

Package Leaflet: Information for the user

Caspofungin Rowex 70mg Powder for concentrate for solution for infusion caspofungin

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

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Caspofungin Rowex is and what it is used for
2. What you need to know before you are given Caspofungin Rowex
3. How to use Caspofungin Rowex
4. Possible side effects
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6. Contents of the pack and other information

1. What Caspofungin Rowex is and what it is used for

What Caspofungin Rowex is

Caspofungin Rowex contains a medicine called caspofungin. This belongs to a group of medicines called antifungals.

What Caspofungin Rowex is used for

Caspofungin Rowex is used to treat the following infections in children, adolescents and adults:

- serious fungal infections in your tissues or organs (called 'invasive candidiasis'). This infection is caused by fungal (yeast) cells called *Candida*.
People who might get this type of infection include those who have just had an operation or those whose immune systems are weak. Fever and chills that do not respond to an antibiotic are the most common signs of this type of infection.
- fungal infections in your nose, nasal sinuses or lungs (called 'invasive aspergillosis') if other anti-fungal treatments have not worked or have caused side effects. This infection is caused by a mould called *Aspergillus*.
People who might get this type of infection include those having chemotherapy, those who have had a transplant and those whose immune systems are weak.
- suspected fungal infections if you have a fever and a low white cell count that have not improved on treatment with an antibiotic. People who are at risk of getting a fungal infection include those who have just had an operation or those whose immune systems are weak.

How Caspofungin Rowex works

Caspofungin Rowex makes fungal cells fragile and stops the fungus from growing properly. This stops the infection from spreading and gives the body's natural defences a chance to completely get rid of the infection.

2. What you need to know before you are given Caspofungin Rowex

Do not use Caspofungin Rowex

- if you are allergic to caspofungin or any of the other ingredients of this medicine (listed in Section 6).

If you are not sure, talk to your doctor, nurse or pharmacist before you are given your medicine.

Warnings and precautions

Talk to your doctor, nurse or pharmacist before you are given Caspofungin Rowex if:

- you are allergic to any other medicines
- you have ever had liver problems - you might need a different dose of this medicine
- you are already taking cyclosporin (used to help prevent organ transplant rejection or to suppress your immune system) – as your doctor may need to run extra blood tests during your treatment
- if you have ever had any other medical problem.

If any of the above applies to you (or you are not sure), talk to your doctor, nurse or pharmacist before you are given Caspofungin Rowex.

Caspofungin Rowex may also cause Serious Cutaneous Adverse Reactions such as Stevens-Johnson Syndrome (SJS) and toxic epidermal necrolysis (TEN).

Other medicines and Caspofungin Rowex

Please tell your doctor, nurse or pharmacist if you are taking, have recently taken or might take any other medicines. This includes medicines obtained without a prescription, including herbal medicines. This is because Caspofungin Rowex can affect the way some other medicines work. Also some other medicines can affect the way caspofungin works.

Tell your doctor, nurse or pharmacist if you are taking any of the following medicines:

- cyclosporin or tacrolimus (used to help prevent organ transplant rejection or to suppress your immune system) as your doctor may need to run extra blood tests during your treatment
- some HIV medicines such as efavirenz or nevirapine
- phenytoin or carbamazepine (used for the treatment of seizures)
- dexamethasone (a steroid)
- rifampicin (an antibiotic).

If any of the above apply to you (or you are not sure), talk to your doctor, nurse or pharmacist before you are given Caspofungin Rowex.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

- Caspofungin has not been studied in pregnant women. It should be used in pregnancy only if the potential benefit justifies the potential risk to the unborn baby.
- Women given caspofungin should not breast-feed.

Driving and using machines

There is no information to suggest that Caspofungin Rowex affects your ability to drive or operate machinery.

This medicinal product contains less than 1 mmol sodium (23 mg) per vial, i.e. essentially “sodium-free”.

3. How to use Caspofungin Rowex

Caspofungin Rowex will always be prepared and given to you by a healthcare professional. You will be given Caspofungin Rowex:

- once each day
- by slow injection into a vein (intravenous infusion)
- over about 1 hour.

Your doctor will determine the duration of your treatment and how much caspofungin you will be given each day. Your doctor will monitor how well the medicine works for you. If you weigh more than 80 kg, you may need a different dose.

Children and adolescents

The dose for children and adolescents may differ from the adult dose.

If you have been given more Caspofungin Rowex than you should

Your doctor will decide how much Caspofungin Rowex you need and for how long each day. If you are worried that you may have been given too much caspofungin, tell your doctor or nurse straight away.

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

4. Possible side effects

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

Tell your doctor or nurse straight away if you notice any of the following side effects – you may need urgent medical treatment:

- rash, itching, feeling warm, swelling of your face, lips or throat or difficulty breathing – you may be having a histamine reaction to the medicine
- difficulty breathing with wheezing or a rash that gets worse – you may be having an allergic reaction to the medicine
- cough, serious breathing difficulties - if you are an adult and have invasive aspergillosis you may be experiencing a serious respiratory problem that could result in respiratory failure
- rash, skin peeling, mucous membrane sores, hives, large areas of peeling skin.

As with any prescription medicine, some side effects may be serious. Ask your doctor for more information.

Other side effects in adults include:

Common: may affect up to 1 in 10 people:

- Decreased haemoglobin (decreased oxygen carrying substance in the blood), decreased white blood cells
- Decreased blood albumin (a type of protein) in your blood, decreased potassium or low potassium levels in the blood.
- Headache
- Inflammation of the vein
- Shortness of breath
- Diarrhoea, nausea or vomiting
- Changes in some laboratory blood tests (including increased values of some liver tests)
- Itching, rash, skin redness or sweating more than usual
- Joint pain
- Chills, fever
- Itching at the injection site.

Uncommon: may affect up to 1 in 100 people:

- Changes in some laboratory blood tests (including disease of blood clotting, platelets, red blood cells and white blood cells).
- Loss of appetite, increase in amount of body fluid, imbalance of salt in the body, high sugar level in the blood, low calcium level in the blood, increase in calcium level in the blood, low magnesium level in the blood, increase in acid level in the blood
- Disorientation, feeling nervous, being unable to sleep
- Feeling dizzy, decreased feeling or sensitivity (especially in the skin), shaking, feeling sleepy, change in the way things taste, tingling or numbness
- Blurred vision, increase in tears, swollen eyelid, yellowing of the whites of the eyes
- Sensation of fast or irregular heartbeats, rapid heartbeat, irregular heartbeat, abnormal heart rhythm, heart failure
- Flushing, hot flush, high blood pressure, low blood pressure, redness along a vein which is extremely tender when touched

- Tightening of the bands of muscle around the airways resulting in wheezing or coughing, fast breathing rate, shortness of breath that wakes you up, shortage of oxygen in the blood, abnormal breath sounds, crackling sounds in the lungs, wheezing, nasal congestion, cough, throat pain
- Belly pain, upper belly pain, bloating, constipation, difficulty swallowing, dry mouth, indigestion, passing gas, stomach discomfort, swelling due to build-up of fluid around the belly
- Decreased flow of bile, enlarged liver, yellowing of the skin and/or whites of the eyes, liver injury caused by a drug or chemical, liver disorder
- Abnormal skin tissue, generalised itching, hives, rash of varying appearance, abnormal skin, red often itchy spots on your arms and legs and sometimes on the face and the rest of the body
- Back pain, pain in an arm or leg, bone pain, muscle pain, muscle weakness
- Loss of kidney function, sudden loss of kidney function
- Catheter site pain, injection site complaints (redness, hard lump, pain, swelling, irritation, rash, hives, leaking of fluid from the catheter into the tissue), inflammation of vein at injection site
- Increased blood pressure and alterations in some laboratory blood tests (including kidney electrolyte and clotting tests), increased levels of the medicines you are taking that weaken the immune system
- Chest discomfort, chest pain, feeling of body temperature change, generally feeling unwell, general pain, swelling of the face, swelling of the ankles, hands or feet, swelling, tenderness, feeling tired.

Side effects in children and adolescents

Very common: may affect more than 1 in 10 people:

- Fever

Common: may affect up to 1 in 10 people:

- Headache
- Fast heartbeat
- Flushing, low blood pressure
- Changes in some laboratory blood tests (increased values of some liver tests)
- Itching, rash
- Catheter site pain
- Chills
- Changes in some laboratory blood tests.

Reporting of side effects

If you get any side effects, talk to your doctor, nurse or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Caspofungin Rowex

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 and the vial as EXP. The expiry date refers to the last day of that month.

Store in a refrigerator (2°C to 8°C).

Reconstituted concentrate: should be used immediately. Stability data have shown that the concentrate for solution for infusion can be stored for up to 24 hours when the vial is stored at 25°C or less and reconstituted with water for injection.

Diluted patient infusion solution: should be used immediately. Stability data have shown that the product

can be used within 24 hours when stored at 25°C or less, or within 48 hours when the intravenous infusion bag (bottle) is stored refrigerated (2 to 8°C) and diluted with compatible infusion solution. 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 to 8°C, unless reconstitution and dilution have taken place in controlled validated aseptic conditions.

Once Caspofungin Rowex has been prepared, it should be used straight away. This is because it does not contain any ingredients to stop the growth of bacteria. Only a trained healthcare professional who has read the complete directions should prepare the medicine (please see below “Instructions of how to reconstitute and dilute Caspofungin Rowex”).

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 Caspofungin Rowex contains

- The active substance is caspofungin. Each vial of Caspofungin Rowex contains 70 mg of caspofungin (as acetate). The concentration of the reconstituted vial is 7.2 mg/ml.
- The other ingredients are sucrose, mannitol, succinic acid and sodium hydroxide.

What Caspofungin Rowex looks like and contents of the pack

Caspofungin Rowex is a sterile, white to off-white compact powder.

Each pack contains one vial of powder.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

Rowex Ltd., Bantry, Co. Cork, Ireland.

Manufacturer

Xellia Pharmaceuticals ApS., Dalslandsgade 11, DK-2300 Copenhagen S, Denmark.

This medicinal product is authorised in the Member States of the EEA under the following names:

Austria	Caspofungin Sandoz 70 mg – Pulver für ein Konzentrat zur Herstellung einer Infusionslösung
Belgium	Caspofungin Sandoz 70 mg poeder voor concentraat voor oplossing voor infusie
Bulgaria	Caspofungin Sandoz Каспофунгин Сандоз
Cyprus	Caspofungin Sandoz
Czech Republic	Caspofungin Sandoz 70 mg
Germany	Caspofungin HEXAL 70 mg Pulver für ein Konzentrat zur Herstellung einer Infusionslösung
Denmark	Caspofungin Sandoz
Estonia	Caspofungin Sandoz
Spain	Caspofungina Sandoz 70 mg polvo para concentrado para solución para perfusión EFG
Finland	Caspofungin Sandoz
France	CASPOFUNGINE SANDOZ 70 mg, poudre pour solution à diluer pour perfusion
Croatia	Kasporfungin Sandoz 70 mg prašak za koncentrat za otopinu za

	infuziju.
Ireland	Caspofungin Rowex 70 mg Powder for concentrate for solution for infusion
Italy	Caspofungin Sandoz
Lithuania	Caspofungin Sandoz 70 mg milteliai infuzinio tirpalo koncentratui
Latvia	Caspofungin Sandoz 70 mg pulveris infūziju šķīduma koncentrāta pagatavošanai
Malta	Caspofungin Sandoz 70mg powder for concentrate for solution for infusion
Netherlands	Caspofungine Sandoz 70 mg, poeder voor concentraat voor oplossing voor infusie
Norway	Caspofungin Sandoz
Poland	Caspofungin Sandoz
Portugal	Caspofungina Sandoz
Romania	Caspofungină Sandoz 70 mg pulbere pentru concentrat pentru soluție perfuzabilă
Sweden	Caspofungin Sandoz
Slovenia	Kaspofungin Sandoz 70 mg prašek za koncentrat za raztopino za infundiranje
Slovakia	Caspofungin Sandoz 70 mg prášok na infúzny koncentrát
United Kingdom	Caspofungin Sandoz 70mg powder for concentrate for solution for infusion PL 04416/1443

This leaflet was last revised in: April 2017.

The following information is intended for medical or healthcare professionals only:

Instructions of how to reconstitute and dilute Caspofungin Rowex:

Reconstitution of Caspofungin Rowex

DO NOT USE ANY DILUENTS CONTAINING GLUCOSE as Caspofungin Rowex is not stable in diluents containing glucose. DO NOT MIX OR CO-INFUSE Caspofungin Rowex WITH ANY OTHER MEDICINES, as there are no data available on the compatibility of Caspofungin Rowex with other intravenous substances, additives, or medicinal products. Visually inspect the infusion solution for particulate matter or discolouration.

INSTRUCTIONS FOR USE IN ADULT PATIENTS

Step 1 Reconstitution of conventional vials

To reconstitute the powder bring the vial to room temperature and aseptically add 10.5 ml of water for injection. The concentrations of the reconstituted vials will be 7.2 mg/ml.

The white to off-white compact lyophilised powder will dissolve completely. Mix gently until a clear solution is obtained. Reconstituted solutions should be visually inspected for particulate matter or discolouration. This reconstituted solution may be stored for up to 24 hours at or below 25°C.

Step 2 Addition of reconstituted Caspofungin Rowex to patient infusion solution

Diluents for the final solution for infusion are: sodium chloride solution for injection, or lactated Ringer's solution. The solution for infusion is prepared by aseptically adding the appropriate amount of reconstituted concentrate (as shown in the table below) to a 250 ml infusion bag or bottle. Reduced volume infusions in 100 ml may be used, when medically necessary, for 50 mg or 35 mg daily doses. Do not use if the solution is cloudy or has precipitated.

PREPARATION OF THE SOLUTION FOR INFUSION IN ADULTS

DOSE*	Volume of reconstituted Caspofungin Rowex for transfer to intravenous bag or bottle	Standard preparation (reconstituted Caspofungin Rowex added to 250 ml) final concentration	Reduced volume infusion (reconstituted Caspofungin Rowex added to 100 ml) final concentration
70 mg	10 ml	0.28 mg/ml	Not Recommended
70 mg (from two 50-mg vials)**	14 ml	0.28 mg/ml	Not Recommended
35 mg for moderate hepatic impairment (from one 70 mg vial)	5 ml	0.14 mg/ml	0.34 mg/ml

* 10.5 ml should be used for reconstitution of all vials

**If 70 mg vial is not available, the 70 mg dose can be prepared from two 50-mg vials

INSTRUCTIONS FOR USE IN PAEDIATRIC PATIENTS

Calculation of Body Surface Area (BSA) for paediatric dosing

Before preparation of infusion, calculate the body surface area (BSA) of the patient using the following formula: (Mosteller Formula)¹

¹ Mosteller RD: Simplified Calculation of Body Surface Area. *N Engl J Med* 1987 Oct 22;317(17): 1098 (letter)

$$BSA (m^2) = \sqrt{\frac{\text{Height (cm)} \times \text{Weight (kg)}}{3600}}$$

Preparation of the 70 mg/m² infusion for paediatric patients >3 months of age (using a 70-mg vial)

- Determine the actual loading dose to be used in the paediatric patient by using the patient's BSA (as calculated above) and the following equation:
 $BSA (m^2) \times 70 \text{ mg/m}^2 = \text{Loading Dose}$
 The maximum loading dose on Day 1 should not exceed 70 mg regardless of the patient's calculated dose.
- Equilibrate the refrigerated vial of Caspofungin Rowex to room temperature.
- Aseptically add 10.5 ml of water for injection.^a This reconstituted solution may be stored for up to 24 hours at or below 25°C.^b This will give a final Caspofungin Rowex concentration in the vial of 7.2 mg/ml.
- Remove the volume of medicine equal to the calculated loading dose (Step 1) from the vial. Aseptically transfer this volume (ml)^c of reconstituted Caspofungin Rowex to an IV bag (or bottle) containing 250 ml of 0.9%, 0.45%, or 0.225% Sodium Chloride Injection, or Lactated Ringers Injection. Alternatively, the volume (ml)^c of reconstituted Caspofungin Rowex can be added to a reduced volume of 0.9%, 0.45%, or 0.225% Sodium Chloride Injection or Lactated Ringers Injection, not to exceed a final concentration of 0.5 mg/ml. This infusion solution must be used within 24 hours if stored at or below 25°C or within 48 hours if stored refrigerated at 2 to 8°C.

Preparation of the 50 mg/m² infusion for paediatric patients >3 months of age (using a 70-mg vial)

- Determine the actual daily maintenance dose to be used in the paediatric patient by using the patient's BSA (as calculated above) and the following equation:
 $BSA (m^2) \times 50 \text{ mg/m}^2 = \text{Daily Maintenance Dose}$
 The daily maintenance dose should not exceed 70 mg regardless of the patient's calculated dose.
- Equilibrate the refrigerated vial of Caspofungin Rowex to room temperature.
- Aseptically add 10.5 ml of water for injection.^a This reconstituted solution may be stored for up to 24

hours at or below 25°C.^b This will give a final Caspofungin Rowex concentration in the vial of 7.2 mg/ml.

4. Remove the volume of medicine equal to the calculated daily maintenance dose (Step 1) from the vial. Aseptically transfer this volume (ml)^c of reconstituted Caspofungin Rowex to an IV bag (or bottle) containing 250 ml of 0.9%, 0.45%, or 0.225% Sodium Chloride Injection, or Lactated Ringers Injection. Alternatively, the volume (ml)^c of reconstituted Caspofungin Rowex can be added to a reduced volume of 0.9%, 0.45%, or 0.225% Sodium Chloride Injection or Lactated Ringers Injection, not to exceed a final concentration of 0.5 mg/ml. This infusion solution must be used within 24 hours if stored at or below 25°C or within 48 hours if stored refrigerated at 2 to 8°C.

Preparation notes:

^a The white to off-white cake will dissolve completely. Mix gently until a clear solution is obtained.

^b Visually inspect the reconstituted solution for particulate matter or discolouration during reconstitution and prior to infusion. Do not use if the solution is cloudy or has precipitated.

^c Caspofungin Rowex is formulated to provide the full labeled vial dose (70 mg) when 10 ml is withdrawn from the vial.