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

The medicine is dispensed with a doctor's prescription only

Zemplar® 1 microgram

Soft capsules

The active ingredient and its quantity:
Each capsule of Zemplar 1 microgram (mcg) contains: paricalcitol 1 microgram (mcg)

For the list of inactive and allergenic ingredients in the preparation, see section 2 "Important information about some of the ingredients of the medicine" and section 6 "Further information".

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 the treatment of your ailment/for you. Do not pass it on to others. It may harm them, even if it seems to you that their ailment/medical condition is similar.

1. WHAT IS THE MEDICINE INTENDED FOR?

The medicine is indicated for the prevention and treatment of secondary hyperparathyroidism in patients who suffer from chronic renal insufficiency (chronic kidney disease at stage 3 or 4) or in patients suffering from renal failure (chronic kidney disease stage 5) and undergoing hemodialysis or peritoneal dialysis.

Therapeutic group: An anti-parathyroid agent.

This medicine is a synthetic form of active vitamin D. Active vitamin D is required for the normal function of many tissues in the body, including the parathyroid gland and bones. In people who have normal kidney function, this form of active vitamin D is produced naturally by the kidneys, but in people with kidney failure, the production of active vitamin D is markedly reduced.
Zemplar therefore provides a source of active vitamin D when the body cannot produce enough active vitamin D, and helps to prevent the consequences of low levels of active vitamin D, namely, high levels of parathyroid hormone, which may cause bone problems. Zemplar is used in adult patients with chronic kidney disease stages 3, 4 and 5.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:
- you are sensitive (allergic) to the active ingredient paricalcitol or to any of the additional ingredients contained in the medicine (for a list of the inactive ingredients, see section 6 "Further information").
- you have very high levels of calcium or vitamin D in your blood.

Your doctor can tell you if these conditions apply to you.

Special warnings regarding use of the medicine
- **Before treatment with Zemplar,** it is important to limit the amount of phosphorus in your diet.
  Phosphate-binding medicines may be needed to control phosphorus levels. If you are taking calcium-based phosphate binders, the doctor may need to adjust your dosage.
- In some patients with chronic kidney disease stage 3 or 4, an increase in the blood levels of a substance called creatinine has been observed. However, this increase does not reflect a reduction in renal function.

Tests and follow-up
- During the course of treatment with this medicine, blood tests should be carried out in order to monitor your treatment.

Children and adolescence
This medicine is not intended for children and adolescents under 18 years of age.

Elderly patients
There is a limited amount of experience in using Zemplar in patients aged 65 years or older. In general, no overall differences in effectiveness or safety were seen between patients aged 65 years or older and younger patients.

Drug interactions
If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.
Some medicines can affect the activity of Zemplar or increase the possibility of side effects.
It is particularly important to inform the doctor if you are taking:
- medicines used to treat fungal infections or oral thrush (e.g., ketoconazole).
- medicines for treating heart problems or blood pressure (e.g., digoxin and diuretics).
- medicines containing a source of phosphate (e.g., medicines to lower blood calcium levels).
- medicines containing calcium or vitamin D, including non-prescription nutritional supplements and multivitamins.
- medicines containing magnesium or aluminium (e.g., certain types of medicines for indigestion [antacids] and phosphate-binding medicines).
- medicines used to treat high cholesterol levels (e.g., cholestyramine).

Use of the medicine and food
Zemplar can be taken with or without food.

Pregnancy, breastfeeding and fertility
- If you are pregnant or breastfeeding, think you may be pregnant or are planning to become pregnant, consult a doctor or pharmacist before taking Zemplar.
- There are no adequate data regarding use of paricalcitol in pregnant women. Potential risk in human use is not known, therefore, paricalcitol should not be used during pregnancy unless clearly necessary.
- It is not known if paricalcitol passes into breast milk. Consult the doctor before breastfeeding while taking Zemplar.

Driving and operating machinery
Zemplar should not affect your ability to drive or operate machinery.

Important information about some of the ingredients of the medicine
Zemplar contains alcohol (ethanol). This medicine contains 0.71 milligram (mg) of alcohol (ethanol) in each soft capsule with 1 microgram (mcg) active ingredient. The amount of alcohol per soft capsule of this medicine is less than or equivalent to 1 milliliter (ml) beer or wine.
The small amount of alcohol in this medicine will not have noticeable effects.

3. HOW SHOULD YOU USE THE MEDICINE?

- Always use the preparation according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain regarding the dosage and treatment regimen of the preparation.
- The dosage and treatment regimen will be determined by the doctor only.
- **Method of administration:** The gel capsules are soft and should therefore be swallowed whole. Do not crush, pulverize or chew the capsules.
- **Do not exceed the recommended dose.**
- The doctor will use laboratory test results in order to determine the dosage appropriate for you.
- After starting treatment with Zemplar, the dosage usually needs adjusting, depending on your response to treatment.

Liver disease
If you have mild to moderate liver disease, there is no need for dosage adjustment. However, there is no experience in patients with severe liver disease.

If you accidentally take a higher dosage
Taking too high a dosage of Zemplar can cause an abnormal increase in blood calcium levels, a condition which can be harmful.

If you took an overdose, or if a child has accidentally swallowed the medicine, or if you experience one of the side effects mentioned below, refer immediately to a doctor, or proceed to a hospital emergency room and bring the package of the medicine with you.

Symptoms which may occur immediately after taking too high a dosage of Zemplar:
- weakness and/or drowsiness
- headache
- nausea or vomiting
- dry mouth
- constipation
- muscle or bone pain
- metallic taste in the mouth

Symptoms which can develop over a longer period of taking too much Zemplar include:
- loss of appetite
- drowsiness
- weight loss
- sore eyes
- runny nose
- itchy skin
- feeling hot and feverish
- loss of sex drive
- severe abdominal pain (due to an inflamed pancreas)
- kidney stones
- changes in blood pressure
- irregular heartbeat (palpitations)
- blood and urine tests results can indicate high levels of cholesterol, urea, nitrogen and liver enzymes
- on rare occasions – mental changes, including: confusion, drowsiness, insomnia or nervousness

If you forget to take the medicine
Take a dose as soon as you remember. However, if it is almost time for your next dose, skip the forgotten dose, and take the next dose at the regular time. Do not take a double dose to compensate for the forgotten dose.
Adhere to the treatment regimen as recommended by the doctor. Even if there is an improvement in your health, do not stop treatment with the medicine without consulting the doctor or pharmacist.

If you stop taking the medicine
It is important to keep taking Zemplar as per the doctor's instructions, unless the doctor has instructed you to stop treatment.

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

If you have further questions regarding use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Zemplar 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.

Refer to the doctor immediately if you notice one of the following side effects:
Allergic reactions (such as: shortness of breath, wheezing, rash, itching, or swelling of the face or lips).
- Common side effects (effects that occur in 1-10 in 100 users):
  - increase in blood calcium levels
  - increase in blood calcium levels and, as a result, increase in blood phosphate levels (in patients with advanced chronic kidney disease)
  - increase in blood phosphate levels
- Uncommon side effects (effects that occur in 1-10 in 1,000 users):
  - pneumonia (lung infection)
  - decreased levels of parathyroid hormone
  - decreased appetite
  - decreased levels of calcium
  - dizziness
  - unusual taste in the mouth
  - headache
  - irregular heartbeat
  - stomach discomfort or pain
  - constipation
  - diarrhea
  - nausea
  - dry mouth
  - heartburn (reflux or indigestion)
  - vomiting
  - acne
  - itchy skin
  - rash
  - allergic skin reaction (hives)
  - muscle cramps
  - muscle pain
  - breast tenderness
  - weakness
  - feeling tired, not feeling well
  - swelling in the legs
  - pain
  - increased levels of creatinine
  - changes in liver function tests

If a side effect occurs, if one of the side effects worsens or if you suffer from a side effect not mentioned in the leaflet, consult the 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 Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting 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, must be kept 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 the doctor.
- Do not use the medicine after the expiry date (exp. date) that appears on the outer package and blister. The expiry date refers to the last day of that month.
- This medicine does not require special storage conditions. It is recommended to store it at room temperature.
- Medicines that are no longer in use must not be disposed via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

- **In addition to the active ingredient, the medicine also contains:**
  medium chain triglycerides, gelatin, glycerol anhydrous, ethanol anhydrous, titanium dioxide, iron oxide (black), butylhydroxytoluene (BHT), black ink opacode® WB, purified water.
- **What the medicine looks like and the contents of the package:**
  The soft 1 mcg Zemplar capsules are oval and grey and have the letters 'ZA' imprinted on them.
  The soft capsules are packaged in a blister that contains 7 capsules. The blisters are packaged in a carton package. There is a total of 7 or 28 capsules in one package.
  Not all package sizes may be marketed.
- **License holder and its address:** AbbVie Biopharmaceuticals Ltd., 4 Haharash St., Hod Hasharon, Israel.
- **Manufacturer and its address:**
  AbbVie Ltd., Vanwall Road, Maidenhead, Berkshire SL6 4UB, United Kingdom.
- **Registration number of the medicine in the National Drug Registry of the Ministry of Health:**
  141-12-31816

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