

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

This medicine is dispensed with a doctor's prescription only

Symdeko 50 mg/ 75 mg & 75 mg
Symdeko 100 mg/150 mg & 150 mg

Film-coated tablets

Active ingredients and their quantities

Symdeko 50 mg/ 75 mg & 75 mg

White film-coated tablets

Each film coated tablet contains tezacaftor 50 mg and ivacaftor 75 mg

Light blue film-coated tablets

Each film coated tablet contains ivacaftor 75 mg

Symdeko 100 mg/150 mg & 150 mg

Yellow film-coated tablets

Each film coated tablet contains tezacaftor 100 mg and ivacaftor 150 mg

Light blue film-coated tablets

Each film coated tablet contains ivacaftor 150 mg

Inactive ingredients and allergens - see section 6 "**Additional information**". See also "**Important information about some of this medicine's ingredients**" in section 2.

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

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

1. What is the medicine intended for?

Symdeko contains a combination of tezacaftor and ivacaftor and is used for the treatment of cystic fibrosis (CF) in patients ages 6 years and older who have inherited the *F508del* mutation (change) from both parents and therefore have the mutation in two copies of the CFTR gene, or who have at least one mutation in the CFTR gene that is responsive to treatment with Symdeko.

Therapeutic group:

Tezacaftor – CFTR corrector

Ivacaftor – Potentiator of the CFTR protein

Symdeko contains two active substances, tezacaftor and ivacaftor that work together to improve the function of the abnormal CFTR protein. Tezacaftor increases the amount of CFTR available and ivacaftor helps the abnormal protein to work more properly.

2. Before using the medicine

Do not use this medicine if:

- You are sensitive (allergic) to the active ingredients (tezacaftor or ivacaftor) or to any of the other ingredients in this medicine (see section 6 "**Additional information**").

Special warnings about using this medicine

Before taking Symdeko, tell your doctor about all of your medical conditions, including if you:

- have or have had liver problems
- have kidney problems

If you have liver problems, your doctor may need to reduce the dose as your liver is not clearing Symdeko as fast as in people who do not have moderate or severe problems with liver function.

Children

Symdeko is not intended for use in children under 6 years of age.

Tests and follow-up

Your doctor will do blood tests to check your liver function:

- before you start taking Symdeko
- every 3 months during your first year of taking Symdeko
- every year while you are taking Symdeko

Your doctor may do blood tests to check the liver function more often if you have had high liver enzymes in your blood in the past.

Abnormality of the eye lens (cataract) has been noted in some children and adolescents treated with SYMDEKO or treated with ivacaftor alone. If you are a child or adolescent, your doctor should perform eye examinations before and during treatment with Symdeko to look for cataracts.

Drug interactions

If you are taking or have recently taken other medicines, including nonprescription medicines and dietary supplements, tell your doctor or pharmacist.

Do not take Symdeko if you are taking:

- rifampin or rifabutin – antibiotic medicines used for treatment of infections
- phenobarbital, carbamazepine, or phenytoin – epileptic seizure medicines
- St. John's wort (*Hypericum perforatum*) – medicine produced from a plant used for treatment of depression

Talk to your doctor before taking Symdeko if you take any of the medicines listed above.

Symdeko may affect the way other medicines work, and other medicines may affect how Symdeko works. The dose of Symdeko may need to be adjusted when taken with certain medicines. Especially tell your doctor if you take:

- Ketoconazole, itraconazole, posaconazole, voriconazole, or fluconazole – antifungal medicines used for the treatment of fungal infections
- Telithromycin, clarithromycin, or erythromycin – antibiotics used for the treatment of bacterial infections
- Cyclosporine, tacrolimus, everolimus, or sirolimus – immunosuppressants
- Digoxin – cardiac glycoside used for the treatment of mild to moderate congestive heart failure and an abnormal heart rhythm called atrial fibrillation
- Warfarin – anticoagulant medicine used to prevent blood clots from forming
- Glimepiride or glipizide – medicines for diabetes used to lower blood sugar levels

Using this medicine and food

Avoid food or drink containing grapefruit during treatment with Symdeko as they may increase the amount of tezacaftor and ivacaftor in your body. Always take Symdeko with food that

contains fat. Examples of fat-containing foods include eggs, butter, peanut butter, cheese pizza, and whole-milk dairy products such as whole milk, cheese and yogurt.

Pregnancy and breastfeeding

If you are pregnant or think that you are pregnant, planning to have a child or are breast-feeding, consult a doctor or pharmacist before using the medicine. There is limited information on the use of Symdeko in pregnant woman. The doctor will help you decide what is best for you.

It is unknown whether tezacaftor or ivacaftor (the active ingredients in Symdeko) are secreted in mother's milk. If you are planning to breastfeed, consult a doctor before taking Symdeko. Your doctor will decide whether to recommend that you stop breast-feeding or for you to stop tezacaftor/ivacaftor therapy.

Driving and using machines

Symdeko can cause dizziness in some people who take it. Do not drive a car, use machinery, or do anything that needs you to be alert until you know how Symdeko affects you.

If a child experiences dizziness while taking Symdeko, it is advised that the child does not ride a bike or do anything else that needs their full attention, until their symptoms disappear.

Important information about some of this medicine's ingredients

Symdeko's light blue tablet contains lactose. If you have been told by the doctor that you have intolerance to some sugars, contact your doctor before taking this medicine.

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 not sure about your dose or about how to take this medicine. Only your doctor will determine your dose and how you should take this medicine.

The recommended dosage is usually:

For patients aged 6 to 11 years weighing less than 30 kg

One white tablet (tezacaftor 50 mg/ivacaftor 75 mg) in the morning and one light blue tablet (ivacaftor 75 mg) in the evening.

- Take the white tablet and the light blue tablet about 12 hours apart.

For patients aged 6 to 11 years weighing more than 30 kg and patients aged 12 years and older

One yellow tablet (tezacaftor 100 mg/ivacaftor 150 mg) in the morning and one light blue tablet (ivacaftor 150 mg) in the evening.

- Take the yellow tablet and light blue tablet about 12 hours apart.

Swallow the tablets whole. There is no information about crushing, splitting, or chewing the tablets.

Do not exceed the recommended dose.

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.

If you forgot to take the medicine at the scheduled time:

- Do not take more than your usual dose of Symdeko to make up for the missed dose.

Patients aged 6 to 11 years weighing less than 30 kg

- If it is **6 hours or less** from the time you usually take the white tablet in the morning or the light blue tablet in the evening, **take the missed dose** with food that contains fat as soon as you can. Then take your next dose at the usual time.
- If it is **more than 6 hours** from the time you usually take the white tablet in the morning or the light blue tablet in the evening, **do not take the missed dose**. Take your next dose at the usual time with food that contains fat.

Patients aged 6 to 11 years weighing more than 30 kg and Patients aged 12 years and older

- If it is **6 hours or less** from the time you usually take the yellow tablet in the morning or the light blue tablet in the evening, **take the missed dose** with food that contains fat as soon as you can. Then take your next dose at the usual time.
- If it is **more than 6 hours** from the time you usually take the yellow tablet in the morning or the light blue tablet in the evening, **do not take the missed dose**. Take your next dose at the usual time with food that contains fat.

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

If you stop taking the medicine, tell your doctor. Before stopping you should discuss the implications with the doctor or the pharmacist.

Do not take medicines in the dark! Check the label and dose each time you take medicine. Wear glasses if you need them.

If you have further questions about using this medicine, consult your doctor or pharmacist.

4. Side effects

Like with all medicines, using Symdeko may cause side effects in some users. Do not be alarmed by this list of side effects. You may not experience any of them.

Serious side effects include:

- Abnormality of the eye lens (cataract)
- Raised levels of liver enzymes in the blood

Consult your doctor immediately if you have any of the following symptoms, which may be a sign of liver problems:

- Pain or discomfort in the upper right stomach area
- Yellowing of your skin or the white part of your eyes
- Loss of appetite
- Nausea or vomiting
- Dark, amber-colored urine

Side effects seen with Symdeko:

Very common side effects (occur in more than one in ten users)

- Headache

Common side effects (occur in 1-10 in 100 users)

- Feeling sick (nausea)
- Blocked nose (sinus congestion)
- Dizziness

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.

Reporting side effects

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. You can also use this link: <https://sideeffects.health.gov.il>

5. How to store the medicine?

Prevent poisoning! To prevent poisoning, keep this, and all other medicines, in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by the doctor.

Do not use Symdeko after the expiry date (exp. date) which is stated on the carton and blister. The expiry date refers to the last day of that month.

Storage conditions

Store below 25°C.

6. Additional information

In addition to the active ingredients, this medicine also contains:

Symdeko 50 mg/ 75 mg & 75 mg

White film-coated tablets

microcrystalline cellulose, hypromellose acetate succinate (HPMCAS), croscarmellose sodium, hypromellose (HPMC), magnesium stearate and sodium lauryl sulfate. The tablet film coat contains opadry white 20A180008 (HPMC 2910/hypromellose, hydroxypropyl cellulose, talc and titanium dioxide).

Light blue film-coated tablets

microcrystalline cellulose, lactose monohydrate, hypromellose acetate succinate, croscarmellose sodium, magnesium stearate, colloidal silicon dioxide and sodium lauryl sulfate. The tablet film coat contains opadry II (blue) 85F105098 (polyvinyl alcohol, titanium dioxide, PEG 3350, talc, FD&C Blue #2/Indigo Carmine Aluminum Lake) and carnauba wax. The printing ink contains opacode black s-1-17823 (shellac, iron oxide black, propylene glycol and ammonium hydroxide).

Symdeko 100 mg/150 mg & 150 mg

Yellow film-coated tablets

microcrystalline cellulose, hypromellose acetate succinate (HPMCAS), croscarmellose sodium, hypromellose (HPMC), magnesium stearate and sodium lauryl sulfate. The tablet film coat contains opadry yellow (HPMC/hypromellose 2910, hydroxypropyl cellulose, titanium dioxide, talc and iron oxide yellow).

Light blue film-coated tablets

microcrystalline cellulose, lactose monohydrate, hypromellose acetate succinate, croscarmellose sodium, magnesium stearate, colloidal silicon dioxide and sodium lauryl sulfate. The tablet film coat contains opadry II (blue) 85F90614 (polyvinyl alcohol, titanium dioxide, PEG 3350, talc, FD&C Blue #2/indigo carmine aluminum lake) and carnauba wax. The printing ink contains opacode black s-1-17823 (shellac, isopropyl alcohol, iron oxide black, n-butyl alcohol, propylene glycol, ammonium hydroxide).

What the medicine looks like and contents of the pack

Each of the strengths of SYMDEKO consists of 2 different tablets.

Symdeko 50 mg/ 75 mg & 75 mg:

- White film-coated tablet debossed with 'V 50' on one face and contains the active ingredients tezacaftor and ivacaftor.
- Light blue film-coated tablet printed with 'V 75' in black ink on one face and contains the active ingredient ivacaftor.

Symdeko 100 mg/150 mg & 150 mg:

- Yellow film-coated tablet debossed with 'V100' on one face and contains the active ingredients tezacaftor and ivacaftor.
- Light blue film-coated tablet printed with 'V 150' in black ink on one face and contains the active ingredient ivacaftor.

Each of the strengths of SYMDEKO is available in a pack containing 56 film-coated tablets. The tablets are packaged in 4 blisters. Each blister contains 14 tablets (7 tezacaftor/ivacaftor and 7 ivacaftor tablets).

Registration holder's name and address

Vertex Pharmaceuticals (U.K.) Limited
7 Rival Street, Tel Aviv-Yafo, Israel

Manufacturer's name and address

Vertex Pharmaceuticals (Europe) Limited
2 Kingdom Street, London, W2 6BD, United Kingdom

Approved in June 2021

Registration number of the medicine in the Ministry of Health's National Drug Registry

Symdeko 50 mg/75 mg & 75 mg: 167-05-36310
Symdeko 100 mg/150 mg & 150 mg: 162-71-35683