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

The medicine is dispensed with a doctor's prescription only

Tavneos

Hard Capsules

Each capsule contains 10 mg Avacopan

Inactive and allergenic ingredients in the preparation - see Section 6 and the section "Important information about some of the ingredients of the medicine".

Read the leaflet carefully in its entirety before using the medicine.
This leaflet contains concise information about the medicine.
If you have 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 it seems to you that their medical condition is similar.

1. Who is the medicine intended for?

Tavneos, in combination with Rituximab or Cyclophosphamide, is designed for the treatment of adult patients with severe and active granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA).

Therapeutic group: Complement system inhibitors

Tavneos contains the active ingredient avacopan, which attaches to a specific protein in the body called the complement 5a receptor.

The complement 5a receptor plays a key role in stimulating inflammation. Tavneos binds to this protein and prevents it from working, thereby reducing inflammation of blood vessels observed in these diseases.

Tavneos can be used together with other treatments prescribed by your doctor.

- Granulomatosis with polyangiitis (GPA) – mainly affects small blood vessels and tissues in the kidneys, lungs, throat, nose and sinuses, but affects other organs as well. Patients develop small lumps (granulomas) in and around the blood vessels, which are formed as a result of tissue damage caused by inflammation.
- Microscopic polyangiitis (MPA) - affects the smaller blood vessels. It usually affects the kidneys, but may also affect other organs.

2. Before using this medicine:

Do not use this medicine if:

- You are sensitive (allergic) to avacopan, or to any of the other ingredients of this medicine (see Section 6).

Special warnings regarding the use of this medicine:

Before the treatment with Tavneos, and during the course of the treatment, tell your doctor if you have previously had, or currently have:

- Symptoms of liver damage, such as nausea or vomiting, feeling tired, loss of appetite, yellowing of the skin or eyes, dark urine, itching, upper stomach pain, a rise in the levels of total bilirubin, the yellow breakdown substance of blood pigment; or a rise in liver enzymes, such as transaminases
- Unexpected bruising and bleeding (these two are common signs of bone marrow failure), any infection
- Hepatitis B, hepatitis C, HIV or tuberculosis
- A heart disease, such as heart attack, heart failure, infection of cardiac blood vessels
- Any type of cancer.

Tavneos is not recommended in patients with:

- Active liver disease
- An active, serious infection

Children and adolescents

Do not administer this medicine to children below the age of 18. There is insufficient information regarding the safety and efficacy of the medicine in this age group.

Tests and follow-up

Your doctor will perform blood tests before the treatment, and when needed during the treatment, in order to test for:

- Any problems with your liver (by measuring liver enzymes and the levels of total bilirubin in the blood)
- Your risk of getting infections (by measuring the white blood cell count).

Your doctor will decide whether to temporarily suspend or permanently discontinue the treatment.

Your doctor will also monitor you for signs and symptoms of an infection called Neisseria meningitidis. This is recommended for adult patients with granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA).

Treatment for the prevention of the lung infection Pneumocystis jirovecii pneumonia is recommended during the treatment with Tavneos.

It is recommended that vaccines be administered before the start of treatment with Tavneos, or when there is no active disease [granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA)].

Severe and often painful swelling under the skin, mainly in the face, has been reported during treatment with Tavneos. If this affects the throat, it can cause breathing difficulties. Stop treatment and seek urgent medical advice in case of any swelling of the face, lips, tongue or throat, or if breathing difficulties occur.

Drug interactions:

If you are taking or have recently taken other medicines, including non-prescription medicines and nutritional supplements, tell your doctor or pharmacist. In particular if you are taking:

- Carbamazepine, phenobarbital, phenytoin - medicines intended for the treatment of epilepsy and other illnesses
- Enzalutamide, mitotane - medicines intended for the treatment of cancer
- Rifampicin - a medicine intended for the treatment of tuberculosis or certain other infections
- Hypericum (St. John's wort) - a herbal medicine used to treat mild depression.

If short-term use of one of these medicines cannot be avoided during treatment with Tavneos, your doctor may regularly check your condition to see how well Tavneos is working.

Tavneos can affect or be affected by the following medicines:

- Alfentanil - a painkiller used during operations performed with anesthetics
- Boceprevir, telaprevir - medicines for the treatment of hepatitis C
- Bosentan - a medicine designed for the treatment of high blood pressure in the lungs, and sores on the fingers and toes called scleroderma
- Clarithromycin, telithromycin - antibiotic medicines administered for the treatment of bacterial infections
- Conivaptan - a medicine for the treatment of low blood sodium levels
- Ciclosporin - a medicine designed to suppress the immune system and prevent transplant rejection; and to treat severe skin diseases and severe eye or joint infections
- Dabigatran - a blood thinning medicine
- Dihydroergotamine, ergotamine - medicines for the treatment of migraine
- Fentanyl - a strong painkiller
- Indinavir, efavirenz, etravirine, lopinavir/ritonavir, nelfinavir, ritonavir, saquinavir - medicines intended for the treatment of HIV infections
- Itraconazole, posaconazole, voriconazole - medicines intended for the treatment of fungal infections
- Ketoconazole - a medicine for the treatment of symptoms caused by excessive production of cortisol by the body, called Cushing's syndrome
- Mibefradil - a medicine for the treatment of irregular heart rhythm and high blood pressure
- Modafinil - a medicine for the treatment of an extreme tendency to fall asleep
- Nefazodone - a medicine for the treatment of depression

- Rapamycin, tacrolimus - medicines that suppress the immune system and prevent transplant rejection.
- Simvastatin – a medicine used to lower levels of total cholesterol, “bad” (LDL) cholesterol and fatty substances called triglycerides in the blood

Use of the medicine with food

Avoid the consumption of grapefruits and grapefruit juice during treatment with Tavneos, as these can influence the efficacy of the medicine.

Pregnancy and breastfeeding
If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

- **Pregnancy -** There is no information about the use of Tavneos in pregnant women. Treatment with this medicine is not recommended for use during pregnancy or in women of childbearing potential not using contraception.
- **Breastfeeding -** There is no information regarding whether avacopan passes into breast milk; therefore, a risk to the baby cannot be ruled out. Your doctor will help you decide whether the treatment with Tavneos should be stopped or whether breastfeeding should be discontinued.

Driving and using machines

Tavneos has no effect, or only a negligible effect, on the ability to drive and to use machines.

Important information about some of the ingredients of the medicine
Tavneos contains the ingredient macrogolglycerol hydroxystearate, which may cause side effects of upset stomach and diarrhea.

3. How should you use the medicine?

Always use this medicine in accordance with your doctor’s instructions. Check with the doctor or pharmacist if you are not sure about the dosage and treatment regimen of the preparation. The dosage and treatment regimen will be determined by the doctor only.

The usual dosage is generally:

3 capsules in the morning and 3 capsules in the evening.

Do not exceed the recommended dose.

Administration form

Swallow the medicine with one glass of water.

<u>Crushing/splitting/chewing</u>

Do not crush, chew or open the capsule. Take the medicine with a meal.

If you accidentally took a higher dose, consult your doctor immediately.

If you forget to take the medicine at the scheduled time

- and you have **more than 3 hours until the next dose**, take the dose you forgot as soon as possible. Take the next dose at the scheduled time.
- and you have **less than 3 hours until the next dose,** do not take the dose you forgot. Take the next dose at the regular time.

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

Adhere to the treatment regimen as recommended by your doctor. Even if there is an improvement in your health, do not stop the treatment with the medicine without consulting your doctor or pharmacist.

If you stop taking the medicine

Stop the treatment and seek urgent medical advice in case of any swelling of the face, lips, tongue or throat, or if breathing difficulties occur. In any other situation, do not stop taking the medicine in the absence of medical advice.

Do not take medicines in the dark! Check the label and dose <u>each time</u> you take a medicine. Wear glasses if you need them.
If you have further questions regarding use of the medicine, consult your doctor or pharmacist.

4. Side effects

As with any medicine, the use of Tavneos may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

Contact your doctor immediately if the following serious side effects occur:

- Very common side effects - effects that occur in more than 1 in 10 users:
- Blood tests showing a rise in:
  - Liver enzymes (a sign of liver problems)
  - Bilirubin: The yellow breakdown product of blood pigment.

- Common side effects - effects that occur in 1-10 in 100 users:
- Lung inflammation (symptoms may be wheezing, difficulty breathing or chest pain).

- Uncommon side effects - effects that occur in 1-10 in 1,000 users:
- A severe allergic reaction that causes swelling under the skin, mainly in the area of the face, and that may cause breathing difficulties (angioedema).

- Side effects of unknown frequency (effects whose frequency has not yet been determined):
- Serious liver injury and bile duct injury (symptoms can be nausea and vomiting, feeling tired, loss of appetite, yellowing of the skin or eyes, dark urine, itching, or upper stomach pain) (see Section 2).

Other side effects may occur, with the following frequencies:

- Very common side effects - effects that occur in more than 1 in 10 users:
- Infection of the upper airways
- Swollen and inflamed throat and nose
- Headache
- Feeling sick (nausea)
- Diarrhea
- Vomiting
- Decreased white blood cell count seen in blood tests.

- Common side effects - effects that occur in 1-10 in 100 users:
- Inflammation of the internal part of the nose that causes sneezing, itching, a runny and stuffy nose
- Urinary tract infection
- Inflammation of the sinuses or bronchi
- Inflammation of the stomach and the lining of the intestines
- Inflammation in the lower airways
- Cellulitis
- Shingles
- Flu
- Candida yeast fungal infection or oral herpes
- Middle ear infection
- A drop in the number of a type of white blood cell, called neutrophils (symptoms can be infections, fever or painful swallowing)
- Upper abdominal pain
- A rise in the blood levels of creatine phosphokinase enzyme (symptoms may be chest pain, confusion, muscle aches, sudden weakness or numbness of the body).

If a side effect occurs, if one of the side effects worsens, or if you suffer from a side effect not mentioned in this leaflet, consult your doctor.

Reporting side effects
Side effects can be reported to the Ministry of Health by clicking on the link “Report Side Effects of Drug Treatment” found on the homepage of the Ministry of Health (www.health.gov.il), which directs you to the online form for the report of side effects, or by entering the link: https://sideeffects.health.gov.il/

5. How should the medicine be stored?

- Avoid poisoning! This medicine and any other medicine should be kept in a safe 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 the doctor.
- Do not use the medicine after the expiry date that appears on the carton packaging and on the bottle after the word “EXP”. The expiry date refers to the last day of that month.

Storage conditions:

There are no special storage conditions.
Keep this medicine in its original box in order to protect it from light.
Do not dispose of this medicine via wastewater or household waste. Ask your pharmacist how to dispose of medicines you no longer use. These measures will help protect the environment.

6. FURTHER INFORMATION:

- In addition to the active ingredient, this medicine also contains:
  polyoxyl-40 hydrogenated castor oil (Macrogolglycerol hydroxystearate), PEG-4000, gelatin, polysorbate 80, red iron oxide (E172), yellow iron oxide (E172), black iron oxide (E172), titanium dioxide (E171), shellac, potassium hydroxide.

- What the medicine looks like and the contents of the package:
  A plastic bottle that contains 30 or 180 capsules.
  Each capsule is composed of two parts, colored yellow and light orange, with the text “CCX168” in black ink.

  Not all pack sizes may be marketed.

- License holder and address: CTS Ltd., 4 HaHarash St., Hod Hasharon, Israel

- Manufacturer name and address:
  Vifor Fresenius Medical Care Renal Pharma Ltd
  Rechenstrasse 37
  9014 St. Gallen
  Switzerland

- Registration number of the medicine in the National Drug Registry of the Ministry of Health: 173-80-37474-99

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