Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986

This medicine is dispensed with a doctor's prescription only

Cresemba® 100 mg capsules

Each capsule contains isavuconazole 100 mg (about 186.3 mg isavuconazonium sulfate)

For a list of inactive ingredients and allergens, see section 6 "Further information".

Read the entire leaflet carefully before using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.

This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar to yours.

1. WHAT IS THIS MEDICINE INTENDED FOR?

Cresemba is indicated in adults for the treatment of:
- invasive aspergillosis.
- mucormycosis in patients for whom treatment with amphotericin B is inappropriate.

Therapeutic group: antifungal of the triazole group
Isavuconazole works by killing or stopping the growth of the fungus which causes the infection.

2. BEFORE USING THIS MEDICINE

Do not use this medicine if:

- You are sensitive (allergic) to the active ingredient or to any of the other ingredients in this medicine (see section 6).
- You have a heart beat problem called 'familial short QT syndrome'.

- You are breastfeeding.
- You are taking any of the following medicines:
  - ketoconazole, for treatment of fungal infections
  - high doses of ritonavir (more than 200 mg every 12 hours), for treatment of HIV
  - rifampicin, rifabutin, for treatment of tuberculosis
  - carbamazepine, for treatment of epilepsy
  - barbiturate medicines like phenobarbital, for treatment of epilepsy and sleep disorders
  - phenytoin, for treatment of epilepsy
  - *Hypericum* (St. John's wort), a herbal medicine for treatment of depression
  - efavirenz, etravirine, for treatment of HIV
  - nafcillin, for treatment of bacterial infections

Special warnings regarding use of the medicine
Before using Cresemba, tell your doctor if:
- You have had an allergic reaction to another 'azole' anti-fungal medicine in the past, such as ketoconazole, fluconazole, itraconazole, voriconazole or posaconazole.
- You are suffering from severe liver disease. Your doctor should monitor you for possible side effects.

Stop taking Cresemba and tell the doctor immediately if you notice any of the following side effects:
- sudden wheezing, difficulty breathing, swelling of the face, lips, mouth or tongue, severe itching, sweating, dizziness or fainting, fast heartbeat or pounding in the chest – these may be signs of a severe allergic reaction (anaphylaxis).

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

Skin problems
Tell your doctor immediately if you develop severe blistering of the skin, mouth, eyes or genitals.

Children and adolescents
Cresemba is not intended for use in children and adolescents below the age of 18 years.

Drug interactions
If you are taking or have recently taken, other medicines, including nonprescription medicines and dietary supplements, tell your doctor or pharmacist. Particularly if you are taking:
- ketoconazole, for treatment of fungal infections
- high doses of ritonavir (more than 200 mg every 12 hours), for treatment of HIV
- rifampicin, rifabutin, for treatment of tuberculosis
- carbamazepine, for treatment of epilepsy
- barbiturate medicines like phenobarbital, for treatment of epilepsy and sleep disorders
- phenytoin, for treatment of epilepsy
- *Hypericum* (St. John's wort), a herbal medicine for treatment of depression
- efavirenz, etravirine, for treatment of HIV
- nafcillin, for treatment of 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 caused by cancer treatments
- prednisone, for treatment of rheumatoid arthritis
- pioglitazone, for treatment of 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 whether the medicines are still having the desired effect:
- ciclosporine, tacrolimus and sirolimus, used to prevent rejection of a transplant
- cyclophosphamide, for treatment of cancer
- digoxin, for treatment of heart failure or uneven heart beats
- colchicine, for treatment of gout attack
- dabigatran etexilate, used to stop blood clots after hip or knee replacement surgery

- clarithromycin, for treatment of bacterial infections
- saquinavir, fosamprenavir, indinavir, nevirapine, lopinavir/ritonavir combination, for treatment of HIV
- alfentanil, fentanyl, for treatment against strong pain
- vincristine, vinblastine, for treatment of cancer
- mycophenolate mofetil (MMF), to treat transplant patients
- midazolam, for treatment of severe insomnia and stress
- bupropion, for treatment of depression
- metformin, for treatment of diabetes
- daunorubicin, doxorubicin, imatinib, irinotecan, lapatinib, mitoxantrone, topotecan, for treatment of different types of cancer.

Pregnancy, breastfeeding, and fertility
If you are pregnant or breastfeeding, 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 instructs you otherwise, because it is not known whether the medicine may affect or harm your unborn baby.

Do not take Cresemba while breastfeeding.

Driving and using machines
Cresemba may make you feel confused, tired or sleepy. The medicine can also make you pass out. Therefore, be very careful when driving or operating machines.

3. HOW TO USE THIS MEDICINE?
Always use this medicine according to your doctor's instructions. Check with your doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the medicine.
The dosage and treatment regimen will be determined by your doctor only.
The standard dosage is usually:
Starting dose for the first two days (48 hours)
The recommended dose is 2 capsules every 8 hours.

Usual dose after the first two days
This dose is started 12 to 24 hours after taking your last starting dose. The recommended dose is 2 capsules once a day.

Do not exceed the recommended dose.

Treatment duration
Continue taking the medicine until your doctor instructs you otherwise. The duration of treatment with Cresemba may be longer than 6 months if your doctor considers this necessary.

Method of administration
Capsules should be taken with or without food. Swallow the capsules whole. Do not chew, crush, dissolve or open the capsules.

If you have accidentally taken a higher dosage
If you have taken an overdose, or if a child has accidentally swallowed some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you.
You may experience more side effects such as:
- headache, feeling dizzy, restless or sleepy
- tingling, reduced sense of touch or reduced sensation in the mouth
- problems being aware of things, hot flushes, anxiety, joint pain
- change in the way things taste, dry mouth, diarrhea, vomiting
- feeling your heart beat, fast heart rate, increased sensitivity to light.

If you forget to take the medicine
If you forget to take this medicine, take the capsule as soon as you remember. However, if it is nearly time for the next dose, skip the forgotten dose.
Do not take a double dose to compensate for the forgotten dose.

Adhere to the treatment as recommended by your doctor.
Even if your health improves, do not stop treatment with this medicine without consulting your doctor.

If you stop taking this medicine
Do not stop taking this medicine unless your doctor has instructed you to do so. It is important to keep taking this medicine as long as your doctor instructs you, in order to make sure that the fungal infection has gone.

Do not take medicines in the dark! Check the label and dose each time you take a medicine. Wear glasses if you need them.
If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Cresemba may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

Stop using this medicine and contact your doctor immediately if you notice any of the following side effects:
- a severe allergic reaction (anaphylaxis) such as sudden wheezing, breathing problems, swelling of the face, lips, mouth or tongue, severe itching, sweating, dizziness or fainting, fast heartbeat or pounding in the chest.

Contact your doctor immediately if you notice any of the following side effects:
- severe blistering of the skin, mouth, eyes or genitals.

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

Common side effects (may affect up to 1 in 10 people):
- low blood potassium level
- 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), diarrhea, stomach pain
- changes in blood tests of liver function
- rash, itching
- kidney failure (symptoms could include swelling of legs)
- chest pain, feeling tired or sleepy

Uncommon side effects (may affect up to 1 in 100 people):
- reduced level of white blood cells - can increase the risk of infection and fever
- reduced level of blood platelets - can increase the risk of bleeding and bruising
- reduced level of red blood cells - can make you feel weak or short of breath or make your skin pale
- severe reduction in the quantity of blood cells - can make you feel weak, cause bruising or make infections more likely
- rash, swelling of the lips, mouth, tongue or throat with difficulty breathing (hypersensitivity)
- low blood sugar levels
- low blood levels of magnesium
- low blood levels of a protein called albumin
- not getting the right goodness from your diet (malnutrition)
- depression, difficulty sleeping
- seizures, fainting or feeling faint, dizziness
- sensation of tingling, tickling, or pricking of the skin (paraesthesia)
- altered mental state (encephalopathy)
- changes in sense of 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 (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
- swelling in the extremities
- feeling weak, very tired, or sleepy or generally out of sorts (malaise)

Side effects with frequency not known:
- anaphylaxis (a severe allergic reaction).

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects or by using the link: https://sideeffects.health.gov.il

5. HOW TO STORE THE MEDICINE?

Prevent poisoning! This and any other medicine should be kept in a closed place, out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by a doctor.
Do not use the medicine after the expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.
Storage conditions: Store below 25°C. Store in the original package in order to protect from moisture.

6. FURTHER INFORMATION

In addition to the active ingredient, this medicine also contains:
Capsule content
magnesium citrate (anhydrous), microcrystalline cellulose, talc, stearic acid, anhydrous colloidal silica.

Capsule shell (body)
hypromellose, water purified, red iron oxide, titanium dioxide, gellan gum, potassium acetate, disodium edetate, sodium laurilsulfate, ink (10A2 Black).

Capsule shell (cap)
hypromellose, water purified, titanium dioxide, gellan gum, potassium acetate, disodium edetate, sodium laurilsulfate, ink (10A2 Black).

Printing ink on the capsule
shellac, propylene glycol, ammonia solution concentrated, potassium hydroxide, black iron oxide.

What the medicine 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 capsule cap marked with "C" in black ink.
Cresemba is packed in a pack containing 14 capsules. Each pack contains 2 aluminium blister trays containing 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.

Registration holder and address: Pfizer PFE Pharmaceuticals Israel Ltd.,
9 Shenkar St., Herzliya Pituach 46725.

Registration number of the medicine in the National Drug Registry of the Ministry of Health:162-03-35594.

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