

**PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS
REGULATIONS (PREPARATIONS) 1986**

This medicine is marketed upon physician's prescription only

PIFELTRO® 100mg FILM-COATED TABLETS

Each film coated tablet contains:

Doravirine 100 mg

For a list of inactive ingredients see section 6 "Further Information". See also section 2.8 "Important information about some of the ingredients of the medicine".

Read all of this leaflet carefully before you start using the medicine.

- This leaflet contains concise information about Pifeltro. If you have any further questions, refer to the doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their medical condition seems similar to yours.

1. WHAT PIFELTRO IS INTENDED FOR?

PIFELTRO is indicated, in combination with other antiretroviral medicinal products, for the treatment of adults infected with HIV-1 without past or present evidence of viral resistance to doravirine.

Pifeltro must be used in combination with other medicines for HIV.

Therapeutic group: a non-nucleoside reverse transcriptase inhibitor (NNRTI).

How Pifeltro works

When used with other medicines, Pifeltro works by preventing HIV from making more viruses in your body. This will help by:

- reducing the amount of HIV in your blood (this is called your 'viral load').
- increasing the number of white blood cells called 'CD4⁺ T'. This can make your immune system stronger. This may reduce your risk of early death or catching infections because your immune system is weak.

2. BEFORE USING PIFELTRO

2.1 Do not use Pifeltro:

- if you are sensitive (allergic) to doravirine or any of the other ingredients of this medicine listed in section 6.
- if you are taking any of the following medicines, which are strong cytochrome P450 CYP3A enzyme inducers. These medicines include, but are not limited to the following:
 - carbamazepine, oxcarbazepine, phenobarbital, phenytoin (medicines for seizures)
 - rifampicin, rifapentine (medicines for tuberculosis)
 - St. John's wort (*Hypericum perforatum*, a herbal remedy used for depression and anxiety) or products that contain it
 - mitotane (a medicine to treat cancer)
 - enzalutamide (a medicine to treat prostate cancer)
 - lumacaftor (a medicine to treat cystic fibrosis)

Do not take Pifeltro if the above applies to you. If you are not sure, talk to your doctor, pharmacist, or nurse before taking Pifeltro. See also section "Interactions with other medicines".

2.2 Special warnings regarding the use of Pifeltro

Talk to your doctor, pharmacist, or nurse before taking Pifeltro.

Severe skin reactions

Severe skin reactions, including Stevens-Johnson syndrome/toxic epidermal necrolysis, have been reported in association with Pifeltro treatment. Stop using Pifeltro and seek medical attention immediately if you notice any of the symptoms related to these serious skin reactions described in section 4.

Immune reactivation syndrome

This can happen when you start taking any HIV medicine, including this medicine. Your immune system may get stronger and begin to fight infections that have been hidden in your body for a long time. Tell your doctor right away if you start having any new symptoms after starting your HIV medicine.

Autoimmune disorders (a condition that occurs when the immune system attacks healthy body tissue) may also occur after you start taking medicines for the treatment of your HIV infection. Autoimmune disorders may occur many months after the start of treatment. If you notice any symptoms of infection or other symptoms such as muscle weakness, weakness beginning in the hands and feet and moving up towards the trunk of the body, palpitations, tremor or hyperactivity, please inform your doctor immediately to seek necessary treatment.

2.3 Children and adolescents

This medicine is not indicated for use in children and adolescents below 18 years of age.

2.4 Interactions with other medicines

If you are taking, or have recently taken, other medicines including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. Especially if you are taking the medicines listed below. This is because other medicines may affect how Pifeltro works, and Pifeltro might affect the way other medicines work.

There are some medicines you must not take with Pifeltro. See list under section “Do not use Pifeltro”.

Talk to your doctor before taking the following medicines with Pifeltro, as your doctor may need to change the dose of your medicines:

- bosentan (a medicine to treat lung disease)
- dabrafenib (a medicine to treat skin cancer)
- lesinurad (a medicine to treat gout)
- modafinil (a medicine to treat excessive sleepiness)
- nafcillin (a medicine to treat some bacterial infections)
- rifabutin (a medicine to treat some bacterial infections such as tuberculosis)
- telotristat ethyl (a medicine to treat diarrhoea in people with carcinoid syndrome)
- thioridazine (a medicine to treat psychiatric conditions such as schizophrenia)

If your doctor decides you should take these medicines with Pifeltro, one tablet of Doravirine should be taken twice daily (approximately 12 hours apart).

Your doctor may check your blood levels or monitor for side effects if you take the following medicines with Pifeltro:

- sirolimus (a medicine used to control your body’s immune response after a transplant)
- tacrolimus (a medicine used to control your body’s immune response after a transplant)

2.5 Using Pifeltro with food

This medicine can be taken with food or between meals.

2.6 Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant, or are planning to have a baby, talk to your doctor about the risks and benefits of taking Pifeltro. It is preferable to avoid the use of this

medicine during pregnancy. This is because it has not been studied in pregnancy and it is not known if it will harm your baby while you are pregnant.

Breast-feeding

Breast-feeding is not recommended in women living with HIV because HIV infection can be passed on to the baby in breast milk.

If you are breast-feeding, or thinking about breast-feeding, you should discuss it with your doctor as soon as possible.

Fertility

There is no information in human on the effect of Pifeltro on fertility.

2.7 Driving and using machines

Pifeltro has a minor influence on the ability to drive or ride a bicycle and use machines. A few of the reported side effects such as dizziness, fatigue or somnolence may affect your ability to drive or to operate machinery.

2.8 Important information about some of the ingredients of the medicine

Pifeltro tablets contain lactose. If you have been told by your doctor that you have an intolerance to lactose, talk to your doctor before taking this medicine.

3. HOW SHOULD YOU USE PIFELTRO?

Always use Pifeltro as instructed by the doctor.

You should check with the doctor or pharmacist if you are not sure regarding the dosage and treatment regimen. This medicine must be used in combination with other medicines for HIV.

The dosage and treatment regimen will be determined by the doctor only.

Usually, the acceptable dosage is 1 tablet once a day. If you take certain medicines, your doctor may need to change the amount of doravirine you take. See section "Interactions with other medicines" for a list of medicines.

Do not exceed the recommended dose.

Method of administration

- Swallow the tablet whole.
 - This medicine can be taken with food or between meals.
- No information is available regarding crushing/splitting/chewing of tablets.

If you have accidentally taken a higher dose than you should

If you have taken an overdose, or if a child has accidentally swallowed the medicine, proceed immediately to a doctor or to a hospital emergency room and bring the package of the medicine with you.

If you have forgotten to take Pifeltro

- It is important that you do not miss or skip doses of this medicine.
- If you forget to take a dose, take it as soon as you remember. But if your next dose is due within 12 hours, skip the dose you missed and take the next one at the usual time. Then continue your treatment as before.
- Do not take a double dose to make up for a missed dose.
- If you are not sure what to do, call your doctor or pharmacist.

If you stop taking Pifeltro

Do not run out of this medicine. Refill your prescription or talk to your doctor before it is all gone.

Do not take medicines in the dark! Check the label and the dose each time you take a medicine.

Wear glasses if you need them.

If you have further questions on the use of the medicine, consult with a doctor or a pharmacist.

4. SIDE EFFECTS

As with any medicine, Pifeltro may cause side effects, in some users.

Do not be alarmed by reading the list of side effects, you may not suffer from any of them.

Do not stop taking this medicine without first talking to your doctor.

Stop using Pifeltro and seek medical attention immediately if you notice any of the following symptoms: reddish non-elevated, target-like or circular patches on the trunk, often with central blisters, skin peeling, ulcers of mouth, throat, nose, genitals and eyes. These serious skin rashes can be preceded by fever and flu-like symptoms (Stevens-Johnson syndrome/toxic epidermal necrolysis). The frequency of these reactions cannot be estimated from the available data.

Other side effects that may occur

Common: may affect up to 1 in 10 people:

- abnormal dreams, difficulty in sleeping (insomnia)
- headache, dizziness, sleepiness
- feeling sick (nausea), diarrhoea, stomach pain, vomiting, wind (flatulence)
- rash
- feeling tired

Blood tests may also show:

- increased levels of liver enzymes (ALT)

Uncommon: may affect up to 1 in 100 people:

- nightmares, depression, anxiety, irritability, confusion, suicidal thoughts
- trouble concentrating, memory problems, tingling of hands and feet, stiff muscles, poor quality sleep
- high blood pressure
- constipation, stomach discomfort, swollen or bloated stomach (abdominal distension), indigestion, soft stools, stomach spasms
- itchiness
- muscle pain, joint pain
- feeling weak, general feeling of being unwell

Blood tests may also show:

- decreased levels of phosphate
- increased levels of liver enzymes (AST)
- increased levels of lipase
- increased levels of amylase
- decreased levels of haemoglobin

Rare: may affect up to 1 in 1,000 people

- aggression, hallucinations, difficulty adjusting to changes, mood changes, sleep walking
- difficulty breathing, enlarged tonsils
- feeling of incomplete defecation
- inflammation of the skin due to allergy, redness on the cheeks, nose, chin or forehead, bumps or pimples on the face
- kidney damage, kidney problems, kidney stones
- pain in the chest, feeling cold, pain, thirst

Blood tests may also show:

- decreased levels of magnesium
- increased levels of creatine phosphokinase

Not known: frequency cannot be estimated from the available data:

- pain in the belly (abdomen) caused by inflammation of the liver

If a side effect appears, if any of the side effects worsens or if you suffer from a side effect not mentioned in this leaflet, consult with the doctor.

Side effects can be reported to the Ministry of Health by using the link "Adverse Drug Reactions Report" at the home page of the Ministry of Health's web site (www.health.gov.il) which refers to the online side effects reporting form, or by using the link: <https://sideeffects.health.gov.il/>.

5. HOW TO STORE PIFELTRO?

- **Avoid Poisoning!** This medicine and any other medicine must be stored in a safe place out of the reach and sight of children and/or infants, in order 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 pack. The expiry date refers to the last day of the indicated month.
- **Storage conditions:**
 - Store in the original package and keep the bottle tightly closed in order to protect from moisture.
 - This medicinal product does not require any special temperature storage conditions. It is recommended to store at room temperature.
 - The bottle contains a desiccant protecting the tablets from moisture. Keep the desiccant inside the bottle and do not throw away until you have finished taking all of the medicine.
 - This medicine should be used within 35 days after first opening of the bottle.
- 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 protect the environment.

6. FURTHER INFORMATION

In addition to the active ingredient Pifeltro also contains:

hypromellose acetate succinate; lactose monohydrate; microcrystalline cellulose E460; croscarmellose sodium E468; magnesium stearate E470b; and silica, colloidal anhydrous E551.

The tablets are film-coated with a coating material containing the following ingredients:

hypromellose E464; titanium dioxide E171; lactose monohydrate; triacetin E1518; and carnauba wax E903.

What Pifeltro looks like and contents of the pack

Pifeltro is available as a white, oval-shaped, film-coated tablet, and is debossed with the corporate logo and 700 on one side and plain on the other side.

Pack size: 1 bottle with 30 film-coated tablets.

Marketing authorisation holder and importer:

Merck Sharp & Dohme (Israel-1996) Company Ltd., 34 Ha'charash St., Hod-Hasharon.

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Drug registration no. listed in the official Registry of the Ministry of Health: 164-62-36060