# SUMMARY OF PRODUCT CHARACTERISTICS

## 1. NAME OF THE MEDICINAL PRODUCT

PANDEV 40 mg Lyophilized Powder for Solution for IV Injection

Sterile

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

**Active substance:**
Each vial contains 45.11 mg pantoprazole sodium sesquihydrate that is equivalent to 40 mg pantoprazole as the active substance.

**Excipients with known effect:**
Edetate disodium……..1 mg
Sodium hydroxide……2 mg
For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Vial containing lyophilized powder for injection.
A homogeneous, white to off-white lyophilized powder, free of visible foreign matter.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

PANDEV is indicated for:

- Reflux esophagitis,
- Gastric and duodenal ulcer,
- The short-term maintenance of hemostasis and prevention of re-bleeding in patients with acute bleeding gastric or duodenal ulcers,
- Zollinger-Ellison Syndrome and other pathological hypersecretory conditions.

### 4.2 Posology and method of administration

**Posology/duration and frequency of administration:**
This medicine should be administered by a healthcare professional and under appropriate medical supervision.
Intravenous administration is recommended only if oral administration is not appropriate. Data are available on intravenous use for up to 7 days. Therefore, as soon as oral therapy is possible, treatment with PANDEV IV should be discontinued and 40 mg pantoprazole p.o. should be administered instead.

For the treatment of duodenal ulcer, gastric ulcer, and moderate to severe reflux esophagitis:
The recommended intravenous dose is one vial (40 mg pantoprazole) per day.

For the short-term maintenance of hemostasis and prevention of re-bleeding in patients with acute bleeding gastric or duodenal ulcers:
In patients with acute bleeding 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/hour for 3 days (72 hours).

For the long-term management of Zollinger-Ellison Syndrome and other pathological

hypersecretory conditions:
Patients should start their treatment with a daily dose of 80 mg. Thereafter, the dose can be titrated up or down as needed using measurements of gastric acid secretion to guide. With doses above 80 mg daily, the dose should be divided and given twice daily. A temporary increase of the dose above 160 mg pantoprazole is possible but this should not be applied longer than required for adequate acid control.

In case a rapid acid control is required, a starting dose of 2 x 80 mg IV is sufficient to manage a decrease of acid output into the target range (< 10 mEq/h) within 1 hour in the majority of patients.

Oral therapy should be initiated as soon as it is clinically confirmed.

**Method of administration**
PANDEV IV is administered by injection.
A ready-to-use solution is prepared by adding 10 mL of sodium chloride 9 mg/mL (0.9 %) physiological saline into the vial containing powder for injection. The prepared solution may be administered directly or may be administered after mixing it with 100 mL sodium chloride 9 mg/mL (0.9 %) solution for injection, with glucose 55 mg/mL (5 %) solution for injection, or with lactated Ringer's injection.
PANDEV must not be mixed with substances other than the specified solvents.
The medicinal product should be administered intravenously over 2 - 15 minutes.
After preparation, the solution must be used within 24 hours.

**Additional information regarding special populations:**
**Renal impairment:**
No dose adjustment is necessary in patients with impaired renal function (see. section 5.2).

**Hepatic impairment:**
A daily dose of 20 mg pantoprazole (half a vial of 40 mg pantoprazole) should not be exceeded in patients with severe liver impairment (see section 4.4). Liver enzymes should also be monitored during PANDEV therapy. PANDEV therapy should be discontinued if elevated liver enzymes occur.

**Pediatric population:**
No adequate clinical experience in the treatment of children is available. Therefore, PANDEV powder for solution for IV injection is not recommended for use in patients below 18 years of age until the necessary data are available.

**Elderly:**
No dose adjustment is necessary in the elderly (see section 5.2).

**4.3 Contraindications**
PANDEV should not be used in patients with known hypersensitivity to the active substance, to substituted benzimidazoles or to any of the other excipients in its composition (see section 6.1).

**4.4 Special warnings and precautions for use**
Hepatic impairment:
In patients with severe liver impairment, particularly those on long-term use, liver enzymes should be monitored regularly during treatment with pantoprazole. In the case of a rise in liver enzymes, PANDEV should be discontinued (see section 4.2).

Gastric malignancy:
In the presence of any alarm symptom (e.g. unintentional significant weight loss, recurrent vomiting, dysphagia, hematemesis, anemia or melena) and in the presence or suspicion of gastric ulcer, malignancy should be excluded. Because pantoprazole may suppress symptoms and delay diagnosis.

Further investigation is to be considered if symptoms persist despite adequate treatment.

Co-administration with HIV protease inhibitors:
Pantoprazole is not recommended for use with HIV protease inhibitors for which absorption is dependent on acidic intragastric pH, such as atazanavir, due to significant reduction in their bioavailability (see section 4.5).

Bone fracture:
Several published observational studies suggest that proton pump inhibitor (PPI) therapy may be associated with an increased risk for osteoporosis-related fractures of the hip, wrist, or spine. The risk of fracture was increased in patients who received high-dose, defined as multiple daily doses, and long-term PPI therapy (a year or longer). Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated.

Observational studies suggest that PPIs may increase the total risk of fractures by 10%–40%. Some of this increase may be related to other risk factors. Patients at risk for osteoporosis should be treated according to current treatment guidelines and receive adequate vitamin D and calcium.

Hypomagnesemia:
Hypomagnesemia, symptomatic and asymptomatic, has been reported rarely in patients treated with PPIs for at least 3 months, and in most cases after a year of therapy. Serious adverse events from hypomagnesemia, such as fatigue, tetany, delirium, convulsions, drowsiness, and ventricular arrhythmias, may occur but may begin insidiously and be overlooked. In most patients, treatment of hypomagnesemia required magnesium replacement and discontinuation of the PPI.
For patients expected to be on prolonged treatment or who take PPIs with digoxin or drugs that may cause hypomagnesemia (e.g., diuretics), health care professionals should consider measuring magnesium levels before starting PPI treatment and periodically during treatment.

Subacute cutaneous lupus erythematosus
Proton pump inhibitors have been associated with very rare cases of subacute cutaneous lupus erythematosus. If lesions occur, especially on sun-exposed areas of the skin, and are accompanied by arthralgia, the patient should seek immediate medical attention and the healthcare professional should consider discontinuing PANDEV therapy. Previous subacute cutaneous lupus erythematosus following proton pump inhibitor therapy increases the risk of the same condition occurring with other proton pump inhibitors.

Laboratory tests:
Serum chromogranin A (CgA) levels increase secondary to drug-induced decreases in gastric acid levels. Increased CgA levels may lead to false-positive results in diagnostic workup for neuroendocrine tumors. To avoid this, PANDEV therapy should be stopped at least 5 days before CgA measurements (see Section 5.1). If CgA and gastrin levels have not returned to reference range after the first measurement, measurements should be repeated 14 days after stopping proton pump

inhibitor therapy. If serial tests are performed (e.g. for monitoring), the tests should be performed in the same laboratory, as reference ranges may vary between tests.

Gastrointestinal infections caused by bacteria

Treatment with PANDEV may cause a slightly increased risk of gastrointestinal infections caused by bacteria such as *Salmonella* and *Campylobacter* or *C. difficile* (see section 5.1).

Long-term treatment:

Patients should be monitored regularly, especially during long-term treatment exceeding 1 year.

Sodium

This medicinal product contains less than 1 mmol (23 mg) per vial, therefore, it is considered 'sodium free'.

## 4.5 Interaction with other medicinal products and other forms of interaction

Medicinal products with pH-dependent absorption pharmacokinetics

Due to its severe and prolonged inhibition of gastric acid secretion, PANDEV may alter the absorption of drugs whose oral bioavailability is pH-dependent (some antifungals such as ketoconazole, itraconazole, posaconazole and some other drugs such as erlotinib).

HIV protease inhibitors

The use of pantoprazole with HIV protease inhibitors, such as atazanavir, whose absorption is dependent on acidic intragastric pH, is not recommended due to significant reduction in their bioavailability (see section 4.4).

If the combination of HIV protease inhibitors with a proton pump inhibitor is necessary, close clinical monitoring (e.g. viral load) is recommended. The daily dose of 20 mg pantoprazole should not be exceeded. The dosage of HIV protease inhibitors may require adjustment.

Coumarin anticoagulants (phenprocoumon and warfarin):

Concomitant administration of pantoprazole with phenprocoumon or warfarin did not affect the pharmacokinetics of warfarin, phenprocoumon or INR. However, in the post-marketing period, increases in the International Normalization Ratio (INR) and prolongation of prothrombin time have been reported in some patients receiving PPIs concomitantly with phenprocoumon or warfarin. Increases in INR and prolongation of prothrombin time may lead to abnormal bleeding and even death. Patients receiving pantoprazole and warfarin or phenprocoumon therapy may require monitoring for increases in INR and prolongation of prothrombin time.

Methotrexate

Concomitant use of high-dose methotrexate (e.g. 300 mg) and a proton pump inhibitor has been reported to increase methotrexate levels in some patients. Therefore, temporary discontinuation of pantoprazole may need to be considered in conditions where high-dose methotrexate is used, such as cancer and psoriasis.

Other interaction studies:

Pantoprazole is metabolized mainly in the liver via the cytochrome P450 enzyme system. The main metabolic pathway is demethylation by CYP2C19 and other metabolic pathways include oxidation by CYP3A4.

Interaction studies conducted with drugs that are metabolized via the same enzyme system such as

carbamazepine, diazepam, glibenclamide, nifedipine, and oral contraceptives containing levonorgestrel and ethinyl estradiol do not imply a clinically significant interaction.

An interaction of pantoprazole with other medicinal products or compounds metabolised using the same enzyme system cannot be excluded.

A range of interaction studies demonstrate that pantoprazole does not interfere with either the metabolism of active substances metabolized by CYP1A2 (such as caffeine, theophylline), CYP2C9 (such as piroxicam, diclofenac, naproxen), CYP2D6 (such as metoprolol), CYP2E1 (such as ethanol) or p-glycoprotein related absorption of digoxin.

There were no interactions with concomitantly administered antacids.

Interaction studies have also been performed on concomitant administration of pantoprazole with antibiotics such as clarithromycin, metronidazole, and amoxicillin. No clinically relevant interaction has been found.

Medicinal products that inhibit or induce CYP2C19:
CYP2C19 inhibitors such as fluvoxamine may increase systemic exposure to pantoprazole. In patients treated with CYP2C19 inhibitors such as fluvoxamine or those with hepatic impairment who are receiving high doses of pantoprazole for long periods, a reduction in the dose of pantoprazole may be considered.

Enzyme inducers that affect CYP2C19 and CYP3A4, such as rifampicin and St. John's wort (*Hypericum perforatum*), may reduce plasma concentrations of PPIs metabolized by these enzyme systems.

**Additional information on special populations:**
No interaction study on special populations has been conducted.

**4.6 Fertility, pregnancy and lactation**
**General principles**
Pregnancy category: B

**Women of childbearing potential/Birth control (Contraception)**
There are no clinically significant data obtained from specific tests conducted with oral contraceptives containing levonorgestrel and ethinyl estradiol (see section 4.5).

**Pregnancy**
Data from a limited number of pregnancy exposures (between 300-1000 pregnancy outcomes) do not indicate adverse effects of pantoprazole on pregnancy or on the health of the fetus/newborn (such as causing malformations or having foeto/neonatal toxicity).
No relevant epidemiological data have been obtained to date. Animal studies have shown reproductive toxicity (see section 5.3). The potential risk for humans is unknown.
Caution should be exercised when used in pregnancy.

**Lactation**
Animal studies have shown excretion of pantoprazole in breast milk. There is insufficient/limited information on the excretion of pantoprazole in human milk, but transfer into breast milk has been

reported. A risk to newborns/infants cannot be excluded. When deciding whether to discontinue breastfeeding or to discontinue/abstain from PANDEV therapy, the benefit of breastfeeding for the child and the benefit of PANDEV therapy for the nursing mother should be taken into account.

**Fertility**
There is no evidence of impaired fertility following administration of pantoprazole in animal studies (see section 5.3).

**4.7 Effects on ability to drive and use machines**
Pantoprazole has no or negligible influence on the ability to drive and use machines.

Adverse drug reactions such as dizziness and visual disturbances may be observed (see section 4.8). In the event of these adverse events, the patient should not drive or operate machinery.

**4.8 Undesirable effects**
Approximately 5 % of patients can be expected to experience adverse drug reactions. The most frequently reported adverse reactions were diarrhea and headache, observed in approximately 1% of patients on both occasions.

The frequency of adverse events, listed by system organ class, is defined as follows:
Very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to < 1/1,000); very rare (< 1/10,000); not known (cannot be estimated from the available data).

| **Frequency**<br><br>**System Organ Class** | **Common (≥ 1/100 to < 1/10)** | **Uncommon (≥ 1/1,000 to < 1/100)** | **Rare (≥ 1/10,000 to < 1/1,000)** | **Very rare (< 1/10,000; including isolated reports)** | **Not known** |
|---|---|---|---|---|---|
| **Blood and lymphatic system disorders** | | | Agranulocytosis | Thrombocytopenia; Leukopenia; Pancytopenia | |
| **Immune system disorders** | | | Hypersensitivity (including anaphylactic shock and anaphylactic reactinos) | | |
| **Metabolism and nutrition disorders** | | | Hyperlipidemias and lipid increases (triglycerides, cholesterol); Weight changes | | Hyponatremia; Hypomagnesemia (see section 4.4); Hypocalcemia[(1)]; Hypokalemia |
| **Psychiatric disorders** | | Sleep disorders | Depression (and all aggravations) | Disorientation (and all aggravations) | Hallucination; Confusion (especially in pre-disposed patients, as well as the aggravation of these |

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|---|---|---|---|---|---|
| | | | | | symptoms in case of pre-existence) |
| **Nervous system disorders** | | Dizziness; Headache | Taste disorders | | Paresthesia |
| **Eye disorders** | | | Disturbances in vision (blurred vision) | | |
| **Gastrointestinal disorders** | Fundic gland polyps (benign) | Nausea / vomiting; Abdominal pain and discomfort, Abdominal distension and bloating; Constipation; Dry mouth; Abdominal distension and bloating; Diarrhea | | | Microscopic colitis |
| **Hepatobiliary disorders** | | Liver enzymes increased (transaminases, γ-GT) | Bilirubin increased | | Hepatocellular injury; Jaundice; Hepatocellular failure |
| **Skin and subcutaneous tissue disorders** | | Allergic reactions such as pruritus, exanthema and rash; Prurit | Urticaria; Angioedema | | Stevens-Johnson syndrome; Lyell syndrome; Erythema multiforme; Photosensitivity; Subacute cutaneous lupus erythematosus (see section 4.4) |
| **Musculoskeletal and connective tissue disorders** | | Fracture of the hip, wrist or spine (see section 4.4) | Arthralgia; Myalgia | | Muscle spasm [(2)] |
| **Renal and urinary tract disorders** | | | | | Interstitial nephritis (with the possibility of progression to renal failure) |
| **Reproductive system and breast disorders** | | | Gynecomastia | | |
| **General disorders and administration site disorders** | Thrombophlebitis at the injection site | Asthenia, fatigue and malaise | Body temperature increased; Edema peripheral | | |

(1) Hypocalcemia associated with hypomagnesemia

(2) Muscle spasm as a result of electrolyte disturbances

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

**4.9 Overdose**
There are no known symptoms of overdose in humans.
Systemic exposure with up to 240 mg administered intravenously over 2 minutes, were well tolerated.
As pantoprazole is extensively protein bound, it is not readily dialyzable.
In the case of an overdose with clinical signs of intoxication, apart from symptomatic and supportive treatment, no specific therapeutic recommendations can be made.

**5. PHARMACOLOGICAL PROPERTIES**
**5.1 Pharmacodynamic properties**
Pharmacotherapeutic group: Proton pump inhibitors
ATC code: A02BC02

Mechanism of Action
Pantoprazole is a substituted benzimidazole that inhibits the secretion of hydrochloric acid in the stomach by specific blockade of the proton pumps of the parietal cells.

Pantoprazole is converted to its active form in the acidic environment in the parietal cells where it inhibits the H+, K+-ATPase enzyme, i.e. the final stage in the production of hydrochloric acid in the stomach. The inhibition is dose-dependent and affects both basal and stimulated acid secretion. In most patients, freedom from symptoms is achieved within 2 weeks. As with other proton pump inhibitors and H2 receptor inhibitors, treatment with pantoprazole reduces acidity in the stomach and thereby increases gastrin in proportion to the reduction in acidity. The increase in gastrin is reversible. Since pantoprazole binds to the enzyme distal to the cell receptor level, it can inhibit hydrochloric acid secretion independently of stimulation by other substances (acetylcholine, histamine, gastrin). The effect is the same whether the product is given orally or intravenously.

Pharmacodynamic effects
The fasting gastrin values increase under pantoprazole. On short-term use, in most cases they do not exceed the upper limit of normal. During long-term treatment, gastrin levels double in most cases. An excessive increase, however, occurs only in isolated cases. As a result, a mild to moderate increase in the number of specific endocrine (ECL) cells in the stomach is observed in a minority of cases during long-term treatment (simple to adenomatoid hyperplasia). However, according to the studies conducted so far, the formation of carcinoid precursors (atypical hyperplasia) or gastric carcinoids as were found in animal experiments (see section 5.3) have not been observed in humans.

During treatment with antisecretory drugs, serum gastrin increases in response to decreased acid

secretion. CgA also increases due to decreased gastric acidity. Increased CgA levels may interfere with investigations for neuroendocrine tumors.

Available published evidence suggests that proton pump inhibitors should be discontinued 5 days to 2 weeks prior to CgA measurements. This is to allow CgA levels, which may be spuriously elevated following PPI therapy, to return to the reference range.

Decreased gastric acidity due to any means including proton pump inhibitors, increases gastric counts of bacteria normally present in the gastrointestinal tract.
Treatment with proton pump inhibitors may lead to slightly increased risk of gastrointestinal infections such as *Salmonella* and *Campylobacter* and, in hospitalized patients, possibly also *Clostridium difficile*.

An influence of a long-term treatment with pantoprazole exceeding one year cannot be completely ruled out on endocrine parameters of the thyroid according to results in animal studies.

**5.2 Pharmacokinetic properties**
**General characteristics**
The pharmacokinetics of pantoprozole do not change after single or repeated dosing.

Absorption:
Absorption information is not applicable, as the medicine is given directly into the bloodstream.

Distribution:
Pantoprazole is approximately 98% bound to serum proteins. Its volume of distribution is approximately 0.15 L/kg.

Biotransformation:
Pantoprazole is almost completely metabolized in the liver. The main metabolic pathway is demethylation by CYP2C19 followed by sulfate conjugation, the other metabolic pathway is oxidation by CYP3A4.

Elimination:
The terminal half-life is approximately one hour and the clearance is approximately 0.1 L/h/kg. A few cases of delayed elimination have been observed. Due to the specific binding of pantoprazole to the proton pumps of parietal cells, the elimination half-life is not proportional to the longer durations of action (inhibition of acid secretion).

Pantoprazole metabolites are eliminated mainly renally (approximately 80%), the remainder in the faeces. The main metabolite in both serum and urine is desmethylpantoprazole, which is conjugated with sulphate. The half-life of the main metabolite (approximately 1.5 hours) is not significantly longer than that of pantoprazole.

Linearity/non-linearity:
In the dose range of 10 to 80 mg, the plasma kinetics of pantoprazole are linear after both oral and intravenous administration.

**Characteristics in patients**
Polymorphic metabolism:

Approximately 3% of the European population lack a functional CYP2C19 enzyme and are called poor metabolizers. In these individuals, the metabolism of pantoprazole is probably mainly catalyzed by CYP3A4. After a single-dose administration of 40 mg pantoprazole, the mean area under the plasma concentration-time curve was 6 times higher in poor metabolizers than in subjects having a functional CYP2C19 enzyme (extensive metabolizers). Mean peak plasma concentrations were increased by 60%. These findings have no implications for the posology of pantoprazole.

Renal impairment:
No dose reduction is required in patients with renal impairment (including dialysis patients). As with healthy subjects, pantoprazole's half-life is short and only very small amounts of pantoprazole are dialyzed. Although the main metabolite has a moderately delayed half-life (2-3 hours), excretion is still rapid and thus any accumulation does not occur.

Hepatic impairment:
Although in patients with liver cirrhosis (classes A and B according to Child) the half-life increased to between 7 and 9 hours and the AUC increased by a factor of 5-7, the maximum serum concentration only increased slightly by a factor of 1.5 compared with healthy subjects.

Pediatric population:
Following administration of single IV doses of 0.8 or 1.6 mg/kg pantoprazole to children aged between 2 and 16 years, there was no significant association between pantoprazole clearance and age or weight. AUC and volume of distribution were in accordance with data from adults.

Geriatric population:
A slight increase in AUC and $C_{max}$ occurred in elderly volunteers when compared with younger volunteers is also not clinically relevant.

**5.3 Preclinical safety data**
Pre-clinical data reveal no special hazard to humans based on conventional studies of safety pharmacology, repeated dose toxicity and genotoxicity.

In the two-year carcinogenicity studies in rats, neuroendocrine neoplasms were found. In addition, squamous cell papillomas were found in the forestomach of rats. The mechanism leading to the formation of gastric carcinoids by substituted benzimidazoles has been carefully investigated and allows the conclusion that it is a secondary reaction to the massively elevated serum gastrin levels occurring in the rat during chronic high dose treatment. In the two-year rodent studies, an increased number of liver tumors was observed in rats and in female mice and was interpreted as being due to pantoprazole's high metabolic rate in the liver.

A slight increase of neoplastic changes of the thyroid was observed in the group of rats receiving the highest dose (200 mg/kg). The occurrence of these neoplasms is associated with the pantoprazole-induced changes in the breakdown of thyroxine in the rat liver. As the therapeutic dose in humans is low, no harmful effects on the thyroid glands are expected.

In a peri-postnatal rat reproduction study designed to evaluate bone development, signs of pup toxicity (mortality, reduced mean body weight, reduced mean body weight gain, and reduced bone development) were observed at exposures approximately 2 times the human clinical exposure ($C_{max}$). Bone parameters were similar between groups at the end of the recovery phase, and body weights tended to be reversible after a drug-free recovery period. Increased mortality was reported

only in weaned rat pups (up to 21 days) and is estimated to correspond to infants up to 2 years of age. The relevance of this finding to the pediatric population is uncertain. In a previous peri-postnatal study in rats at a lower dose of 3 mg/kg, no adverse effects were observed when compared to the lower dose of 5 mg/kg.

Investigations revealed no evidence of impaired fertility or teratogenic effects.

Penetration of the placenta was investigated in the rat and was found to increase with advanced gestation. As a result, concentration of pantoprazole in the fetus is increased shortly before birth.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Edetate disodium
Sodium hydroxide

### 6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

### 6.3 Shelf life

The shelf life is 24 months.
After reconstitution, or reconstitution and dilution, chemical and physical in use stability has been demonstrated for 24 hours at room temperature below 25° C.
From a microbiological point of view, the product should be used immediately.
If not used immediately, in-use storage times and conditions are the responsibility of the user.

### 6.4 Special precautions for storage

Store at room temperature below 25°C, protected from light.
Keep the vial in the outer carton in order to protect from light.
For storage conditions of the reconstituted and diluted medicinal product, see section 6.3.

### 6.5 Nature and contents of container

As the primary packaging materials, the injection comprises 12 mL transparent, colorless Type I glass vial with a gray colored bromobutyl rubber notched stopper and blue flip-off cap. Each vial enclosed in an outer carton with a package leaflet.

### 6.6. Special precautions for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local requirements.

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 powder. The reconstituted solution is no less clear than an equal volume of solvent or water. This solution may be administered directly or may be administered after mixing it with 100 mL sodium chloride 9 mg/mL (0.9 %) solution for injection, with glucose 55 mg/mL (5 %) solution for injection, or with lactated Ringer's injection. Glass or plastic containers should be used for dilution.

After reconstitution, or reconstitution and dilution, chemical and physical in use stability has been demonstrated for 24 hours at room temperature below 25° C.

PANDEV should not be mixed with solvents other than those stated.
The medicine should be administered intravenously over 2-15 minutes.

The contents of the vial are for single use only. Any product that has remained in the container or the visual appearance of which has changed (e.g. if cloudiness or precipitation is observed) should be disposed of in accordance with local requirements.

**7. MARKETING AUTHORIZATION HOLDER**
DEVA Holding A.Ş.
Halkalı Merkez Mah. Basın Ekspres Cad. No.:1
34303 Küçükçekmece-İSTANBUL/TÜRKİYE

**8. MARKETING AUTHORIZATION NUMBER**
2015/805

**9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION**
Date of first authorization : 07.10.2015
Date of last renewal :

**10. DATE OF REVISION OF THE TEXT**