

Package leaflet: Information for the patient

Symkevi 50 mg/75 mg film-coated tablets
Symkevi 100 mg/150 mg film-coated tablets
tezacaftor/ivacaftor

- ▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

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

What is in this leaflet

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

1. What Symkevi is and what it is used for

Symkevi contains two active substances, tezacaftor and ivacaftor. The medicine helps lung cells to work better in some patients with cystic fibrosis (CF). CF is an inherited condition in which the lungs and the digestive system can become clogged with thick, sticky mucus.

Symkevi works on a protein called CFTR (*cystic fibrosis transmembrane conductance regulator*), which is damaged in some people with CF (who have a mutation in the *CFTR* gene). Ivacaftor causes the protein to work better while tezacaftor increases the amount of protein at the cell surface. Symkevi is normally taken with ivacaftor, another medicine.

Symkevi taken with ivacaftor is for long-term treatment of patients aged 6 and over who have CF with certain genetic mutations that result in reduced amount and/or function of the CFTR protein.

Symkevi taken with ivacaftor helps your breathing by improving your lung function. You may also notice that you do not get ill as often and/or that it is easier to gain weight.

2. What you need to know before you take Symkevi

Do not take Symkevi

- **If you are allergic** to tezacaftor, ivacaftor, or any of the other ingredients of this medicine (listed in section 6).

Talk to your doctor, without taking the tablets, if this applies to you.

Warnings and precautions

- **Talk to your doctor if you have liver problems**, or have had them previously. Your doctor may need to adjust your dose.
- Your doctor will do some **blood tests to check your liver** before and during treatment with Symkevi, especially if your blood tests showed high liver enzymes in the past. Increased liver enzymes in the blood have been seen in patients with CF receiving Symkevi.

Tell your doctor right away if you have any symptoms of liver problems. These are listed in section 4.

- **Your doctor may do eye examinations** before and during treatment with Symkevi. Cloudiness of the eye lens (cataract) without any effect on vision has occurred in some children and adolescents receiving this treatment.
- **Talk to your doctor if you have kidney problems**, or you have previously had them.
- **Talk to your doctor** before starting treatment if you have received **an organ transplant**.

Children under 6

Symkevi is not to be used in children under the age of 6 years. It is not known if Symkevi is safe and effective in children under 6.

Other medicines and Symkevi

Tell your doctor or pharmacist if you are taking, have recently taken, or might take any other medicines. Some medicines can affect how Symkevi works or may make side effects more likely. In particular, tell your doctor if you take any of the medicines listed below. Your doctor may change the dose of one of the medicines if you take any of these.

- **Antifungal medicines** (used for the treatment of fungal infections). These include ketoconazole, itraconazole, posaconazole, voriconazole and fluconazole.
- **Antibiotic medicines** (used for the treatment of bacterial infections). These include telithromycin, clarithromycin, erythromycin, rifampicin and rifabutin.
- **Anticonvulsant medicines** (used for the treatment of epilepsy and epileptic seizures or fits). These include phenobarbital, carbamazepine and phenytoin.
- **Herbal medicines**. These include St. John's wort (*Hypericum perforatum*).
- **Immunosuppressants** (used after an organ transplantation). These include ciclosporin, tacrolimus, sirolimus and everolimus.
- **Cardiac glycosides** (used for the treatment of some heart conditions). These include digoxin.
- **Anticoagulant medicines** (used to prevent blood clots). These include warfarin.
- **Medicines for diabetes**. These include glimepiride and glipizide.

Symkevi with food and drink

Avoid food or drinks containing grapefruit during treatment as these may increase the side effects of Symkevi by increasing the amount of Symkevi in your body.

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 taking this medicine.

- **Pregnancy:** It may be better to avoid using this medicine during pregnancy. Your doctor will help you decide what is best for you and your child.
- **Breast-feeding:** It is not known if tezacaftor or ivacaftor pass into breast milk. Your doctor will consider the benefit of breast-feeding for the child and the benefit of treatment for you to help you decide whether to stop breast-feeding or to stop treatment.

Driving and using machines

Symkevi can make you dizzy. If you feel dizzy, do not drive, cycle or use machines unless you are not affected.

Symkevi contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially ‘sodium-free’.

3. How to take Symkevi

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

There are different strengths of Symkevi for different age groups. Check you have been given the right dose (below).

Symkevi is usually taken with ivacaftor.

Age	Morning (1 tablet)	Evening (1 tablet)
6 to < 12 years weighing < 30 kg	tezacaftor 50 mg/ivacaftor 75 mg	ivacaftor 75 mg
6 to < 12 years weighing ≥ 30 kg	tezacaftor 100 mg/ivacaftor 150 mg	ivacaftor 150 mg
12 years and older	tezacaftor 100 mg/ivacaftor 150 mg	ivacaftor 150 mg

Take the tablets about 12 hours apart.

Take both Symkevi and ivacaftor tablets with food that contains fat. Meals or snacks that contain fat include those prepared with butter or oils or those containing eggs. Other fat-containing foods are:

- Cheese, whole milk, whole milk dairy products, yogurt, chocolate
- Meats, oily fish
- Avocados, hummus, soy-based products (tofu)
- Nuts, fat-containing nutritional bars or drinks

The tablets are for oral use.

Swallow the tablet whole. Do not chew, crush or break the tablets before swallowing.

You must keep using all your other medicines, unless your doctor tells you to stop.

If you have liver problems, either moderate or severe, your doctor may need to reduce the dose of your tablets, because your liver will not process the medicine as fast as usual.

If you take more Symkevi than you should

Contact your doctor or pharmacist for advice. If possible, take your medicine and this leaflet with you. You may get side effects, including those mentioned in section 4 below.

If you forget to take Symkevi

- If you forget to take either your morning Symkevi or evening ivacaftor tablet, and you remember **within 6 hours** of the scheduled time you should have taken the tablet, take the forgotten tablet at once.
- If **more than 6 hours** have passed, do not take the forgotten tablet. Just wait, and take your next tablet at the usual time.
- **Do not** take 2 tablets to make up for a missed dose.

If you stop taking Symkevi

Your doctor will tell you how long you need to keep using Symkevi. It is important to take this medicine regularly. Do not make changes unless your doctor tells you.

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

4. Possible side effects

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

Possible signs of liver problems

Increased liver enzymes in the blood are very common in patients with CF. These may be a sign of liver problems:

- Pain or discomfort in the upper right area of the stomach (abdominal) area
- Yellowing of the skin or the white part of the eyes
- Loss of appetite
- Nausea or vomiting
- Dark urine

Tell your doctor straight away if you have any of these symptoms.

Side effects seen with Symkevi:

Very common

(may affect more than 1 in 10 people)

- Headache
- Common cold

Common

(may affect up to 1 in 10 people)

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

Side effects seen with ivacaftor:

Very common

- Upper respiratory tract infection (the common cold), including sore throat and nasal congestion
- Headache
- Dizziness
- Stomach (abdominal) ache
- Diarrhoea
- Increased liver enzymes in the blood
- Rash
- Changes in the type of bacteria in mucus

Common

- Runny nose
- Ear pain, ear discomfort
- Ringing in the ears
- Redness inside the ear
- Inner ear disorder (feeling dizzy or spinning)
- Sinus congestion
- Redness in the throat
- Breast mass

Uncommon

(may affect up to 1 in 100 people)

- Ear congestion
- Breast inflammation
- Enlargement of the breast in males
- Nipple changes or pain

Additional side effects in children and adolescents

Side effects in children and adolescents are similar to those observed in adults.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance, website: www.hpra.ie.

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

5. How to store Symkevi

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 package after EXP. The expiry date refers to the last day of that month.

This medicine does not require any special storage conditions.

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 Symkevi contains

The active substances are tezacaftor and ivacaftor.

Symkevi 50 mg tezacaftor/75 mg ivacaftor film-coated tablets

Each film-coated tablet contains 50 mg of tezacaftor and 75 mg of ivacaftor.

The other ingredients are:

- Tablet core: Hypromellose acetate succinate, sodium laurilsulfate (E487), hypromellose 2910 (E464), microcrystalline cellulose (E460(i)), croscarmellose sodium (E468), and magnesium stearate (E470b).
- Tablet film coating: Hypromellose 2910 (E464), hydroxypropyl cellulose (E463), titanium dioxide (E171), talc (E553b).

Symkevi 100 mg tezacaftor/150 mg ivacaftor film-coated tablets

Each film-coated tablet contains 100 mg of tezacaftor and 150 mg of ivacaftor.

The other ingredients are:

- Tablet core: Hypromellose acetate succinate, sodium laurilsulfate (E487), hypromellose (E464), microcrystalline cellulose (E460(i)), croscarmellose sodium (E468), and magnesium stearate (E470b).
- Tablet film coating: Hypromellose 2910 (E464), hydroxypropyl cellulose (E463), titanium dioxide (E171), talc (E553b), and iron oxide yellow (E172).

What Symkevi looks like and contents of the pack

Symkevi 50 mg/75 mg film-coated tablets are white, oval-shaped tablets stamped with “V50” on one side and plain on the other.

Symkevi 100 mg/150 mg film-coated tablets are yellow, oval-shaped tablets stamped with “V100” on one side and plain on the other.

Symkevi is available in the following pack size:

Pack size of 28 tablets (4 blister cards, each with 7 tablets).

Marketing Authorisation Holder

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Other sources of information

Detailed information on this medicine is available on the European Medicines Agency website: <http://www.ema.europa.eu>. There are also links to other websites about rare diseases and treatments.