Package leaflet: Information for the patient

Zemplar 5 micrograms/ml solution for injection

paricalcitol

Read all of this leaflet carefully before you are given 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, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Zemplar is and what it is used for

Zemplar contains the active substance paricalcitol, which is a synthetic form of active vitamin D.

Active vitamin D is required for the normal functioning of many tissues in the body, including the parathyroid gland and bones. In people who have normal kidney function, this active form of vitamin D is naturally produced by the kidneys, but in 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 and helps to prevent the consequences of low levels of active vitamin D, in patients with chronic kidney disease namely high levels of parathyroid hormone which can cause bone problems. Zemplar is used in adult patients with kidney disease Stages 5.

2. What you need to know before you are given Zemplar

You should not be given Zemplar
- if you are allergic to paricalcitol or any of the other ingredients of this medicine (listed in section 6).
- if you have very high levels of calcium or vitamin D in your blood.

Your doctor will be able to tell you if these conditions apply to you.

Warnings and precautions
Talk to your doctor or nurse before being given Zemplar.

- before the treatment begins, it is important to limit the amount of phosphorus in your diet. Examples of foods high in phosphorous include tea, soda, beer, cheese, milk, cream, fish, chicken or beef liver, beans, peas, cereals, nuts, and grains.
- phosphate-binding medicines, which keep phosphate from being absorbed from your food, may be needed to control phosphorus levels.
- if you are taking calcium-based phosphate binders, the doctor may need to adjust your dose.
- your doctor will need to do blood tests to monitor your treatment.

Other medicines and Zemplar
Tell your doctor, nurse or pharmacist if you are taking, have recently taken or might take any other medicines.

Some medicines may affect the action of this medicine or may increase the likelihood of side effects. It is particularly important to tell your doctor if you are taking any of the following medicines:

- to treat fungal infections such as candida or thrush, (for example ketoconazole)
- to treat heart problems or high blood pressure (for example digoxin, diuretics or water pills)
- that contain a source of phosphate (for example, medicines to lower calcium levels in the blood)
- that contain calcium or vitamin D, including supplements and multivitamins that can be bought without a prescription
- that contain magnesium or aluminium, for example some types of indigestion medicines (antacids) and phosphate-binders

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

It is not known if it is safe for pregnant women to use this medicine, therefore its use is not recommended during pregnancy or if you may become pregnant.

It is not known if paricalcitol passes into human breast milk. Tell your doctor before breast-feeding while taking Zemplar.

Driving and using machines
Zemplar may make you feel dizzy, which can affect your ability to drive safely or use heavy machines.

Do not drive or use machines if you feel dizzy.

Zemplar contains ethanol
This medicine contains up to 1.3 g of ethanol (alcohol) in each dose which is equivalent to about 18 mg/kg. The amount in each dose of this medicine is equivalent to about 32 ml beer or 13 ml wine.

The amount of alcohol in this medicine is not likely to have an effect in adults and adolescents, and its effects in children are not likely to be noticeable. It may have some effects in younger children, for example feeling sleepy.

The alcohol in this medicine may alter the effects of other medicines. Talk to your doctor or pharmacist if you are taking other medicines.

If you are pregnant or breast-feeding, talk to your doctor or pharmacist before you are given this medicine.

If you are addicted to alcohol, talk to your doctor or pharmacist before you are given this medicine.

3. How Zemplar is used

Your doctor will use the results of your laboratory tests to decide the correct starting dose for you. Once treatment with Zemplar has started, the dose may be adjusted, based upon the results of routine laboratory tests. Using your lab results, your doctor will help determine the correct dose of Zemplar for you.

Zemplar will be given by a doctor or nurse while you are having your treatment on the kidney machine. It will be given through the tube (bloodline) that is used to connect you to the machine. You will not need to have an injection because Zemplar can be put directly into the tube that is being used for your treatment. You will not be given Zemplar more frequently than every other day and not more than three times a week.

If you are given too much Zemplar

Too much Zemplar can cause abnormally high levels of calcium in the blood, which can be harmful. Symptoms which can appear soon after taking too much Zemplar may include a feeling of weakness and/or drowsiness, headache, nausea (feeling sick) or vomiting (being sick), a dry mouth, constipation, pains in muscles or bones and a metallic taste in the mouth.

If you experience high level of calcium in your blood after taking Zemplar, your doctor will ensure you receive the appropriate treatment to return your calcium to normal limits. Once your calcium levels return to normal limits, you may be given Zemplar at a lower dose.

Your doctor will be checking your blood levels. If you experience any of the above, seek medical advice immediately.

Symptoms which can develop over a longer period of receiving too much Zemplar include loss of appetite, drowsiness, weight loss, sore eyes, a runny nose, itchy skin, feeling hot and feverish, loss of sex drive and severe abdominal pain (due to an inflamed pancreas) and kidney stones. Your blood pressure may be affected and heart beat irregularities (palpitations) can occur. The results of blood and urine tests may show high cholesterol, urea, nitrogen and raised levels of liver enzymes. Zemplar may rarely cause mental changes including confusion, drowsiness, insomnia or nervousness.

Zemplar contains 30% by volume of Propylene glycol as an ingredient. Cases of poisonous effects related to the high doses of Propylene glycol have only rarely been reported and would not be expected when being given to kidney patients on a kidney machine because Propylene glycol is removed from the blood during dialysis.

If you receive too much Zemplar, or experience any of the above, seek medical advice immediately.

4. Possible side effects

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

Various allergic reactions have been seen with Zemplar. **Important: Tell your doctor or nurse immediately if you notice any of the following side effects:**

- shortness of breath
- difficulty breathing or swallowing
- wheezing
- rash, itchy skin, or including hives
- swelling of the face, lips, mouth, tongue or throat

Tell your doctor or nurse if you notice any of the following side effects:

Common (may affect up to 1 in 10 people):
- low levels of parathyroid hormone
- high levels of calcium (feeling sick or being sick, constipated or confused); phosphorous in the blood (probably no symptoms but it can make bones more likely to break)
- headache
- unusual taste in the mouth
- itchy skin

Uncommon (may affect up to 1 in 100 people):
- blood infection, pneumonia (lung infection), sore throat, infections in the vagina, influenza
- breast cancer
- decreased number of red cells (anaemia – feeling weak, shortness of breath, looking pale); decreased number of white cells (more likely to get infections); swollen glands in the neck, armpit and/or groin
- high levels of parathyroid hormones
- high levels of potassium in the blood, low levels of calcium in the blood, loss of appetite
- confusion, which is sometimes severe (delirium), personality disorders (not feeling like yourself), agitation (feeling jittery, anxious), problems sleeping, nervousness
- coma (a deep state of unconsciousness during which the person cannot respond to the environment), stroke, fainting, muscular spasms in arms and legs, even during sleep, decreased touch sensation, tingling or numbness, dizziness
- increased pressure in the eye, pink eye (itchy/crusty eyelids)
- earache
- heart attack, irregular/fast heartbeat
- low blood pressure, high blood pressure
- fluid on the lungs, asthma, wheezing, difficulty breathing, nose bleeds, cough
- bleeding from the rectum, inflammation of the colon, diarrhoea, stomach ache, difficulty swallowing, constipation, nausea, vomiting, dry mouth
- skin rash with itchy blisters, hair loss, excessive hair growth, excessive and unpredictable sweats
- joint pain, joint stiffness, back pain, muscle twitching, muscle pain
- breast pain, difficulty having an erection
- abnormal way of walking, general swelling or localised swelling of the ankles, feet and legs, injection site pain, fever, chest pain, unusual tiredness or weakness, a general feeling of discomfort, thirst
- increased bleeding time (blood will not clot so quickly), increase of a liver enzyme, change in laboratory test results, weight loss

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

- swelling of the face, lips, mouth, tongue or throat which may cause difficulty in swallowing or breathing; itchy skin (hives); stomach bleeding.

You may not be able to tell if you have some of the side effects listed above unless you are told so by your doctor.

If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor, nurse or pharmacist immediately.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly (see details below).

Ireland:

HPRA Pharmacovigilance

Website: www.hpra.ie

United Kingdom:

Yellow Card Scheme
Website: www.mhra.gov.uk/yellow card or search for MHRA Yellow Card in the Google Play or Apple App Store

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

5. How to store Zemplar

Keep this medicine out of the sight and reach of children.

This medicinal product does not require any special storage conditions.
Zemplar should be used immediately after opening.

Do not use this medicine after the expiry date which is stated on the carton after EXP. The expiry date refers to the last date of that month.

Do not use this medicine if you notice particles or discolouration.

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 Zemplar contains

- The active substance is paricalcitol. Each ml of solution contains 5 micrograms of paricalcitol.

The other ingredients are: ethanol (alcohol), propylene glycol, and water for injections.

What Zemplar looks like and contents of the pack

Zemplar solution for injection is a watery, clear and colourless solution, free from visible particles.
It is supplied in containers with 5 glass ampoules of 1 ml or 2 ml or 5 glass vials of 1 ml or 2 ml.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:
In Ireland: AbbVie Limited, Citywest Business Campus, Dublin 24, Ireland
In the UK: AbbVie Ltd, Maidenhead, SL6 4UB, UK

Vial Manufacturer:
AbbVie S.r.l. S.R.148 Pontina km 52 snc 04011 Campoverde di Aprilia (LT), Italy

This medicinal product is authorised in the Member States of the EEA under the following names:

Austria: Zemplar 5 Mikrogramm/ml - Injektionslösung

Czech Republic: Zemplar
Germany: Zemplar 5 Mikrogramm/ml Injektionslösung
Ireland: Zemplar 5 micrograms/ml solution for injection
Italy: Zemplar 5 microgrammi/ml soluzione iniettabile
Netherlands: Zemplar, oplossing voor injectie 5 microgram/ml
Portugal: Zemplar 5 microgramas/ml solução Injetável
Slovakia: Zemplar 5 mikrogramov/ml injekčný roztok
Spain: Zemplar 5 microgramos/ml solución inyectable
Sweden: Zemplar 5 mikrogram/ml injektionsvätska, lösning
United Kingdom: Zemplar 5 micrograms/ml solution for injection

This leaflet was last revised in April 2020.

For information in large print, tape, CD or Braille, phone 01628 561090 (UK) or 01 428 7900 (Ireland).

----------[perforation to separate the user instruction from the patient information leaflet]----------

The following information is intended for healthcare professionals only:

Zemplar 5 microgram/ml solution for injection

Preparation of solution for injection

Zemplar 5 microgram/ml solution for injection is intended for single use only. As with all drugs administered through injection, the diluted solution should be inspected for particles and discoloration, prior to administration.

Compatibility

Propylene glycol interacts with heparin and neutralises its effect. Zemplar solution for injection contains propylene glycol as an excipient and should be administered through a different injection port than heparin.

This medicinal product must not be mixed with other medicinal products.

Storage and shelf life

Parenteral medicinal products should be inspected visually for particulate matter and discoloration prior to administration. The solution is clear and colourless.

This medicinal product does not require any special storage conditions.

This medicinal product has a shelf life of 3 years (vial) or 2 years (ampoule).

Posology and Method of Administration

Zemplar solution for injection is administered via haemodialysis access.

Adults
1) Initial Dose should be calculated based on baseline parathyroid hormone (PTH) levels:

The initial dose of paricalcitol is based on the following formula:

Initial dose (micrograms) = $\frac{\text{baseline intact PTH level in pmol/l}}{8}$

OR

= $\frac{\text{baseline intact PTH level in pg/ml}}{80}$

and administered as an intravenous (IV) bolus dose no more frequently then every other day at any time during dialysis.

The maximum dose safely administered in clinical studies was as high as 40 micrograms.

2) Titration Dose:

The currently accepted target range for PTH levels in end-stage renal failure subjects undergoing dialysis is no more than 1.5 to 3 times the non-uremic upper limit of normal, 15.9 to 31.8 pmol/l (150-300 pg/ml), for intact PTH. Close monitoring and individual dose titration are necessary to reach appropriate physiological endpoints. If hypercalcaemia or a persistently elevated corrected Ca x P product greater than 5.2 mmol2/l2 (65 mg2/dl2) is noted, the dosage should be reduced or interrupted until these parameters are normalised. Then, paricalcitol administration should be reinitiated at a lower dose. Doses may need to be decreased as the PTH levels decrease in response to therapy.

The following table is a suggested approach for dose titration:

Suggested Dosing Guidelines (Dose adjustments at 2 to 4 week intervals)	
iPTH Level Relative to Baseline	**Paricalcitol Dose Adjustment**
Same or increased	Increase by 2 to 4 micrograms
Decreased by < 30%	
Decreased by ≥ 30%, ≤ 60%	Maintain
Decreased > 60%	Decrease by 2 to 4 micrograms
IPTH < 15.9 pmol/l (150 pg/ml)	