

CRESEMBA[®] Capsules (Isavuconazonium sulfate)

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, pharmacist or nurse.
- 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, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

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2. What you need to know before you take Cresemba
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1. What Cresemba is and what it is used for

What Cresemba is

Cresemba is an anti-fungal medicine that contains the active substance isavuconazole.

How Cresemba works

Isavuconazole works by killing or stopping the growth of the fungus, which causes the infection.

What Cresemba is used for

Cresemba is used in adults to treat the following fungal infections:

- invasive aspergillosis, caused by a fungus in the 'Aspergillus' group;
- mucormycosis, caused by a fungus belonging to the 'Mucorales' group in patients for whom a treatment with amphotericin B is not appropriate.

2. What you need to know before you take Cresemba

Do not take Cresemba:

- if you are allergic to isavuconazole or any of the other ingredients of this medicine (listed in section 6),
- if you have a heart beat problem called 'familial short QT syndrome',
- **if you are using any of the following medicines:**
 - ketoconazole, used for fungal infections,
 - high doses of ritonavir (400 mg every 12 hours), used for HIV,
 - rifampicin, rifabutin, used for tuberculosis,
 - carbamazepine, used for epilepsy,
 - barbiturate medicines like phenobarbital, used for epilepsy and sleep disorders,
 - phenytoin, used for epilepsy,
 - St. John's wort, a herbal medicine used for depression,

- efavirenz, etravirine, used for HIV,
- nafcillin, used for bacterial infections.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before taking Cresemba:

- if you have had an allergic reaction to other 'azole' anti-fungal treatments in the past, such as ketoconazole, fluconazole, itraconazole, voriconazole or posaconazole,
- if you are suffering from severe liver disease. Your doctor should monitor you for possible side effects

Look out for side effects

Stop taking Cresemba and tell your doctor straight away if you notice any of the following side effects:

- rash, swelling of your lips, mouth, tongue or throat with difficulty breathing - these may be signs of an allergic reaction (hypersensitivity).

Changes in your liver function

Cresemba can sometimes affect your liver function. Your doctor may carry out blood tests while you are taking this medicine.

Skin problems

Tell your doctor straight away if you get severe blistering of the skin, mouth, eyes or genitals.

Children and adolescents

Cresemba should not be used in children or adolescents younger than 18 years because there is no information on use in this age group.

Other medicines and Cresemba

Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines. Some medicines may affect the way Cresemba works or Cresemba may affect the way they work, if they are taken at the same time.

In particular, do not take this medicine and tell your doctor or pharmacist if you are taking any of the following medicines:

- ketoconazole, used for fungal infections,
- high doses of ritonavir (400 mg every 12 hours), used for HIV,
- rifampicin, rifabutin, used for tuberculosis,
- carbamazepine, used for epilepsy,
- barbiturate medicines like phenobarbital, used for epilepsy and sleep disorders,
- phenytoin, used for epilepsy,
- St. John's wort, a herbal medicine used for depression,
- efavirenz, etravirine, used for HIV,
- nafcillin, used for bacterial infections.

Unless your doctor tells you otherwise, do not take this medicine and tell your doctor or pharmacist if you are taking any of the following medicines:

- rufinamide or other medicines which decrease the QT interval on the heart tracing (ECG),
- aprepitant, used to prevent nausea and vomiting by cancer treatment,
- prednisone, used for rheumatoid arthritis,
- pioglitazone, used for diabetes.

Tell your doctor or pharmacist if you are taking any of the following medicines, as a dose adjustment or monitoring may be required to check that the medicines are still having the

desired effect:

- ciclosporin, tacrolimus and sirolimus, used for after having a transplant, called 'immuno-suppressants',
- cyclophosphamide, used for cancer,
- digoxin, used to treat heart failure or an uneven heart beat,
- colchicine, used for gout attack,
- dabigatran etexilate, used to stop blood clots after hip or knee replacement surgery,
- clarithromycin, used for bacterial infections,
- saquinavir, amprenavir, nelfinavir, indinavir, delavirdine, nevirapine, lopinavir/ritonavir combination, used for HIV,
- alfentanil, fentanyl, used against strong pain,
- vincristine, vinblastine, used for cancer,
- mycophenolate mofetil (MMF), used in transplant patients,
- midazolam, used for severe insomnia and stress,
- bupropion, used for depression,
- metformin, used for diabetes,
- daunorubicin, doxorubicin, imatinib, irinotecan, lapatinib, mitoxantrone, topotecan, used for different sorts of cancer.

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 for advice before using this medicine.

Do not take Cresemba if you are pregnant, unless your doctor tells you otherwise. This is because it is not known if it may affect or harm your unborn baby.

Do not breast-feed if you are taking Cresemba.

Driving and using machines

Cresemba may make you feel confused, tired or sleepy. It can also make you pass out. If this happens, do not drive or use machines.

3. How to take Cresemba

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

Starting dose for the first two days (48 hours)

The recommended dose is two capsules three times a day (every 8 hours).

Usual dose after the first two days

This is started 12 to 24 hours after your last starting dose. The recommended dose is two capsules once a day.

You will take this dose until your doctor tells you otherwise. The duration of treatment with Cresemba may be longer than 6 months if your doctor considers this necessary.

Capsules can be taken with or without food. Swallow the capsules whole. Do not chew, crush, dissolve or open the capsules.

If you take more Cresemba than you should

If you take more Cresemba than you should, talk to a doctor or go to a hospital straight away. Take the medicine pack with you so the doctor knows what you have taken.

You may have more side effects such as:

- headache, feeling dizzy, restless or sleepy,
- tingling, reduced sense of touch or sensation in the mouth,
- problems being aware of things, hot flushes, anxiety, joint pain,
- changes in the way things taste, dry mouth, diarrhoea, vomiting,
- feeling your heart beat, faster heart rate, being more sensitive to light.

If you forget to take Cresemba

Take the capsules as soon as you remember. However, if it is nearly time for the next dose, skip the missed dose.

Do not take a double dose to make up for a forgotten dose.

If you stop taking Cresemba

Do not stop taking Cresemba unless your doctor has told you to do so. It is important to keep taking this medicine as long as your doctor tells you. This is to make sure that the fungal infection has gone.

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

4. Possible side effects

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

Stop taking Cresemba and tell your doctor straight away if you notice any of the following side effects:

- rash, swelling of your lips, mouth, tongue or throat with difficulty breathing - these may be signs of an allergic reaction (hypersensitivity).

Tell your doctor straight away if you notice any of the following side effects:

- severe blistering of the skin, mouth, eyes or genitals.

Other side effects

Tell your doctor, pharmacist or nurse if you notice any of the following side effects:

Common: may affect up to 1 in 10 people

- low potassium in your blood,
- decreased appetite,
- hallucinations (delirium),
- headache,
- sleepiness,
- inflamed veins that could lead to blood clots,
- shortness of breath or sudden and severe difficulty breathing,
- feeling sick (nausea), being sick (vomiting), diarrhoea, stomach pain,
- changes in blood tests of liver function,
- rash, itching,
- kidney failure,
- chest pain, feeling tired or sleepy.

Uncommon: may affect up to 1 in 100 people

- reduced white blood cells - can increase your risk of infection and fever,
- reduced blood cells called 'platelets' - can increase your risk for bleeding or bruising,
- reduced red blood cells - can make you feel weak or short of breath or make your skin

- pale,
- severe reduction in blood cells - can make you feel weak, cause bruising or make infections more likely,
- rash, swelling of your lips, mouth, tongue or throat with difficulty breathing (hypersensitivity),
- low blood sugar levels,
- low blood levels of magnesium,
- low levels in the blood of a protein called 'albumin',
- not getting the right goodness from your diet (malnutrition),
- depression, difficulty sleeping,
- seizure, fainting or feeling faint, dizziness,
- sensation of tingling, tickling, or pricking of the skin (paraesthesia),
- altered mental state (encephalopathy),
- changes in taste (dysgeusia),
- feeling of 'spinning' or being dizzy (vertigo),
- heart beat problems - may be too fast or uneven, or extra heart beats – this may show in your heart tracing (electrocardiogram or ECG),
- problems with the blood circulation,
- low blood pressure,
- wheezing, very fast breathing, coughing up blood or blood-stained sputum, nose bleeding,
- indigestion,
- constipation,
- feeling bloated (abdominal distension),
- enlarged liver,
- inflammation of the liver,
- problems with the skin, red or purple spots on the skin (petechiae), inflamed skin (dermatitis), hair loss,
- back pain,
- feeling weak, very tired, or sleepy or generally out of sorts (malaise).

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

5. How to store Cresemba

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

Store in the original packaging in order to protect from moisture.

Do not use this medicine after the expiry date which is stated on the label after EXP.

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 Cresemba contains

- The active substance is isavuconazole. Each capsule contains 186.3 mg isavuconazonium sulfate, corresponding to 100 mg isavuconazole.
- The other ingredients ingredients are:
 - Capsule content: magnesium citrate (anhydrous), microcrystalline cellulose, talc, anhydrous colloidal silica, stearic acid.
 - Capsule shell: hypromellose, water, red iron oxide (E172) (capsule body only), titanium dioxide (E171), gellan gum, potassium acetate, disodium edetate, sodium laurilsulfate.
 - Printing ink: shellac, propylene glycol, potassium hydroxide, black iron oxide (E172).

What Cresemba looks like and contents of the pack

Cresemba 100 mg capsules are capsules with a reddish-brown body marked with “100” in black ink and a white cap marked with “C” in black ink.

Cresemba is available in cartons that contain 14 capsules. Each carton contains 2 aluminium blisters pack, with 7 capsules each.

Each capsule pocket is connected to a pocket that contains ‘desiccant’ to protect the capsule from moisture.

Do not puncture the blister containing the desiccant.

Do not swallow or use the desiccant.

December 2018
Hong Kong