

Package Leaflet: Information for the user

Caspofungin Hikma 50 mg powder for concentrate for solution for infusion Caspofungin Hikma 70 mg powder for concentrate for solution for infusion

Caspofungin

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

What is in this leaflet

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

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

What Caspofungin Hikma is

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

What Caspofungin is used for

Caspofungin 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 works

Caspofungin 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 Hikma

Do not use Caspofungin Hikma

- 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 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.

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

Other medicines and Caspofungin Hikma

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 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^[1]_{SEP}
- 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.

Pregnancy and breast-feeding

Ask your doctor for advice before taking any medicine, if you are pregnant or breast-feeding or think you are pregnant.

- 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 affects your ability to drive or operate machinery.

3. How to use Caspofungin Hikma

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

You will be given Caspofungin:

- 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 Hikma than you should

Your doctor will decide how much Caspofungin 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 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 heart beats, rapid heart beat, irregular heart beat, 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 heart beat
- 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 [the national reporting system listed in Appendix V](#). By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Caspofungin Hikma

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 (the first two numbers are the month; the next four numbers are the year). The expiry date refers to the last day of that month.

Store in a refrigerator (2 °C to 8 °C).

Once Caspofungin 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 Hikma”).

If not used immediately, the solution may be stored for up to 24 hours at 25°C or less, or for 48 hours when the intravenous infusion bag (bottle) is stored refrigerated (2 to 8°C) and diluted with sodium chloride solution 9 mg/ml (0.9 %), 4.5 mg/ml (0.45 %), or 2.25 mg/ml (0.225 %) for infusion, or lactated Ringer’s solution. 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.

Do not use the solution if you notice any signs of discolouration or suspended particles.

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 Hikma contains

- The active substance is caspofungin.

Caspofungin Hikma 50 mg powder for concentrate for solution for infusion

Each vial of Caspofungin Hikma contains 50 mg of caspofungin (as acetate).

Caspofungin Hikma 70 mg powder for concentrate for solution for infusion

Each vial of Caspofungin Hikma contains 70 mg of caspofungin (as acetate).

- The other ingredients are sucrose, manitol, hydrochloric acid (for pH-adjustment), sodium hydroxide (for pH-adjustment), carbon dioxide (for pH-adjustment) (please see section 2. What you need to know before you are given Caspofungin).

What Caspofungin Hikma looks like and contents of the pack

Lyophilised sterile white to off-white compact powder. The reconstituted solution is clear.

Caspofungin Hikma 50 mg powder for concentrate for solution for infusion

10 ml Type I glass vial with a bromobutyl rubber and a plastic cap with a red aluminum band.

Caspofungin Hikma 70 mg powder for concentrate for solution for infusion

10 ml Type I glass vial with a bromobutyl rubber and a plastic cap with an orange aluminum band.

Each pack contains one vial of powder.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

Hikma Farmacêutica (Portugal) S.A.

Estrada do Rio da Mó, 8, 8A 8B, Fervença,
2705-906 Terrugem, Sintra,
Portugal

Manufacturer

Pharmadox Healthcare, Ltd

KW20A Kordin Industrial Park, Paola, PLA 3000, Malta

or

Galenicum Health, S.L.U.

Sant Gabriel, 50. Esplugues de Llobregat 08950 Barcelona Spain

or

SAG Manufacturing S.L.U.

Ctra. N-I, Km 36 San Agustín de Guadalix, 28750, Madrid, Spain

or

Hikma Italia S.p.A.

Viale Certosa, 10, 27100, Pavia (PV), Italy

This leaflet was last revised in 05/2023

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

Instructions of how to reconstitute and dilute Caspofungin Hikma:

Reconstitution of Caspofungin Hikma

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

Caspofungin Hikma 50 mg powder for concentrate for solution for infusion

INSTRUCTIONS FOR USE IN ADULT PATIENTS (50 mg vial)

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 5.2 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 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.

50 mg vial: PREPARATION OF THE SOLUTION FOR INFUSION IN ADULTS

DOSE*	Volume of reconstituted Caspofungin for transfer to	Standard preparation (reconstituted Caspofungin added)	Reduced volume infusion (reconstituted Caspofungin added)
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	intravenous bag or bottle	to 250 ml) final concentration	to 100 ml) final concentration
50 mg	10 ml	0.20 mg/ml	-
50 mg at reduced volume	10 ml	-	0.47 mg/ml
35 mg for moderate hepatic impairment (from one 50 mg vial)	7 ml	0.14 mg/ml	-
35 mg for moderate hepatic impairment (from one 50 mg vial) at reduced volume	7 ml	-	0.34 mg/ml

*10.5 ml should be used for reconstitution of all vials

INSTRUCTIONS FOR USE IN PAEDIATRIC PATIENTS (50 mg vial)

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: (Mosteller¹ Formula)

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

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

1. 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.

2. Equilibrate the refrigerated vial of Caspofungin to room temperature.
3. 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 concentration in the vial of 5.2 mg/ml.
4. 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 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 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.

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

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

1. 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:

$$\text{BSA (m}^2\text{)} \times 50 \text{ mg/m}^2 = \text{Daily Maintenance Dose}$$

The daily maintenance dose should not exceed 70 mg regardless of the patient's calculated dose.

2. Equilibrate the refrigerated vial of Caspofungin to room temperature.
3. 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 concentration in the vial of 5.2 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 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 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 discoloration during reconstitution and prior to infusion. Do not use if the solution is cloudy or has precipitated.
- c** Caspofungin is formulated to provide the full labeled vial dose (50 mg) when 10 ml is withdrawn from the vial.

Caspofungin Hikma 70 mg powder for concentrate for solution for infusion

INSTRUCTIONS FOR USE IN ADULT PATIENTS (70 mg vial)

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 discoloration. This reconstituted solution may be stored for up to 24 hours at or below 25°C.

Step 2 Addition of reconstituted Caspofungin 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.

70 mg vial: PREPARATION OF THE SOLUTION FOR INFUSION IN ADULTS

DOSE*	Volume of reconstituted Caspofungin for transfer to intravenous bag or bottle	Standard preparation (reconstituted Caspofungin added to 250 ml) final concentration	Reduced volume infusion (reconstituted Caspofungin 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 vial.

INSTRUCTIONS FOR USE IN PAEDIATRIC PATIENTS (70 mg vial)

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)

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

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

1. 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.
2. Equilibrate the refrigerated vial of Caspofungin to room temperature.
 3. 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 concentration in the vial of 7.2 mg/ml.
 4. 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 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 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)

1. 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:

$$\text{BSA (m}^2\text{)} \times 50 \text{ mg/m}^2 = \text{Daily Maintenance Dose}$$

The daily maintenance dose should not exceed 70 mg regardless of the patient's calculated dose.

2. Equilibrate the refrigerated vial of Caspofungin to room temperature.
3. 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 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 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 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 discoloration during reconstitution and prior to infusion. Do not use if the solution is cloudy or has precipitated.
- c** Caspofungin is formulated to provide the full labeled vial dose (70 mg) when 10 ml is withdrawn from the vial.