PATIENT INFORMATION LEAFLET

ZYGOSİS 40 mg lyophilized powder for solution for i.v. injection
For intravenous use only.
Sterile

- ***Active Substance:*** Each vial contains 45.1 mg pantoprazole sodium sesquihydrate equivalent to 40 mg pantoprazole.
- ***Excipient(s):*** Disodium edetate dihydrate, sodium hydroxide, water for injection.

Read all of this leaflet carefully before you start using 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 or nurse.*
- *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.*
- *During the use of this medicine, tell that you are using this medicine when you go to a doctor or hospital.*
- *Follow these instructions exactly as written. Do not use* ***higher or lower*** *dose other than your recommended dose.*

In this leaflet;

headlines are included.

1. What ZYGOSİS is and what it is used for

ZYGOSİS is a white to almost white powder for solution. It turns into a clear solution when reconstituted. It comes in a colorless glass vial containing 40 mg powder. It is packed in 1 vial.

ZYGOSİS is a medicine known as “proton pump inhibitor”. It reduces the formation of acid in your stomach. It is used for treating acid-related diseases of the stomach.

ZYGOSİS is used for treating;

- Inflammation and pain in the esophagus due to the regurgitation of stomach acid to the esophagus (esophageal reflux disease),
- ulcers in the upper part of the intestine (duodenal ulcer) or in the stomach (gastric ulcer),
- hemorrhage or the recurrence of bleeding in acute ulcers of the stomach or upper intestines,

- Conditions such as Zollinger-Ellison-Syndrome producing too much acid in the stomach.

2. What you need to know before you use ZYGOSİS

Do not use ZYGOSİS:

If;

- you are allergic (hypersensitive) to the active substance, pantoprazole or to one of the excipients of ZYGOSİS, benzimidazoles (drugs used for fungal diseases),
- you are allergic to medicines containing other proton pump inhibitors.

Warnings and precautions

If;

- Please tell your doctor if you have severe liver problems, if you ever had problems with your liver in the past. Your doctor will regularly check your liver enzymes during treatment with ZYGOSİS, especially in long-term use. In the case of a rise of the liver enzymes, ZYGOSİS should be discontinued.
- You are taking a medicine containing atazanavir (for the treatment of HIV-infection) at the same time as ZYGOSİS, tell your doctor
- Tell your doctor if you have osteoporosis (bone loss). Because like all proton pump inhibitors, ZYGOSİS may slightly increase the risk of fracture in the hip, wrist or spine, especially in patients with osteoporosis, in the elderly and in the presence of other risk factors, at high-doses and over a long period (more than one year). In this case, your doctor may recommend to use ZYGOSİS at a lower dose or for a shorter period.
- Tell your doctor if you have already been diagnosed with hypomagnesemia (low levels of magnesium mineral in your blood). ZYGOSİS, like all proton pump inhibitors, can lead to hypomagnesemia after at least 3 months of treatment (usually longer than 1 year). In this case, your doctor may decide to prescribe magnesium supplements or continue your ZYGOSİS treatment for a shorter period of time. Tell your doctor if you feel that your heart beat is abnormally fast, slow or irregular, if you feel fatigue or dizziness, have muscle spasms or a seizure during your ZYGOSİS treatment. These symptoms may be associated with hypomagnesemia. Also, tell your doctor if you are using any other drugs. Hypomagnesemia may also cause a decrease in potassium and calcium levels in the blood. If necessary, your doctor may request regular monitoring of your blood magnesium level.
- Tell your doctor if you are having neuroendocrine tumor diagnostic tests, because ZYGOSİS, like all proton pump inhibitors, may affect the results of these tests.
- Like all proton pump inhibitors, ZYGOSİS may slightly increase the number of bacteria that are normally present in the upper gastrointestinal tract, and therefore the risk of infection (*Salmonella and Campylobacter or C.difficiale*).
- If you use drugs that thicken or thin blood, such as warfarin and phenprocoumon, you may need further checks.
- Tell your doctor **IMMEDIATELY** if you notice any of the following symptoms:
  - An unintentional loss of weight,
  - Vomiting, especially if repeated,
  - Vomiting blood; looks like dark coffee grounds in your vomit.

- Blood in your stools; may be black or tar
- Difficulty or pain in swallowing
- You look pale and feel weak (anemia)
- Chest pain
- Stomach pain,
- Severe and/or persistent diarrhea.

If these warnings apply or applied to you, please consult your physician.

ZYGOSİS may alleviate the symptoms of cancer and could cause delay in diagnosing it. Your doctor may therefore decide to run some tests to rule out cancer. If your symptoms continue during your treatment, further investigations may be required.

ZYGOSİS with food and drink
No interaction with food and drinks because of the route of administration.

Pregnancy
Please consult your physician or pharmacist before taking the drug.

There are no adequate data from the use of pantoprazole in pregnant women. If you are pregnant or think you may be pregnant, you should use pantoprazole only if your doctor considers the benefit for you greater than the potential risk for your unborn baby.

If you realize that you are pregnant during your treatment, immediately consult your physician or pharmacist.

Breast-feeding
Please consult your physician or pharmacist before taking the drug.

Excretion into human milk has been reported. It should be used in breastfeeding mothers only if the benefit is greater than the potential risk for the baby.

Driving and using machines
ZYGOSİS has no or negligible influence on the ability to drive and use machines.

If you experience side effects like dizziness or disturbed vision, you should not drive or operate machines.

Important information regarding some of the excipients contained in ZYGOSİS
This medicinal product contains less than 1 mmol (23 mg) of sodium in each vial; in fact, “it does not contain sodium”.

Other medicines and ZYGOSİS
ZYGOSİS may influence the effectiveness of other medicines, so tell your doctor if you are taking;

- Medicines used to treat fungal infections such as ketoconazole, itraconazole and

posaconazole or some cancer medicines such as erlotinib whose absorption depends on the acid level in the stomach (pH) because Pantoprazole may stop their absorption and decrease their efficacy.

- If you use a drug which affects blood clotting (such as phenprocumon/warfarin), it is recommended to monitor your blood coagulation values after the start and discontinuation of pantoprazole and during irregular use.
- Medicines used to treat HIV-infection such as atazanavir.
- Methotrexate (used to treat rheumatoid arthritis, psoriasis, and cancer) - if you are taking methotrexate your doctor may temporarily stop your treatment by ZYGOSİS because pantoprazole can increase levels of methotrexate in the blood.
- Fluvoxamine (used to treat depression and other psychiatric diseases) - if you are taking fluvoxamine your doctor may reduce the dose.
- Rifampicin (used to treat infections).
- St. John's Wort (Hypericum perforatum) (used to treat mild depression).
- Pantoprazole is metabolized in the liver. An interaction may occur between pantoprazole and other drugs that are metabolized in the liver. However, specific tests were performed with the following drugs and no clinical significance was observed:
    - Carbamazepine (medication for epilepsy and mood changes),
    - Diazepam (used to relieve anxiety),
    - Nifedipine (used for the treatment of high blood pressure),
    - Glibenclamide (blood glucose lowering),
    - Birth control pills (containing levonorgestrel and ethinyl estradiol),
- There were no interactions with concomitantly administered antacids. Antacids are usually used in the form of a chewable tablet or syrup, which is used to instantly reduce stomach acid.

If you are taking or have recently taken any other medicines, including medicines without a prescription, tell your doctor or pharmacist.

3. How to use ZYGOSİS

Instructions regarding correct use and dosage/administration frequency:

Ulcers in the upper part of the intestine (duodenal ulcer) or in the stomach (gastric ulcer) or inflammation and pain in the esophagus due to the regurgitation of stomach acid to the esophagus (esophageal reflux disease):

1 vial a day (40 mg pantoprazole).

Short-term maintenance of hemostasis and prevention of re-bleeding in patients with acute bleeding gastric or duodenal ulcers:

In patients with acute hemorrhagic gastric or duodenal ulcers, 80 mg should be administered as a bolus infusion over 2-15 minutes, followed by a continuous intravenous infusion of 8 mg/h given over 3 days (72 hours).

Treatment of conditions and as Zollinger-Ellison-Syndrome producing too much acid in the stomach.

2 vials a day (80 mg pantoprazole).

Your doctor may adjust the dose, depending on the amount of stomach acid you produce.

If you are prescribed more than two vials (80 mg) a day, the injections will be given in two equal doses.

Your doctor may prescribe a temporary dose of more than four vials (160 mg) a day. If your stomach acid level needs to be controlled rapidly, a starting dose of 160 mg (four vials) should be enough to lower the amount of stomach acid sufficiently.

Method of administration:

A doctor or a nurse will administer the daily dose to you as an injection into a vein over a period of 2-15 minutes.

Various age groups:

Use in children:
ZYGOSİS is not recommended in children under 18 years.

Use in elderly:
ZYGOSİS may be used in elderly without dose adjustment.

Special cases:

Renal failure:
Dose adjustment is not required in patients with impaired renal function.

Hepatic failure:
In patients with severe liver problems, the daily dose of 20 mg (half a vial) should not be exceeded.

If you are under the impression that the effect ZYGOSİS is too strong or weak, consult your physician or pharmacist.

If you take more ZYGOSİS than you should
There are no known symptoms of overdose.

If you have used ZYGOSİS more than you should have or more than prescribed, consult a physician or a pharmacist.

If you forget to use ZYGOSİS

If you forget to take your medicine, do not take double dose to make up for the missed dose. Continue your treatment with the next dose according to the posology prescribed by your doctor.

Do not double-dose to make up for forgotten doses.

If you stop using ZYGOSİS

Your doctor will tell you how long your treatment will take with ZYGOSİS. Do not discontinue treatment early, because the symptoms of your disease may recur or be aggravated.

4. Possible side effects

Like all medicines, ZYGOSİS may cause side effects in patients sensitive to its ingredients.

Side effects are classified following below levels of frequency.

Very common (may affect more than 1 in 10 people)
Common (may affect less than 1 in 100 people)
Uncommon (may affect less than 1-10 in 1000 people)
Rare (may affect less than 1-10 in 10,000 people)
Very Rare (may affect less than 1 in 10,000 people)
Not known (Cannot be estimated from the available data)

If any of the following reactions happen stop taking ZYGOSİS and tell your doctor IMMEDIATELY or contact the casualty department at your nearest hospital:

- **Very serious allergic reactions (frequency rare):** swelling of the tongue and/or throat, difficulty in swallowing, hives (nettle rash), allergic facial swelling (Quincke's oedema/angioedema), severe dizziness with very fast heartbeat and heavy sweating.

- **Serious skin conditions (frequency not known):** Sudden, widespread blistering of the skin and rapid deterioration of your general condition, irritation (including slight bleeding) in the eyes, nose, mouth/lips or genitals (may be the signs of Stevens-Johnson-Syndrome, Erythema multiforme and Lyell-Syndrome), sensitivity to light, subacute cutaneous lupus erythematosus (redness around the neck, on the back, in front of the body and on the surface of the arms).

- **Other serious conditions (frequency not known):** yellowing of the skin or whites of the eyes (severe damage to liver cells, jaundice) or fever, hives, and enlarged kidneys sometimes with painful urination and lower back pain (serious inflammation of the kidneys) possibly leading to kidney failure.

These are all very serious side effects.

If you experience one of these side effects, it means that you are severely allergic to ZYGOSİS.

You may need urgent medical attention or to be hospitalized.

If you notice any of the following side effects, tell your doctor:

- **Common:**
  Inflammation of the wall of the vein and blood clotting on the injection site; benign polyps in the stomach.
- **Uncommon:**
  Headache; dizziness; diarrhea; feeling sick, vomiting; bloating and flatulence; constipation; dry mouth; abdominal pain and discomfort; allergic reactions such as redness, itching, skin rash; fatigue sleep disorders.
  Taking a proton pump inhibitor like pantoprazole, especially over a period of more than one year, may slightly increase your risk of fracture in the hip, wrist or spine. Tell your doctor if you have osteoporosis or if you are taking corticosteroids which can increase the risk of osteoporosis.
- **Rare:**
  Distortion or complete lack of the sense of taste; disturbances in vision such as blurred vision; hives (urticaria); pain in the joints; muscle pains; weight changes; raised body temperature; high fever; swelling of the extremities (peripheral edema); allergic reactions; depression; breast enlargement in males (gynecomastia).
- **Very rare:**
  Disorientation.
- **Unknown:**
  Seeing or hearing things that don't actually exist, especially in predisposed patients (hallucination), loss of time and space harmony and confusional state (confusion); decreased sodium level in blood (hyponatremia), feeling of tingling, prickling, pins and needles, burning or freezing sensation (paresthesia); skin redness and rash, possibly with pain in the joints. If you are on ZYGOSİS for more than three months it is possible that the levels of magnesium in your blood may fall. Low levels of magnesium (hypomagnesemia) can be seen as fatigue, involuntary muscle contractions, disorientation, convulsions, dizziness and increased heart rate. Low levels of magnesium can also lead to a reduction in potassium or calcium levels in the blood. Your doctor may decide to perform regular blood tests to monitor your levels of magnesium.

Side effects identified through blood tests:

- **Uncommon:**
  Increase in liver enzymes.

- **Rare:**
  Increase in blood bilirubin; increase in triglyceride levels (fats) in the blood, sharp drop in circulating white blood cells (associated with high fever).

- **Very rare:**
  Reduction in the number of blood cells (platelets) which allow coagulation (this may cause you to bleed more than normal); reduction in the number of white blood cells (this may lead to more frequent infections); coexisting abnormal reduction in the number of red blood cells, white blood cells, and the blood cells enabling coagulation (platelets).

If you notice any side effect not mentioned in this leaflet, please inform your doctor or pharmacist.

5. How to store ZYGOSİS

Keep ZYGOSİS out of the sight and reach of children, and in its original packaging.

Store at room temperature below 25°C.

Use in compliance with the expiry date.

Do not use ZYGOSİS after the expiration date printed on its packaging.

If you notice any irregularities in the product and/or its packaging, do not use ZYGOSİS.

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.

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This patient leaflet was approved on 30.12.2019.

THE FOLLOWING INFORMATION IS INTENDED FOR HEALTHCARE PROFESSIONALS ONLY:

A ready-to-use solution is prepared by injecting 10 ml of sodium chloride 9 mg/ml (0.9%) solution for injection into the vial containing the dry powder. This solution may either be administered directly or after mixing it with 100 ml sodium chloride 9 mg/ml (0.9%) solution for injection or glucose 55 mg/ml (5%) solution for injection. Glass or plastic containers should be used for dilution.

ZYGOSİS should not be prepared or mixed with solvents other than those stated.

After preparation, the solution must be used within 12 hours. From a microbiological point of view, the product should be used immediately.

If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 12 hours, at no more than 25°C.

The medicine should be administered intravenously over 2-15 minutes.

The content of the vial is for single intravenous use only. Any product that has remained in the container or whose visual appearance has changed (e.g. if cloudiness or precipitation is observed) must be discarded.