organs (mild bleeding) (these may be symptoms of severe skin reacktions like Stevens Johnson Syndrome, Erythema Multiforme and Lyell Syndrome) and sensitivity to light

• **Other very serious diseases (unknown frequency degree):** Yellowing on the skin or white parts of the eyes (severe damage in liver cells, jaundice) or growth in kids accompanied by fever, urticaria and painful urine and low back pain (severe nephritis)

All of these are very serious adverse effects.

If you have one of these, it means you have a serious allergy against PANZOL®. You may need emergency medical intervention or admitting to a hospital.

If you recognize any of the below, tell your physician:

• **Uncommon** (1 to 10 in 1000 patients)

Headache; dizziness; diarrhea, not feeling good; vomiting; stomach bloating and gas; constipation; dryness of the mouth; stomach pain; allergic reactions like erythema, itchiness and skin rash; asthenia, sleep disorders

The risk of fracture on hips, wrists or spine increases in patients particularly who use proton pump inhibitor like pantoprazole for longer than one year. If you have osteoporosis disease or you use corticosteroids increasing the osteoporosis risk.

• **Rare** (1 to 10 in 10000 patients)

Deterioriation or complete loss of tasting; visual disorders like blurred vision; rash (urticaria); arthralgia; muscle pains; gaining/losing weight; increase of body temperature; high fever; swelling on hands and feet (peripheral edema); allergic reactions; depression; breast augmentation in men (gynecomastia)

• **Very rare** (less than 1 in 10000 patients)

Orientation disorder

• **Not known** (It cannot be estimated from the available data):

Seeing or hearing things that don't exist especially disposed patients (hallucination), loss of time and space harmony and wooziness (confusion); decrease in blood sodium level (hyponatremia). If you are using PANZOL® for more than three months, it's possible that magnesium levels in your blood increase. Decrease in magnesium level (hypomagnesemia), fatigue, involuntary myotonia, orientation disorder, spasms, dizziness and increase in the pulse. Decrease in magnesium level may also cause potassium and calcium levels in your blood. Your doctor may want regular tests to monitor the magnesium levels in your blood.

Adverse effects determined by blood tests:

• **Uncommon** (1 to 10 in 1000 patients):

Increase in liver enzymes

• **Rare** (1 to 10 in 10000 patients):

Increase in bilirubin level in blood; increase in triglyceride (fat) level in blood, sudden decrease (accompanied by high fever) in number of white blood celss (leucocyte).

• **Very rare** (less than 1 in 10000 patients)

Decrease in number of blood cell (blood platelets) ensuring coagulation in blood (this case may cause more bleeding than normal); decrease in number of white blood celss (leucocyte) (this case may cause more frequent infections); abnormal decrease in all red blood cells (erythrocyte), white blood cells (leucocyte) and blood cells ensuring the coagulation (blood platelets).

Reporting the adverse effects.

If you develop an adverse effect which is included or not included in the Package Insert, talk to your doctor, pharmacist or nurse. Also, please report the adverse effects you have encountered to Turkish Pharmacovigilance Center (TUFAM), via clicking "Drug Adverse Effect Report" icon on www.titck.gov.tr or via calling the adverse effect report line on 0 800 314 00 08. By reporting the developed side-effects, you will contribute to obtain more information about the safety of the medicine you are using.

If you encounter any adverse effect that is not included in this package insert, inform your doctor or pharmacist.

5. Storage of PANZOL®

Keep PANZOL® out of the sight and reach of children and in its package.

Store at room temperature below 25˚C in a dry place away from light..

Use in line with expiry date.

Do not use PANZOL® after the expiry date on the package.

If you notice defects in product and/or packaging, do not use PANZOL®.

License Holder:

Biofarma İlaç San. ve Tic. A.Ş.
Akpınar Mah. Osmangazi Cad. No:156
Sancaktepe/İstanbul

Site of Manufacture:

Biofarma İlaç San. ve Tic. A.Ş.
Akpınar Mah. Osmangazi Cad. No:156
Sancaktepe/İstanbul

This package insert was approved on 25.07.2014.

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PACKAGE INSERT

PANZOL® 20 mg Enteric Coated Tablet
It is taken orally.

• ***Drug substance:*** Pantoprazole sodium sesquihydrate equivalent to 20 mg pantoprazole in each tablet.

• ***Excipients:*** Mannitol (E421), calcium carbonate (E170), crospovidone, vinylpyrrolidone-vinyl acetate copolymer, sucrose stearate (E473), calcium stearate, hydroxypropyl methyl cellulose (E464), titanium dioxide (E171), triacetine (E1518), methacrylic acid copolymer, talk (E553b), triethyl citrate (E1505), colloidal silicon dioxide (E551), sodium bicarbonate (E500), yellow iron dioxide (E172), sodium lauryl sulphate

Please read this PACKAGE INSERT carefully before you start to use the medicine since it contains information that is important for you.

- *Keep this package insert. You may need to read it later.*
- *If you have additional questions, please consult your doctor or pharmacist.*
- *This medicine is personally prescribed for you, do not give it to others.*
- *Tell your doctor that you are using this medicine when you apply to a doctor or a hospital during the use of this medicine.*
- *Please comply with the information in this package insert exactly. Do not use* ***higher or lower*** *dose of the medicine than the one recommended to you.*

In This Package Insert:

Topics are included.

1. What is PANZOL® and what is it used for?

• PANZOL® is put into use in tablets (enteric coated) coated with a special substance that prevents the dissolution of the drugs in stomach. Each tablet contains 20 mg pantoprazole (as pantoprazole sodium sesquihydrate) as drug substance.

• Pantoprazole, drug substance of PANZOL®, is included in a drug group named as "proton pump inhibitor". It shows effect by minimizing the amount of acid produced in your stomach. It's used for the treatment of deseases in the stomach and intestine related with the acid.

• PANZOL® is put on the market in blister packages containing 28 tablets. Tablets in the blister are yellow, oval, biconvex and unnotched.

PANZOL®:

5 in adults and children older than:

• In short term (up to 8 weeks at most) treatment and relief of symptoms of erosive esophagitis (occurence of tissue damage on the surface of esophagus) formed with gastroesophageal reflux (foods and acid escaping from the stomach to esophagus),

• In long term treatment of reflux esophagitis (inflammation of esophagus as a result of escaping of foods and acid from the stomach to esophagus) and prevention of the recurrence.

In adults:

• In treatment of mild reflux disease (foods and acids escaping from the stomach to esophagus) and symptoms related to the disease,

• It's administered to the patients that receive continuous nonsteroidal anti-inflammatory drug treatment (NSAII, for example ibuprofen) and that are proved to have gastric and duodenal ulcer endoscopically.

2. Points to take into consideration before using PANZOL®

DO NOT USE PANZOL® in following cases

If;

• If you are allergic (hypersensitivity) to pantoprazole drug substance or one of the excipients in the composition of PANZOL®, benzimidazoles (medicines used for fungus diseases),

• If you are allergic to other drugs containing proton pump inhibitor,

do not use PANZOL®.

TAKE SPECIAL CARE WHILE USING PANZOL® in following cases

If;

• If you have severe hepatic impairment, if you had a problem with your liver, report to your doctor. During the treatment with PANZOL®, your doctor will check your liver enzymes regularley, especially when it's used for a long time. In case of increase of liver enzymes, you should stop using PANZOL®.

• You must be careful if sources of B12 vitamin have decreased or if you posess risk factors for vitamin deficiency. Pantoprazole, like all other gastric acid inhibitors, may minimize the absorption of B12 vitamin.

• If you have been using PANZOL® for more than 1 year, tell your doctor. In that case, probably your doctor will keep you under regular observation. If you recognize new and extraordinary symptoms, you should mention about these when you see your doctor.

• Treatment with PANZOL® may suppress the symptoms related with the cancer and eventually delay the diagnosis. Therefore, before PANZOL® treatment, your doctor may run some tests to ensure that

you are not cancer patient. If your symptoms continue during your treatment, further examinations may be necessary.

- If you have osteoporosis disease, tell your doctor. Like all other proton pump inhibitors, when PANZOL® is used in high doses and for long time (more than 1 year) in patients with osteoporosis, in elder patients and in cases of other risk factors, it may increase the risk of fracture in wrists and spine. In that case, your doctor may recommend you to use PANZOL® in lower doses or for shorter time.
- If you were diagnosed with hypomagnesemia (low magnessium mineral level in your stomach) before, tell your doctor. Like all other proton pump inhibitors, PANZOL® may cause hypomagnesemia after the treatment for at least 3 months (generally, more than 1 year). In that case, your doctor may decide that you should take magnessium supplement or continue PANZOL® treatment for a shorter time. In case you feel that your heart beats abnormally fast, slow or arrhythmically durin your PANZOL® treatment, if you have fatigue or dizziness feeling, muscle spasm or seizure, tell your doctor. These symptoms may be related with hypomagnesemia. Furthermore, in case there are other medicines you take, tell them your doctor as well. Hypomagnesemia may cause decrease in potassium and calcium levels in the blood. In case your doctor deems necessary, he/she would want to monitor the magnesium level in your blood regularly.
- If you are udnergoing neuroendocrine tumor diagnosis tests, tell your doctor, because like all other proton pump inhibitors, PANZOL® may cause the result of these tests.

Like all other proton pump inhibitors, PANZOL® may increase the number of some bacteria that normally exist in upper gastrointestinal tract and therefore the risk of infection (*Salmonellia* and *Campylobacter*) even a little.

- If it's used to prevent the ulcers triggered by the non-steroidal anti-inflammatory agents (painkiller not in the form of steroid, inflammation inhibitor) (NSAI), PANZOL® should be limited to the patients requiring continuous NSAI medication with high adverse affect risk in gastrointestinal system (for example; over age 65; with ulcer or gastrorrhegia.
- If you take anticoagulants or blood thinners like warfarin and phenprocoumon, you may need to have further tests.

- If you notice one of the following, consult your doctor **IMMEDIATELY**:
  - Unexpected weight loss,
  - Recurrent vomiting,
  - Dysphagia,
  - Hematemesis,
  - Looking pale and feeling light-headed (anemia/)
  - Blood in stool
  - Severe and continuous diarrhea

If these warnings apply for you, even in the past, please consult your doctor.

Taking PANZOL® with food and drinks

PANZOL® should be swallowed 1 hour before dinner as whole with an amount of water without chewing or breaking.

Pregnancy

Please consult your doctor or pharmacist before using this medicine.

There isn't sufficient data on use of pantoprazole in pregnancy. If you are pregnant or you think that you are pregnant, but, in case your doctor thinks that estimated benefit of the medicine is more than the risk of damaging your unborn baby, then you should use pantoprazole.

If you notice you are pregnant during your treatment, consult to your doctor or pharmacist immediately.

Lactation

Please consult to your doctor or pharmacist before using this medicine.

It was reported that pantoprazole seeps into breat milk. It should only be used in nursing mothers in case the benefit of the medicine to the mother is more than damaging the baby.

Ability to drive and use machines

If you experience dizziness and visual impairment, do not drive and use machine

Important information about some of the ingredients of PANZOL®

PANZOL® contains a sugar named sucrose.. If you have been told by your physician before that you have intolerance against some sugars (your body showing negative reaction to some sugars), consult your physician before taking this medicinal product.

This medicinal product contains sodium less than 1 mmol (23 mg) in each tablet; so basically it "doesn't contain sodium".

PANZOL® contains 14,75 mg mannitol in each dose. No warning is required for its dose.

Using with other medicines

- Pantoprazole may decrease the absorption and minimize the effects of medicines to prevent the fungal infection like ketoconazole, itraconazole and posaconazole, absorption of which depends on the acid level in the stomach (pH) and some anti-cancer drugs like erlotinip.
- Proton pump inhibitors decrease the absorption of the medicines used in the treatment of HIV (AIDS) like atazanavir. Proton pump inhibitors including the pantoprazole are not recommended to be used with atazanavir.
- Pantoprazole is metabolized. Similarly, there may be interaction between pantoprazole and other medicines metabolized in the liver. In addition, special tests were made with the following drugs and no interaction was observed with clinical importance.
- Carbamazepine (epilepsy and mood disorder drug)
- Diazepam (used to prevent anxiety disorder)
- Nifedipine (used in the treatment of high blood pressure)
- Glibenclamide (antidiabetic)
- Birth control pills (containing levonorgestrel and ethinyl estradiol)

If you are using a drug assisting the blood clotting (like phenprocoumon/warfarin), it's recommended to monitor the blood clotting values after start and termination of pantoprazole treatment and during the irregular administration.

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- No interaction iss observed with antacids. Antacis are used to reduce the gastric acid immediately and generally in chewing tablet or syrup form.

If you are using a prescribed or non-prescribed medicine currently, or have used recently, please inform your doctor or doctor about these.

3. How is PANZOL® used?

- **Instructions for proper use and dose/dosing intervals:**

in adults and children older than 5 years old:

- In short term (up to 8 weeks at most) treatment and relief of symptoms of erosive esophagitis (occurence of tissue damage on the surface of esophagus) formed with gastroesophageal reflux (foods and acid escaping from the stomach to esophagus),

Recommended dose is 1 PANZOL® 20 mg per day. Do not exceed 20 mg PANZOL® a day for children under 40 kg.

- In long term treatment of reflux esophagitis (inflammation of esophagus as a result of escaping of foods and acid from the stomach to esophagus) and prevention of the recurrence.

It's recommended to use PANZOL® 20 mg once a day as maintenance dose for long-term treatment; in case of recurrence, increase the dose to 40 mg per day. After the elimination of recurrence, the dose may be decreased to 20 mg pantoprazole again. Do not exceed 20 mg PANZOL® a day for children under 40 kg.

In adults:

- In treatment of mild reflux disease (foods and acids escaping from the stomach to esophagus) and symptoms related to the disease (acid indigestion, acid escaping to esophagus, dyscatapoxia):

Symptoms are eliminated generally in 2-4 weeks and related esophagitis requires generally a 4-week treatment. If this is not enough, normally in following 4-week period, recovery is ensured. When the symptoms are elliminated, recurrence of the symptoms may be taken under control by applying a treatment regime for PANZOL® 20 mg a day according to the needs. In case sufficient symptom control is not achieved through this treatment regime applied according to the needs, it may be proceeded to the continuous treatment.

- It's administered to the patients that receive continuous nonsteroidal anti-inflammatory drug treatment (NSAII, for example ibuprofen) and that are proved to have gastric and duodenal ulcer endoscopically.

Recommended dose is 1 PANZOL® 20 mg per day.

Administration route and method:

PANZOL® should not be chewed or broken; it should be swallowed as whole with an amount of water one hour before dinner.

Various age groups:

Pediatric use:

It shouldn't be administered to the children under 5.

Geriatric use:

PANZOL® may be used in elder patients without dose arrangement.

Special administration conditions:

Renal failure:

PANZOL® may be used in patients with renal failure without dose arrangement.

Liver failure:

20 mg pantoprazol dose per day shouldn't be exceeded in the patients with severe liver impairment.

If you have the impression that the effect of PANZOL® is either very potent or very weak, please talk to your physician or pharmacist.

If you used more PANZOL® than you should:

There is no known symptoms for overdose.

If you have taken more PANZOL® than you should, consult a doctor or pharmacist.

If you forget to use PANZOL®:

If you forget to take your medicine, do not take double doses to make up the missed dose. Continue your treatment with next dose, according to the dosage regime that your doctor deemed suitable.

Do not take double doses to make up the missed dose.

Possible effects after the discontinuation of PANZOL® treatment:

Your doctor shall provide information for how long your treatment will continue with PANZOL®. Do not quit the treatment earlier because the symptoms of your disease may come back or get worse.

4. What are possible adverse effects?

As with all drugs, there may be adverse effects in the individuals who are sensitive to any of ingredients of PANZOL®.

Adverse effects are classified according to the following frequency degrees:

Very common (1 out of 10 patients)
Common (1 to 10 in 100 patients)
Uncommon (1 to 10 in 1000 patients)
Rare (1 to 10 in 10000 patients)
Very rare (less than 1 in 10000 patients)
Not known (It cannot be estimated from the available data)

Stop taking PANZOL® if you experience one of the conditions below and inform your physician or apply to the emergency department of the nearest hospital IMMEDIATELY:

- **Very serious allergic diseases (rare):** Swelling on tongue and/or throat, swallowing difficulty/indigestion, rash (urticaria), asphyxiation, allergic swelling on face (Quincke disease/angioedema), very fast heart beat and dizziness accompanied by sweating.
- **Very serious skin diseases (unknown freqeuncy degree):** Fulminant, common, bubbling painful rashes on the skin, deterioration in general health status, irritation on eyes, nose, mouth/lips and sexual