Package leaflet: Information for the patient

Topotecan 1 mg powder for concentrate for solution for infusion
Topotecan 4 mg powder for concentrate for solution for infusion
topotecan

Read all of this leaflet carefully before you start using 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 or nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Topotecan is and what it is used for

Topotecan contains the active substance topotecan which helps to kill tumour cells.

Topotecan is used to treat:
- ovarian cancer or small cell lung cancer that has come back after chemotherapy
- advanced cervical cancer if surgery or radiotherapy is not possible. In this case Topotecan treatment is combined with medicines containing cisplatin.

2. What you need to know before you use Topotecan

Do not use Topotecan
- if you are allergic to topotecan or any of the other ingredients of this medicine (listed in section 6);
- if you are breast-feeding. You should stop breast-feeding before starting treatment with Topotecan;
- if your blood cell counts are too low.

Tell you doctor if you think any of these could apply to you.

Warnings and precautions
Talk to your doctor before using Topotecan:
- if you have any kidney problems. Your dose of Topotecan may need to be adjusted. Topotecan is not recommended in case of severe kidney impairment;
- if you have liver problems. Topotecan is not recommended in case of severe liver impairment;
- if you suffer from lung inflammation with signs such as cough, fever and difficulties in breathing, see also section 4 “Possible side effects”.

Topotecan may cause a decrease in the number of blood clotting cells (platelets). This can lead to severe bleeding from relatively small injuries such as a small cut. Rarely, it can lead to more severe bleeding (haemorrhage). Talk to your doctor for advice on how to minimize the risk of bleeding.

The incidence of side effects is more frequent in patients who are in poor general health. The doctor will evaluate your general health during the treatment and you should tell him/her in case you have fever, infection or are in some ways feeling unwell.

Children and adolescents
The experience in children and adolescents is limited and treatment is therefore not recommended.

Other medicines and Topotecan
Tell your doctor if you are taking, have recently taken or might take any other medicines.

Pregnancy, breast-feeding and fertility

Pregnancy
Topotecan should not be used in pregnant women, unless clearly necessary. If you are or think you might be pregnant, tell your doctor immediately.

Breast-feeding
You must not breast-feed while on treatment with Topotecan.

Contraception in males and females
If you are a woman, you should not get pregnant during treatment with topotecan and for at least 6 months after last dose.
If you are a man, you should take adequate precautions to ensure that your partner does not become pregnant during your treatment with topotecan and for at least 90 days after last dose
Effective contraception methods should be used to avoid becoming pregnant or fathering a child while on treatment with Topotecan. Ask your doctor for advice.

Fertility
Patients who are concerned about their fertility should ask their doctor for counselling on fertility and family planning options prior to starting treatment.

Driving and using machines
Topotecan can make you feel tired or weak. If you experience this, do not drive or use machines.

Information on sodium content
This medicine contains less than 1 mmol sodium (23 mg) per vial, i.e. essentially ‘sodium-free’.

3. How to use Topotecan

Your dose of Topotecan will depend on:
- the disease being treated,
- your body surface area (m^2),
- the results of blood tests carried out before and during treatment,
- how well you tolerate treatment.

Adults
Ovarian cancer and small cell lung cancer
The usual dose is 1.5 mg per m^2 of body surface area once daily for 5 days. This treatment cycle will normally be repeated every three weeks.

Cervical cancer
The usual dose is 0.75 mg per m^2 of body surface area once daily for 3 days. This treatment cycle will normally be repeated every three weeks.
For cervical cancer, it will be used together with another anticancer medicines containing cisplatin. For more information about cisplatin, please refer to the corresponding package leaflet.

Patients with impaired kidney function
Your doctor might need to reduce your dose based on your kidney function.

How Topotecan is prepared
Topotecan is supplied as a powder for concentrate for solution for infusion. The powder must be dissolved, and the resulting concentrate further diluted before administration.

How Topotecan is given
A doctor or nurse will give you the reconstituted and diluted Topotecan solution as an infusion (drip), usually into your arm, over about 30 minutes.

If you are given too much Topotecan
As this medicine is being given by your doctor or nurse, it is unlikely that you will be given too much. In the unlikely event of an overdose, your doctor will monitor you for side effects. Tell your doctor or nurse if you have any concerns about the amount of medicine that you receive.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects
You must tell your doctor **immediately** if you experience any of the following serious side effects. They may require hospitalisation and could even be life-threatening.

- **Infections** (very common; may affect more than 1 in 10 people), with signs such as:
  - fever
  - serious decline of your general condition
  - local symptoms, such as sore throat or burning sensation when urinating
  - severe stomach pain, fever and possibly diarrhoea (rarely with blood) can be signs of bowel inflammation (neutropenic colitis)

Topotecan may reduce your ability to fight infections.

- **Lung inflammation** (rare; may affect up to 1 in 1,000 people), with signs such as:
  - difficulty in breathing
  - cough
  - fever

The risk of developing this severe condition (interstitial lung disease) is higher if you currently have lung problems, or if you have received previous radiation treatment or medicines that affected your lungs, see also section 2 “Warnings and precautions”. This condition can be fatal.

- **Severe allergic (anaphylactic) reactions** (rare; may affect up to 1 in 1,000 people), with signs such as:
  - swelling of the face, lips, tongue or throat, difficulty breathing, low blood pressure, dizziness and itchy rash.

Other side effects with Topotecan include:

Very common side effects (may affect more than 1 in 10 people)
- Feeling generally weak and tired, which can be symptoms of a decrease in the number of red blood cells (anaemia). In some cases you may need a blood transfusion.
- Decrese in number of circulating white blood cells (leucotyes) in the blood. Abnormal low number of neutrophil granulocytes (a type of white blood cell) in the blood, with or without fever.
- Unusual bruising or bleeding, sometimes severe, caused by a decrease in the number of blood clotting cells (platelets).

- Weight loss and loss of appetite (anorexia); tiredness; weakness.
- Feeling sick (nausea), vomiting; diarrhoea; stomach pain; constipation.
- Inflammation of the lining of the mouth and digestive tract.
- Fever.
- Infections.
- Hair loss.

Common side effects (may affect up to 1 in 10 people)
- Allergic (hypersensitivity) reactions (including rash).
- Abnormal high level of bilirubin, a waste product produced by the liver during breakdown of red blood cells. Symptoms may include yellow skin (jaundice).
- Decrease in the number of all blood cells (pancytopenia).
- Feeling unwell.
- Serious blood infection, which can be fatal.
- Itching (pruritus).

Rare side effects (may affect up to 1 in 1,000 people)
- Swelling caused by fluid build-up (angioedema) e.g. around the eyes and lips as well as hands, feet and throat. If severe it may cause breathing difficulties.
- Itchy rash (or hives).

Very rare side effects (may affect up to 1 in 10,000 people)
- Mild pain and inflammation at the site of injection due to accidental administration of the medicinal product into the surrounding tissue (extravasation) e.g. by leakage.

If you are being treated for cervical cancer, you may get side effects from the other medicine (cisplatin) that you will be given along with Topotecan.

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 the 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 Topotecan

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 vial and carton.

Keep the vial in the outer carton in order to protect from light.

Storage after reconstitution and dilution
Chemical and physical stability of the concentrate has been demonstrated for 24 hours at 25 ± 2°C, in normal light conditions and 24 hours at 2°C to 8°C, protected from light.

The physico-chemical stability of the medicinal product solution obtained after dilution in solutions for infusion (NaCl 0.9% and Glucose 5%) has been demonstrated for 4 hours at room temperature, in normal lighting conditions, on samples reconstituted and stored for 12 hours and respectively 24 hours at 25ºC ± 2ºC and then diluted.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and

would normally not be longer than 24 hours at 2°C to 8°C, unless reconstitution/dilution has taken place in controlled and validated aseptic conditions.

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

6. Contents of the pack and other information

What Topotecan contains

The active substance is topotecan. Each vial contains 1 mg or 4 mg topotecan (as hydrochloride). After reconstitution 1 ml concentrate contains 1 mg topotecan.
- The other ingredients are: mannitol (E421), tartaric acid (E334), hydrochloric acid (E507) and sodium hydroxide (see section 2).

What Topotecan looks like and contents of the pack

Topotecan is supplied in type I colourless glass vials with grey bromobutylic stopper and aluminium seals with plastic flip-off caps. Vials may or may not be sheathed in a protective sleeve. Vials contain either 1 mg or 4 mg of topotecan.

Each pack contains one vial.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder
Accord Healthcare Limited
Sage House
319 Pinner Road
North Harrow
Middlesex
HA1 4HF
United Kingdom

Manufacturer
S.C. Sindan-Pharma S.R.L.
11 Ion Mihalache Blvd
Bucharest
Romania

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The following information is intended for healthcare professionals only:

Topotecan

INSTRUCTIONS ON USE

Guidelines for the safe handling and disposal of antineoplastic agents

1. Reconstitution and dilution of the medicinal product must be performed by trained personnel.
2. The preparation should be performed in a designated area under aseptic conditions.
3. Adequate protective disposable gloves, goggles, gown and mask should be worn.
4. Precautions should be taken to avoid the medicinal product accidentally coming into contact with the eyes. In the event of contact with the eyes, irrigate with large amounts of water. Then seek medical evaluation by a physician.
5. In case of skin contact, thoroughly wash the affected area with large amount of water. Always wash hands after removing gloves.
6. Pregnant staff should not handle the cytotoxic preparation.
7. Adequate care and precautions should be taken in the disposal of items (syringes, needles, etc.) used to reconstitute and/or dilute cytotoxic medicinal products. Any unused product or waste material should be disposed of in accordance with local requirements.

Reconstitution and dilution prior to administration

Before infusion, Topotecan powder for concentrate for solution for infusion must be reconstituted with an appropriate volume of water for injections, as follows:

- Topotecan 1 mg with 1.1 ml water for injections (as it contains 10% overage of fill)
- Topotecan 4 mg with 4 ml water for injections

Reconstitution will result in a concentrate containing 1 mg topotecan per ml.
This concentrate (1 mg/ml) must be diluted prior to administration.

The volume of reconstituted concentrate corresponding to the calculated individual dose should be further diluted with either sodium chloride 9 mg/ml (0.9%) solution for injection or 50 mg/ml (5%) glucose solution for infusion, to a final concentration of between 25 and 50 microgram per ml in the solution for infusion, for example:

	Volume for 25 microgram/ml solution	**Volume for 50 microgram/ml solution**
1 ml of 1 mg/ml topotecan solution	Add 39 ml to give 40 ml	Add 19 ml to give 20 ml
4 ml of 1 mg/ml topotecan solution	Add 156 ml to give 160 ml	Add 76 ml to give 80 ml

Storage after reconstitution and dilution
Chemical and physical stability of the concentrate has been demonstrated for 24 hours at 25 ± 2°C in normal light conditions, and for 24 hours at 2°C to 8°C when protected from light.

Chemical and physical stability of the solution obtained **after dilution** of the concentrate in sodium chloride 9 mg/ml (0.9%) solution for injection or 50 mg/ml (5%) glucose solution for infusion has been demonstrated for 4 hours at 25 ± 2°C, in normal lighting conditions .The concentrates tested were reconstituted and stored at 25 ± 2°C for 12 hours and 24 hours respectively after reconstitution, and then diluted.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2°C to 8°C, unless reconstitution/dilution has taken place in controlled and validated aseptic conditions.

Disposal
Any unused product or waste material should be disposed of in accordance with local requirements.

All items for administration or cleaning, including gloves, should be placed in high-risk, waste disposal bags for high-temperature incineration. Liquid waste may be flushed with large amounts of water.