience pain, feel tired, have nausea, vomiting and diarrhoea, so it is best you try to remain comfortable and to have somebody with you. If you have any pain do take the painkillers that your doctor prescribed to you.
- The ToP will occur with vaginal bleeding that can be heavier than your menstrual bleeding, contains blood clots and a gelatinous white ball is sometimes visible. Bleeding can happen very quickly after taking Topogyne® but it may also happen hours later.
  - The embryo may be expelled within a few hours after taking Topogyne® or during the next few days.
  - Bleeding lasts for an average of 12 days after you take Mifegyne®. **You must return to your medical centre within 14-21 days for a check up as bleeding is not in any way a proof of complete expulsion.**
- After a ToP, fertility resumes immediately.

You must speak with your doctor about the best contraceptive method for you and start using contraception the same day as the termination of pregnancy is confirmed.

Contact your doctor immediately in case:

- You **vomit** within 30 minutes of taking Topogyne®. Your physician will determine whether another dose of Topogyne® is necessary.
- You have **abnormal bleeding** in terms of duration and amount of blood (seek medical advice if you bleed for more than 12 days and/or need more than 2 sanitary pads per hour for 2 hours).
- You have severe abdominal **pain** that persists despite taking painkillers.
- You have a **fever** or if you are feeling cold and shivering.

During the follow-up visit your doctor will check if the expulsion is complete. If the ToP fails and you decide to carry on with the pregnancy, you should be aware that there is a risk of birth defects in newborns associated with misoprostol use. You should take this into consideration when making a decision to carry your pregnancy to term or not:

- If you decide to continue with the termination of your pregnancy a new procedure will be used. Your doctor will advise you of the options.
- In case you choose to carry your pregnancy to term, make sure you have a special follow-up with careful pre-natal monitoring and repeated ultrasound examinations in a specialised clinic.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in the Patient Information Leaflet. You can also report side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard
By reporting side effects you can help provide more information on the safety of this medicine.

IF AT ANY TIME you are worried or if the following occurs :

- **fever** lasting longer than 24 hours
- **pain** that persists despite taking painkillers
- significant and persistent **blood loss** (use of more than 2 sanitary pads per hour for 2 hours)
- faintness, or any question

Please contact your doctor or go to the prescribing centre :

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For the follow-up visit
please come to the office on :

_____ / _____ / _____ at _____ h ___

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MATERIAL FOR HEALTHCARE PROFESSIONALS

How to manage the risk to your patients in Medical Termination of Pregnancy (MToP)

Please consult the mifepristone and misoprostol SmPC/prescribing information before performing a MToP.

As a reminder, the approved protocol up to 49 days of amenorrhea is the following:

- Mifepristone: **600 mcg** oral dose
- Misoprostol: **400 mcg** oral dose (i.e. 1 tablet of Topogyne®) 36 to 48 h after mifepristone intake

Unlike other misoprostol tablets, each Topogyne® tablet contains 400 mcg misoprostol, **so one Topogyne® tablet only must be given.**

The management of the risk to the patient consists of two steps:

1. Counselling
2. Verification of complete expulsion during the follow-up visit which must take place within a period of 14 to 21 days after administration of the mifepristone

To minimize the risk associated with Topogyne®, you are advised to counsel your patient regarding the following.

1. Information to be taken into account during the counselling

Patient medical history

MToP method is suitable for most patients. However, due to the prostaglandin intake, you have to consider the following pre-existing conditions before the start of the procedure:

- **scarred uterus,**
- **cardiovascular risks (e.g. being aged over 35 years with chronic smoking, hyperlipidemia, diabetes),**
- **established cardiovascular disease**
- **Rhesus negative**

What to do:

- Discuss the medical history with the patient
- Treat the patient with caution when they have the pre-existing conditions

Fertility

This method has no influence on the fertility of the patient.

What to do:

- Discuss the choice of the contraception method with the patient preferably during the counselling visit in order to prescribe the most suitable method to her and provide advice on when to start the contraception following the Medical ToP.

Bleeding

Vaginal bleeding is a normal part of the abortion procedure and the patient should be made aware of this.

What to do:

Instruct the patient on the following:

- Occurrence and intensity of prolonged vaginal bleeding:
  - Bleeding can start very quickly after misoprostol intake
  - Expulsion can occur within 4 hours, or during the next few days
  - Duration of bleeding can last up to 12 days
- To contact physician immediately in case of abnormal bleeding:
  - If more than 12 days and/or
  - If more than 2 sanitary pads per hour for 2 hours are needed
- Bleeding is not in any way proof of complete expulsion therefore a follow-up visit is required to confirm termination of the pregnancy
- If persistent bleeding occurs after the follow-up visit patient needs to contact the doctor
- Persistence of vaginal bleeding could signify incomplete abortion and appropriate treatment should be considered.

Note down on safety card:

- Phone number and address of the prescribing centre so patient can contact you or another physician should they need to
- Date of follow-up visit for the patient

Infections

Toxic or septic shocks following infections are very rare. However some serious or fatal cases have been reported following MToP performed with misoprostol given other than oral (i.e. vaginally). No cases have been reported so far when misoprostol was taken by the approved oral route.

These infections are the consequence of atypical pathogens.

What to do:

Instruct the patient on the following:

- Contact physician immediately in case of
  - Fever
  - Pain despite intake of painkillers

2. Verification of complete expulsion

The medical ToP procedure consists in 3 steps:

- Mifegyne® intake,
- Topogyne® intake,
- and the follow-up visit.

If the medical abortion is done with the regimen mentioned in the Topogyne® SmPC, the risk of ongoing pregnancy is below 1%. This risk increases when other regimens are used. In case of ongoing pregnancy, it is essential for the patient to be informed about the potential risks due to Mifegyne®/Topogyne® to decide to carry the pregnancy to term or not.

What to do:

During follow-up visit verify complete expulsion

In case the medical ToP method failed, inform the patient about her choices:

- Terminate the pregnancy. In this case a second different method for ToP should be used
- Carry the pregnancy to term.

In case the patient decides to carry the pregnancy to term:

- It is important to inform the patient about the risk of malformations of the newborn due to the exposure to drug(s)
- Provide information on special follow up appointments with ultrasound scan monitoring in a specialized centre.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected
adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

Please also inform Exelgyn Pharmacovigilance department (pv@nordicpharma.com).

A safety card to fill out is available for the patient in the patient information leaflet. Please, note down the relevant contact details and prescribing centre to be used by the patient in case of disorders following the procedure.