PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

PANZYGA®

Immunoglobulin Intravenous (Human)

Solution for Infusion, 100 mg/mL, intravenous use

Prescription Medication, passive immunizing agent
Presentation sizes: 10 mL, 25 mL, 50 mL, 100 mL, 200 mL and 300 mL
ATC-Code: J06B A02

Manufactured by:
Octapharma
72 rue du Maréchal Foch
67380 Lingolsheim, France

and

Octapharma Pharmazeutika Produktionsges. m.b.H.
Oberlaaer Strasse 235
1100 Vienna, Austria

Manufactured for:
Octapharma Canada Inc.
308-214 King St W
Toronto, ON M5H 3S6
Canada

Date of Initial Approval:
Jun 24, 2016

Date of Revision:
May 19, 2021

Submission Control No: 240691

RECENT MAJOR LABEL CHANGES

Indications, Pediatrics, Geriatrics: <MON, YYYY>
Dosage and administration, recommended dosage and dosage adjustment, administration: <MON, YYYY>

Not applicable sections or subsections are omitted from this Product Monograph. Remaining sections and subsections are not renumbered.

TABLE OF CONTENTS

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

Panzyga® is indicated for:

- The treatment of patients with primary immune deficiency (PID) and secondary immune deficiency (SID).
- The treatment of patients with immune thrombocytopenic purpura (ITP).
- The treatment of patients with moderate to severe Guillain-Barré Syndrome (GBS).
- The treatment of patients with chronic inflammatory demyelinating polyneuropathy (CIDP)

1.1 Pediatrics

Treatment of primary and secondary immune deficiencies (age range 2-17 years): Based on the data submitted and reviewed by Health Canada, the safety and efficacy of *Panzyga*® in pediatric patients has been established; therefore, Health Canada has authorized an indication for pediatric use. (see section 15 CLINICAL TRIALS, Treatment of Primary Humoral deficiency (PID))

Treatment of ITP and CIDP
The safety and effectiveness of *Panzyga*® has not been established in pediatric patients with ITP and CIDP.

1.2 Geriatrics

Geriatrics (> 65 years of age):

Clinical studies of *Panzyga*® in patients with PID and ITP did not include sufficient numbers of subjects > 65 years to determine whether they respond differently from younger subjects.

In the clinical study in CIDP the safety and effectiveness of *Panzyga*® in subjects older than 65 years was similar to those 65 years of age and younger. In total 36 patients older than 65 years were included in this clinical trial.

Patients > 65 years of age may be at increased risk for developing certain adverse reactions such as thromboembolic or acute renal events. Ensure adequate hydration and use minimum practicable infusion rates.

2 CONTRAINDICATIONS

Panzyga® is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see Dosage Forms, Strengths, Composition and Packaging.
Panzyga® is contraindicated in patients who have had an anaphylactic or severe systemic reaction to the administration of a human immunoglobulin preparation.
Panzyga® is contraindicated in individuals with selective IgA deficiency with known anti-IgA antibodies.

3 SERIOUS WARNINGS AND PRECAUTIONS BOX

Serious Warnings and Precautions

- The physician should discuss the risks and benefits of this product with the patient, before prescribing or administering to the patient (see 8 WARNINGS AND PRECAUTIONS – General).
- There is clinical evidence of an association between the administration of immunoglobulins and thromboembolic events such as myocardial infarction, stroke, pulmonary embolism and deep vein thromboses. Therefore, caution should be exercised when prescribing and administering immunoglobulins.
- In general the risk factors for thromboembolic events include: obesity, advance age, hypertension, diabetes mellitus, history of vascular disease or thrombotic episodes, acquired or inherited thrombophilic disorders, prolonged periods of immobilisations, severely hypovolemic patients, diseases which increase blood viscosity, hypercoagulable conditions, use of estrogens, indwelling central vascular catheters, and cardiovascular risk factors.
- Thrombosis may occur even in the absence of known risk factors.

(see 8 WARNINGS AND PRECAUTIONS – Thromboembolic events)

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

Patients should be adequately hydrated before infusion of *Panzyga*®. In patients with risk factors (such as pre-existing renal insufficiency, diabetes mellitus, hypovolemia, overweight, concomitant nephrotoxic medications, or over the age of 65), *Panzyga*® should be administered at the minimum rate of infusion practicable.
The patient's vital signs should be observed and monitored carefully throughout the infusion. Patients should be observed for at least 20 minutes after administration.

4.2 Recommended Dose and Dosage Adjustment

Treatment of Primary and Secondary Immunodeficiency

The usual dose of *Panzyga*® is between 200 to 800 mg/kg body weight (2-8 mL/kg) administered every 3 to 4 weeks. The dosage may be adjusted over time to achieve the desired trough levels of IgG (at least 5 g/L) and clinical responses.

Treatment of Immune Thrombocytopenic Purpura

Panzyga® to be administered at a total dose of 2 g/kg, divided into 2 doses of 1 g/kg (10 mL/kg) given on 2 consecutive days. Treatment can be repeated if a relapse occurs.

Treatment of Guillain-Barré Syndrome

Information on the dose and duration of use of *Panzyga*® in GBS is based on data from a systematic review for IVIG[1]; *Panzyga*® may be administered as a total dose of 2 g/kg (20 mL/kg) given in divided doses over two to five consecutive days.

Treatment of Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

The recommended loading dose is 2 g/kg, divided into two daily doses of 1 g/kg (10 mL/kg) given on two consecutive days followed by a maintenance dose of 1 - 2 g/kg (10-20 mL/kg) every 3 weeks.

Measles Exposure

Guidance for measles post-exposure prophylaxis has been provided by the National Advisory Committee on Immunization (NACI) and should be consulted[2].
Individuals already receiving replacement IVIg at 400 mg/kg body weight or higher every month are considered protected against measles if the last dose of IVIG was received within three weeks prior to measles exposure. For patients receiving a dose below 400 mg/kg and/or when the interval since last infusion is longer than 3 weeks administration of a single dose of 400 mg/kg bodyweight as soon as possible and within 6 days of exposure is recommended.

4.3 Administration

For intravenous use only. Prior to use, allow *Panzyga*® to reach ambient room temperature.
Panzyga® is not supplied with an infusion set. If an in-line filter is used the pore size should be 0.2-200 microns.
Insert needle (not larger than 16 gauge to prevent the possibility of coring) only once, within the stopper area delineated (by the raised ring for penetration). Penetrate the stopper perpendicular to its plane and within the ring.

Infusion Rate

The initial infusion rate should be maintained for 30 minutes. Following the initial infusion (see table below), the infusion rate may be gradually increased every 15-30 minutes to a maximum of 14 mg/kg/min (0.14 mL/kg/min) in PID/SID, to 8 mg/kg/min (0.08 mL/kg/min) in chronic ITP, and to a maximum of 12 mg/kg/min (0.12 mL/kg/min) in CIDP, as tolerated.

Indication	Initial Infusion Rate* (first 30 minutes)	Maximum Infusion Rate in *Panzyga*® Patients (as tolerated)
PID/SID	1 mg/kg/min	14 mg/kg/min
Chronic ITP in adults	1 mg/kg/min	8 mg/kg/min
CIDP in adults	1 mg/kg/min	12 mg/kg/min

Patients naive to immunoglobulin G (IgG) or patients who have switched from alternative IVIG brands may experience a higher frequency of minor events than those well maintained on

[1] Hughes RA, Swan AV, van Doorn PA. Intravenous immunoglobulin for Guillain-Barré syndrome. The Cochrane database of systematic reviews. 2014;9:CD002063.
[2] Tunis MC, Salvadori MI, Dubey V, Baclic O. Updated NACI recommendations for measles post-exposure prophylaxis, CCDR 2018; volume 44-9: 226-30

regular therapy. Monitor the patient carefully throughout the infusion. Certain adverse drug reactions may be related to the rate of infusion. Slowing or stopping the infusion usually allows the symptoms to disappear promptly. Once the symptoms subside, the infusion may then be resumed at a lower rate.

In all patients, IVIG administration requires adequate hydration before starting the infusion. For patients at risk of renal dysfunction or thromboembolic events, administer *Panzyga*® at the minimum infusion rate practicable. Monitor urine output, serum creatinine levels, and if possible, avoid concomitant use of loop diuretics in such risk patients. Discontinue *Panzyga*® if renal function deteriorates.

Precautions

Panzyga® should not be mixed with other medicinal products. A separate intravenous line should be used for the infusion. Do not use the product after expiry date.

4.5 Missed Dose

A missed dose should be administered as soon as possible.

5 OVERDOSAGE

Overdose may lead to fluid overload, particularly in the elderly and in patients with impaired renal function.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

To help ensure the traceability of biologic products, including biosimilars, health professionals should recognise the importance of recording both the brand name and the non-proprietary (active ingredient) name as well as other product-specific identifiers such as the Drug Identification Number (DIN) and the batch/lot number of the product supplied.

Table – Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Intravenous use	10 % Solution for infusion	Glycine Waiter for injections

Panzyga® is supplied in a single-use bottle containing the labeled amount of functionally active IgG. The components used in the packaging for *Panzyga*® are latex-free. *Panzyga*® is a 100 mg/mL solution for intravenous infusion.

The following dosage forms are available:

Fill Size	**Grams IgG**
10 mL	1 g
25 mL	2.5 g
50 mL	5 g

100 mL	10 g
200 mL	20 g
300 mL	30 g

Nature and Contents of Container
Each 100 mg/mL of *Panzyga*® contains the active ingredients: Immunoglobulin Intravenous (Human), one milliliter (mL) of solution contains 100 mg of protein of which ≥ 96% is immunoglobulin. Each package contains 1 glass bottle of *Panzyga*® ready to use and the package leaflet.

Composition:

Human normal immunoglobulin G (IgG)	100 mg/mL
Glycine	15.0 – 19.5 mg/mL
Water for injections	1 mL

7 DESCRIPTION

Panzyga® (Immunoglobulin Intravenous (Human), 10%) is a sterile liquid preparation of highly purified immunoglobulin G (IgG) and is prepared from large pools of human plasma (see 8 WARNINGS AND PRECAUTIONS - General).

8 WARNINGS AND PRECAUTIONS

Please see also the Serious Warnings and Precautions Box at the beginning of Part I: Health Professional Information.

General
Products made from human plasma may contain infectious agents, such as viruses and theoretically, the variant Creutzfeldt-Jakob disease (vCJD) agent that can cause disease. The risk that such products will transmit an infectious agent has been reduced by screening plasma donors for prior exposure to certain viruses, by testing for the presence of certain current virus infections, and by inactivating and/or removing certain viruses.
Standard measures to prevent infections resulting from the use of medicinal products prepared from human blood or plasma include selection of donors, screening of individual donations and plasma pools for specific markers of infection and the inclusion of effective manufacturing steps for the inactivation/removal of viruses. The pathogen safety of *Panzyga*® is ensured through dedicated steps, in particular by the solvent/detergent treatment which inactivates enveloped viruses and by a nanofiltration (20 nm) for removal of both enveloped and non-enveloped viruses. In addition, an ion-exchange chromatography removes non-enveloped viruses. Furthermore, the nanofiltration and ion-exchange chromatography also remove potentially present infectious prion protein. However, as with all products prepared from human blood or plasma, the risk of transmission of infectious agents cannot be fully excluded.

Driving and Operating Machinery
Panzyga has no or negligible influence on the ability to drive and use machines. However, patients who experience adverse reactions during treatment should wait for these to resolve before driving or operating machines.

Hematologic
IVIG products can contain blood group antibodies which may act as hemolysins and induce in vivo coating of red blood cells (RBCs) with immunoglobulin, causing a positive direct

antiglobulin reaction and, rarely, hemolysis. Hemolytic anaemia can also develop subsequent to *Panzyga*® therapy due to enhanced RBC sequestration (see 9 ADVERSE REACTIONS). IVIG recipients should be monitored for clinical signs and symptoms of hemolysis (see 8 WARNINGS AND PRECAUTIONS: Monitoring and Laboratory Tests).

Hypersensitivity/Anaphylactic reaction
True hypersensitivity reactions are rare. They can occur in patients with anti-IgA antibodies. IVIG is not indicated in patients with selective IgA deficiency where the IgA deficiency is the only abnormality of concern.

Monitoring and Laboratory Tests
The patient's vital signs should be observed and monitored carefully throughout the infusion. If side effects occur, the infusion should be slowed or stopped until the symptoms subside. The infusion may then be resumed at a lower rate that is comfortable for the patient.
After injection of IVIG, the transitory rise in the various passively transferred antibodies may result in misleading positive results in serological tests, e.g. CMV serology.
Passive transmission of antibodies to erythrocyte antigens (e.g., A, B, and D) may cause a positive direct or indirect antiglobulin (Coombs') test.
If signs and/or symptoms of hemolysis are present after IVIG infusion, appropriate confirmatory laboratory testing should be done [see 8 WARNINGS AND PRECAUTIONS].
Because of the potentially increased risk of thrombosis, baseline assessment of blood viscosity should be considered in patients at risk for hyperviscosity, including those with cryoglobulins, fasting chylomicronemia/markedly high triacylglycerols (triglycerides), or monoclonal gammopathies [see 8 WARNINGS AND PRECAUTIONS].

Neurologic
Aseptic meningitis syndrome (AMS) has been reported to occur infrequently in association with IVIG treatment. AMS usually begins within several hours to two days following treatment. The signs include severe headache (migraine-like), neck stiffness, drowsiness, fever, inability to stand bright light, painful eye movements, and nausea and vomiting. The condition usually reverses without ill effects when treatment is stopped. AMS may occur more frequently in association with high dose (2 g/kg) IVIG treatment. Patients with a history of migraine appear to be more susceptible. Preventive measures to avoid the occurrence of aseptic meningitis include careful risk/benefit evaluation in patients with history of migraine, premedication with analgesics with or without caffeine, proper hydration and maintenance of good fluid intake throughout treatment, and slow infusion rates.

Renal
Cases of acute renal failure have been reported in patients receiving IVIG therapy especially with preparations containing sucrose: Panzyga does not contain sucrose.
Periodic monitoring of renal function and urine output is particularly important in patients judged to have a potential increased risk of developing acute renal failure. Renal function, including measurement of blood urea nitrogen (BUN) and serum creatinine, should be assessed before the initial infusion of PANZYGA® and at appropriate intervals thereafter. For patients judged to be at risk of developing renal dysfunction because of pre-existing renal insufficiency, or predisposition to acute renal failure (such as those with diabetes mellitus, sepsis, paraproteinemia, or hypovolemia, those who are obese, those who use concomitant nephrotoxic medicinal products, or those who are over 65 years of age), *Panzyga*® should be administered at the minimum rate of infusion practicable. If renal function deteriorates, consider discontinuing *Panzyga*®.

Respiratory
Transfusion-related acute lung injury (TRALI) has been rarely reported after treatment with IVIG products.

Transfusion related acute lung injury (TRALI)
Transfusion-related Acute Lung Injury (TRALI) is characterized by severe respiratory distress, pulmonary edema, hypoxemia, normal left ventricular function, and fever and typically occurs within 1 to 6 hours following transfusion. IVIG recipients should be monitored for pulmonary adverse reactions. Patients with TRALI may be managed using oxygen therapy with adequate ventilatory support. If TRALI is suspected, appropriate tests should be performed for the presence of antineutrophil antibodies in both product and the patient's serum.

Thromboembolic events
There is clinical evidence of an association between the administration of immunoglobulins and thromboembolic events such as myocardial infarction, stroke, pulmonary embolism and deep vein thromboses.
Although thrombosis may occur in the absence of known risk factors, certain conditions pose an increased risk. These include advanced age, history of vascular disease or thrombotic episodes, acquired or inherited hypercoagulable states, prolonged periods of immobilisation, severe dehydration, diseases which increase blood viscosity, use of estrogens, indwelling central vascular catheters, and cardiovascular risk factors (including obesity, hypertension, diabetes mellitus).
Baseline assessment of blood viscosity should be considered in patients at risk for hyperviscosity, including those with cryoglobulins, fasting chylomicronemia / markedly high triacylglycerols (triglycerides), hyperfibrinogenemia or monoclonal gammopathies. Patients at risk of hyperviscosity should be monitored for signs and symptoms of thrombosis and blood viscosity assessed (see 8 WARNINGS AND PRECAUTIONS: Monitoring and Laboratory Tests).

8.1 Special Populations

8.1.1 Pregnant Women

The safety of *Panzyga*® for use in human pregnancy and during lactation has not been established in controlled clinical trials and therefore should only be given with caution to pregnant woman and breast-feeding mothers.

8.1.2 Breast-feeding

Immunoglobulins are excreted into the milk and may contribute to the transfer of protective antibodies to the neonate.

8.1.3 Pediatrics

Pediatrics (2-17 years of age): The listed warnings and precautions apply both to adults and children.

8.1.4 Geriatrics

Geriatrics (> 65 years of age): *Panzyga*® should be used with caution in patients over 65 years of age who are judged to be at increased risk of developing renal failure. In most cases, additional risk factors have been identified, such as pre-existing renal insufficiency, diabetes mellitus, dehydration, overweight, or concomitant nephrotoxic medications.

9 ADVERSE REACTIONS

9.1 Adverse Reaction Overview

Replacement Therapy:

The most common adverse reactions observed at a rate of >5% in subjects in clinical trials were: headache, abdominal pain, fever, nausea, and fatigue.

Immune Thrombocytopenic Purpura in adults:

The most common adverse reactions observed at a rate of >5% in subjects in clinical trials were: headache, fever, nausea, vomiting, dizziness, and anemia.

Chronic Inflammatory Demyelinating Polyneuropathy:

The most common adverse reactions observed at a rate of >5% in subjects in clinical trials were: headache, pyrexia, dermatitis.

The most serious adverse reaction observed with *Panzyga*® treatment during clinical trials was aseptic meningitis in one subject during the ITP trial and headache and vomiting in one subject during the CIDP trial.

9.2 Clinical Trial Adverse Reactions

Because clinical trials are conducted under very specific conditions, the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.

Clinical trials in patients with primary immune deficiency (PID):
Clinical trials safety data for patients needing IgG replacement therapy derived from 2 prospective studies in patients with PID: Study 1 was conducted in 51 children and adults. Subjects received *Panzyga*® at a dose between 200 to 800 mg/kg body weight every 3 or 4 weeks. Subjects participated in the study for a mean of 360 days. Infusions were initiated at a rate of 1 mg/kg/minute for the first 30 minutes, and, if tolerated, could be advanced to a maximum tolerated rate not exceeding 8 mg/kg/minute. The mean age of subjects was 26.8 years (range: 2 to 65 years). This study was followed by an extension study (Study 2) that evaluated the safety of *Panzyga*® administered at higher infusion rates in 21 subjects that successfully had completed the first study. Nineteen of the 21 enrolled patients received *Panzyga*® up to the maximum allowed infusion rate of 14 mg/kg/minute.

Clinical trial in patients with chronic immune thrombocytopenic purpura (ITP):
Study 3 was conducted in 40 adult subjects with chronic **ITP**. Patients received *Panzyga*® at a dose of 2 g/kg, administered daily as 1 g/kg intravenous infusions on 2 consecutive days. All patients except 1 received at least 1 infusion with the highest rate of 8 mg/kg/minute. Pre-

medication to alleviate potential adverse drug reactions was not allowed in the study. One subject was withdrawn from the study due to an adverse event (worsening of ITP).

Clinical trial in patients with chronic inflammatory demyelinating polyneuropathy (CIDP):
In Study 4 (prospective, double-blind, randomized, multicenter Phase III study), overall 142 patients with CIDP aged between 18 and 83 years (median: 59 years) were enrolled. After a Wash-out Phase, during which the current medication (immunoglobulins or corticosteroids) was reduced stepwise until the patient deteriorated, patients were randomized 1:2:1 to receive first a loading dose of 2 g/kg and then either 0.5 g/kg, 1.0 g/kg or 2.0 g/kg *Panzyga*® for 7 maintenance infusions at 3-week intervals during the 24-week Dose-evaluation Phase. The majority of infusions were given divided in 2 equal parts given over 2 consecutive days.
All 142 patients in this study received at least 1 dose of study medication. Overall, a total of 982 infusions were given. Infusions were initiated at a rate of 1 mg/kg/minute for the first 30 minutes, and, if tolerated, could be advanced to a maximum tolerated rate of 12 mg/kg/minute. The median maximum infusion rate was 12 mg/kg/min throughout the study in all treatment groups. Premedication was only allowed for patients experiencing adverse events during 2 consecutive infusions. A total of 11 patients (7.75%) received premedication. In one patient the adverse reaction of dermatitis allergic led to discontinuation.

Frequency of adverse drug reactions in clinical studies with *Panzyga*®

MedDRA System Organ Class (SOC) according to the sequence:	**Adverse Reaction**	**Frequency per Infusion[1)]**
Blood and lymphatic system disorders	Leukopenia, anemia	Uncommon
Nervous system disorders	Headache --- Dizziness, somnolence, hypoesthesia	Common --- Uncommon
Cardiac disorders	Tachycardia	Uncommon
Vascular disorders	Hypertension	Uncommon
Respiratory, thoracic and mediastinal disorders	Cough	Uncommon
Gastrointestinal disorders	Nausea --- Vomiting, abdominal pain	Common --- Uncommon
Skin and subcutaneous tissue disorders	Dermatitis --- Rash, skin exfoliation, urticaria, pruritus, erythema	Common --- Uncommon
General disorders and administration site conditions	Pyrexia --- Chills, asthenia, influenza-like illness, chest pain, fatigue, chest discomfort	Common --- Uncommon

MedDRA System Organ Class (SOC) according to the sequence:	Adverse Reaction	Frequency per Infusion[1)]
Investigations	Blood lactate dehydrogenase increased, transaminases increased, alanine aminotransferase increased, aspartate aminotransferase increased	Uncommon

1) Frequencies have been evaluated according to the following convention: common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100).

Within each Organ Class, adverse reactions are presented in order of decreasing seriousness.

9.3 Less Common Clinical Trial Adverse Reactions

Nervous System Disorders: Meningitis aseptic (subclinical case)
General Disorders and Administration Site Conditions: Feeling cold, infusion site pruritus, pain, peripheral swelling
Gastrointestinal Disorders: Abdominal discomfort, diarrhoea
Vascular Disorders: Hypotension
Investigations: Hemoglobin decreased, hepatic enzyme increased
Blood and Lymphatic System Disorders: Haemolysis
Respiratory, thoracic and Mediastinal Disorders: Tachypnoea, dyspnoea
Muscoskeletal and Connective Tissue Disorders: Muscoskeletal pain, arthralgia, muscoskeletal stiffness, myalgia
Ear and Labyrinth Disorders: Ear pain
Eye Disorders: Eye pruritus

9.4 Abnormal Laboratory Findings: Hematologic, Clinical Chemistry and Other Quantitative Data

There were no significant abnormal laboratory findings.

9.6 Post-Market Adverse Reactions

Common Post Marketing Adverse Drug Reactions

The following adverse reactions have been identified during post-approval use of *Panzyga*® or other IVIG products. Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency or to establish a causal relationship to IVIG products:

ADRs reported during post-approval use of *Panzyga*®:

- *Blood and lymphatic system disorders:* neutropenia/decreased neutrophil count
- *Immune system disorders:* Anaphylactic reaction, hypersensitivity
- *Psychiatric disorders:* Anxiety
- *Nervous system disorders:* Paraesthesia, tremor

- *Musculoskeletal and connective tissue disorders:* Pain in extremity, neck pain, muscle spasm
- *General disorders and administration site conditions:* Feeling hot, malaise
- *Vascular disorders:* thromboembolic events
- *Injury, poisoning and procedural complications:* Transfusion related acute lung injury (TRALI)

ADRs reported during post-approval use of immunoglobulin products:

- *Blood and lymphatic system disorders:* Pancytopenia
- *Immune system disorders:* Anaphylactic shock, anaphylactoid reaction, angioedema, face edema, allergic reaction
- *Metabolic and nutritional disorders:* Fluid overload, (pseudo)hyponatremia
- *Psychiatric disorders:* Agitation, confusional state, nervousness
- *Nervous system disorders:* Coma, loss of consciousness, seizures, (acute) encephalopathy, cerebrovascular accident, stroke, migraine, speech disorder, photophobia
- *Cardiac disorders:* Myocardial infarction, cardiac arrest, angina pectoris, bradycardia, palpitations, cyanosis
- *Vascular disorders:* (Deep vein) thrombosis, peripheral circulatory failure/collapse, phlebitis, pallor
- *Respiratory, thoracic and mediastinal disorders:* Apnea, Acute Respiratory Distress Syndrome (ARDS), respiratory failure, pulmonary embolism, pulmonary edema, bronchospasm, hypoxia, wheezing
- *Hepatobiliary disorders:* Hepatic dysfunction
- *Skin and subcutaneous tissue disorders:* Stevens-Johnson syndrome, epidermolysis, eczema, alopecia
- *Musculoskeletal and connective tissue disorders:* Back pain
- *Renal and urinary disorders:* Acute renal failure, osmotic nephropathy, renal pain
- *General disorders and administration site conditions:* Hot flush, flushing, edema, hyperhidrosis, lethargy, burning sensation, injection site reaction
- *Investigations:* Oxygen saturation decreased, falsely elevated erythrocyte sedimentation rate, positive direct antiglobulin (Coombs') test

10 DRUG INTERACTIONS

10.3 Drug-Drug Interactions

Human IVIG should not be mixed with other medicinal products, including IVIG from other manufacturers. A separate intravenous line should be used for the infusion. Interactions with other drugs have not been established.

In order to infuse any product that may remain in the infusion tubing at the end of the infusion the tubing may be flushed with either 0.9% (9 mg/ml) saline or 5% (50 mg/ml) dextrose solution.

IgG administration may impair the efficacy of live attenuated virus vaccines such as measles, mumps, rubella and varicella for at least six weeks, and possibly up to three months. In some cases, where large doses are given this period may be as long as one year.

10.4 Drug-Food Interactions

Interactions with food have not been established.

10.5 Drug-Herb Interactions

Interactions with herbal products have not been established.

10.6 Drug-Laboratory Test Interactions

See subsection Monitoring and Laboratory Tests under section 8 WARNINGS AND PRECAUTIONS.

11 ACTION AND CLINICAL PHARMACOLOGY

11.1 Mechanism of Action

Treatment of Primary and Secondary Immunodeficiency

Panzyga® contains a broad spectrum of antibody specificities against bacterial, viral, parasitic, and mycoplasma agents that are capable of both opsonizing and neutralizing of pathogens and toxins.

Treatment of Immune Thrombocytopenic Purpura:

The mechanism of action of IVIGs in the treatment of ITP is not fully understood. One possible mechanism may be the inhibition of the elimination of autoantibody-reacted platelets from the blood circulation by IgG-induced Fc-receptor blockade of phagocytes. Another proposed mechanism is the down-regulation of platelet autoantibody-producing B cells by anti-idiotypic antibodies in IVIG.

Treatment of Guillain-Barré Syndrome and Chronic Inflammatory Demyelinating Polyneuropathy:

The mechanism of action of *Panzyga*® in the treatment of GBS has not been fully elucidated. Immunoglobulins have multiple actions, which often operate in concert with each other. The main mechanisms of action which are likely relevant to the efficacy of the *Panzyga*® in autoimmune neuromuscular disorders include effects on the metabolism of autoantibodies, inhibition of complement binding and prevention of membraneolytic attack complex formation, modulation or blockade of Fc receptors on macrophages, and suppression of pathogenic cytokines and other immunoregulatory molecules.

11.2 Pharmacodynamics

Panzyga® contains mainly immunoglobulin G (IgG) with a broad spectrum of antibodies against various infectious agents reflecting the IgG activity found in the donor population. *Panzyga*®, which is prepared from pooled material from not less than 3500 donors, has an IgG subclass distribution similar to that of native human plasma. Adequate doses of *Panzyga*® can restore abnormally low IgG level to the normal range

11.3 Pharmacokinetics

Treatment of Primary and Secondary Immunodeficiency

In the PID study, 50 pediatric and adult subjects underwent pharmacokinetic assessments. Subjects received infusions of *Panzyga*® (200 to 800 mg/kg body weight) every 3 (n=21) to 4 (n=29) weeks for 12 months. Pharmacokinetic samples were collected between the 7th and 9th *Panzyga*® infusion, depending on the individual treatment schedule.

Key Pharmacokinetic Parameters for *Panzyga*®

Parameter#	**3-Weeks Interval [n=21]**	**4-Weeks Interval [n=29]**
C_{max} [g/L]	21.8	17.4
T_{max} [h]	3.0	2.5
AUC_{tau} [g*hr/L]	7581	7578
$T_{1/2}$ [days]	36.6[1]	42.6[2]

#For T_{max}, median is given; for all other parameters, mean values are presented. [1]n=20; [2]n=27.

Treatment of Immune Thrombocytopenic Purpura

Pharmacokinetic studies with *Panzyga*® have not been performed in patients with ITP.

Chronic Inflammatory Demyelinating Polyneuropathy and Guillain Barré Disease

Pharmacokinetic studies with *Panzyga*® have not been performed in patients with CIDP or GBS.

Special Populations and Conditions

No specific pharmacokinetic studies have been performed in patients at increased risk, such as elderly subjects or patients with renal or hepatic impairment.

Pediatrics

The results of the pharmacokinetic studies in the different pediatric age groups are summarized in the following table, with a comparison to adults.

Pharmacokinetic Characteristics by Different Age Groups (median values)

	Pediatric Population		*Adults*
	Children	*Adolescents*	
	≥ 2 to <12 yrs	≥ 12 to <16 yrs	≥ 16 to ≤75 yrs
Parameter [Unit]	*N=13*	*N=12*	*N=26*
C_{max} [g/L]	18.6	19.3	17.1

C_{min} [g/L]	10.7	9.3	10.1
AUC_{tau} [g*hr/L]	6957	6826	7224
$T_{1/2}$ [days]	36	33	37

12 STORAGE, STABILITY AND DISPOSAL

Panzyga® can be stored at +2 °C to +8 °C for 36 months from the date of manufacture. Within this shelf-life the product may be stored up to 12 months at ≤ 25°C. After the storage at ≤ 25°C the product must be used or discarded. Do not use product after expiry date.

Do not freeze. Protect from exposure to light. Keep in a safe place out of the reach and sight of children.

13 SPECIAL HANDLING INSTRUCTIONS

Panzyga® should be inspected visually for particulate matter and discolouration prior to administration. Do not use non-homogenous solutions, or those that have a deposit. Any remaining fraction should be discarded. *Panzyga*® should be warmed up to room or body temperature before use.

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

PART II: SCIENTIFIC INFORMATION

14 PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: *Panzyga*®, Immunoglobulin Intravenous (Human)

Chemical name: Immunoglobulin G (Human)

Molecular formula and molecular mass: not applicable

Structural formula: not applicable

Physicochemical properties: The molecular weights range from 146 to 170 kD. Immunoglobulins have a common structure with four polypeptide chains. Two heavy chains and two non-glycosylated light chains. Human IgG is divided in four subclasses IgG1, IgG2, IgG3 and IgG4 due to minor differences in the amino sequence. The isoelectric point varies between 5.0 and 9.5

Product Characteristics

Panzyga® is a ready-to-use, sterile, 10% protein liquid preparation of polyvalent human immunoglobulin G (IgG) for intravenous administration employing precipitations, filtrations and chromatographic steps. *Panzyga*® is prepared from large pools of at least 3,500 donations of human plasma by cold ethanol fractionation. Pathogen inactivation/removal is accomplished by a solvent/detergent (S/D) method, a nanofiltration (20 nm), supplemented by ion-exchange chromatography.
After addition of glycine the 10% IgG solution is sterile filtered and filled into glass vials. The final product is salt free and no dilution with saline solution is needed prior to its administration. In the manufacturing process of Panzyga measures have been implemented to reduce the possible content of procoagulant factors. Furthermore a sensitive batch release test has been implemented (thrombin generation assay (TGA)), to detect increased thromboembolic potential.

Viral Inactivation

The pathogen safety of *Panzyga*® is ensured through dedicated steps, in particular by the solvent/detergent treatment which inactivates enveloped viruses such as HIV, hepatitis B (HBV) and hepatitis C (HCV) virus and by nanofiltration (20 nm) for removal of both enveloped viruses and non-enveloped viruses such as hepatitis A virus (HAV) and parvovirus B19. In addition, an ion-exchange chromatography removes non-enveloped viruses as validated for model viruses of hepatitis A and parvovirus. Furthermore, the nanofiltration and ion-exchange chromatography also remove potentially present infectious prion protein of an experimental agent of transmissible spongiform encephalopathy (TSE), considered a prudent model for Creutzfeldt-Jakob disease (CJD) and its variant form (vCJD).

15 CLINICAL TRIALS

Efficacy and Safety Studies

Treatment of Primary Humoral Immunodeficiency (PID)

In a prospective, open-label, single-arm, multicenter study in 51 children and adults with PID, subjects received *Panzyga*® at a dose between 200 to 800 mg/kg body weight every 3 or 4 weeks. Subjects participated in the study for a mean of 360 days. Infusions were initiated at a rate of 1 mg/kg/min for the first 30 minutes, and, if tolerated, could be advanced to a maximum tolerated rate not exceeding 4 mg/kg/min. The mean age of subjects was 26.8 years (range: 2 to 65 years).
The primary efficacy endpoint was the number of episodes of serious bacterial infections per patient per year. Serious infection included pneumonia, bacteremia or sepsis, osteomyelitis/septic arthritis, visceral abscesses, or bacterial meningitis. Secondary efficacy variables included: occurrence of any infection of any kind or seriousness; time to resolution of infections; use of antibiotics; the number of days of work/school missed; the number and days of hospitalizations; and the number of episodes of fever.
For the primary endpoint, the observed rate was 0.08 serious bacterial infections per patient per year (4 infections over 50.2 patient-years).
Only 1 adult patient was hospitalized due to an infection for a number of 4 days (overall rate of days in hospital per person-year: 0.080). Episodes of fever were observed for less than 25% of all patients. The mean resolution time was 14 days for serious bacterial infections and 18 days for other infections. Approximately 50% of all patients missed at least 1 day of work or school due to infections, with an annual rate of less than 4 days/person year.

PID Pivotal Study – Summary of Efficacy Results

Category	***Result***	***Unit***
Number of subjects	51	Subjects
Total number of subject days	18,349	Days
Annual rate of confirmed serious bacterial infections (SBIs)*	0.080	SBIs/person-year ♦
Annual rate of other infections	3.682	Inf./person-year
Number of subjects (%) with use of antibiotics	42 (82.4%)	Subjects (%)
Annual rate of use of antibiotics	87.301	Days/person-year
Absences from work or school due to Infection, number of days (%)	183 (1.0%)	Days (%)
Annual rate of absences from work or school due to infection	3.643	Days/person-year
Hospitalization due to infection, number of days	4	Days
Annual rate of hospitalizations due to infection	0.080	Days/person-year

* Defined as bacteremia/sepsis, bacterial meningitis, osteomyelitis/septic arthritis, bacterial pneumonia and visceral abscess
♦ Upper 1-sided 99% confidence interval: 0.503

Throughout the entire study, the serum IgG trough levels were nearly constant for both treatment schedules and were above the required trough levels of about 5-6 g/L. The calculated pharmacokinetic parameters showed that the minimum concentration of IgG was at least 6.8 g/L for both treatment intervals.

This study was followed by an extension study which was carried out in order to assess the tolerability of *Panzyga*® when administered at higher infusion rates (from 0.08 mL/kg/min up to 0.14 mL/kg/min). In total, 21 patients were enrolled. No patient was pre-medicated prior to any infusion. The product was well tolerated and all patients completed the study as planned. Study medication related AEs were reported in 2 children and 2 adults; the most commonly reported reactions were nausea and headache.

Replacement therapy in the pediatric population: *Panzyga*® was evaluated in 26 pediatric subjects (age range 2-17 years). Pharmacokinetics, efficacy and safety were similar to those in adults. No specific dose requirements were necessary to achieve the targeted serum IgG levels in the pediatric subjects.

Treatment of Chronic Immune Thrombocytopenic Purpura (ITP) in Adults

A prospective, open-label, single-arm, multicenter study assessed the efficacy, safety, and tolerability of *Panzyga*® in 40 subjects with chronic ITP and a platelet count of 20 x 10^9/L or less. Subjects ranged in age from 18 to 72 (median: 32 years); 43% were female and 57% were male.

Subjects received a 2 g/kg dose of *Panzyga*® administered as two daily 1 g/kg intravenous doses, given on 2 consecutive days. All but one patient received the maximum infusion rate of 8 mg/kg/minute, starting at 1 mg/kg/minute. Platelet counts were measured on Days 1 to 8, 15, and 22.

The primary measure of efficacy was an increase in platelet count to at least 50 x 10^9/L within 7 days after the first infusion (responders).

Secondary efficacy measurements included maximum platelet count, the time to reach a platelet count of at least 50 x 10^9/L within the first 7 days, the duration of that response (i.e. the number of days the platelet count remained in excess of 50 x 10^9/L), and the regression of hemorrhages in subjects who had bleeding at baseline were observed.

Of the 36 subjects in the full analysis set, 29 responded to *Panzyga*® with a rise in platelet counts to at least 50 x 10^9/L within 7 days after the first infusion.

The mean maximum platelet count achieved in the 36 subjects was 237 x 10^9/L.

Maximum Platelet Count (x10^9/L)

	ITP subjects (n=36)
Median and range	196.3 (8 to 1067)
Mean ± standard deviation	236.9 ± 205.2

The median time to reach a platelet response of at least 50 x 10^9/L was 2 days (range: 1 to 4 days) after the first infusion. The duration of platelet response was analyzed for the 29 subjects who achieved a response within 7 days after the first infusion, the median duration of platelet response in these subjects was 14 days (range: 1 to 20 days).

Time to and Duration of Platelet Response (Responders Only)

	Time to Platelet Response (Days)	Duration of Platelet Response (Days)
	ITP Subjects All (n=36)	ITP Subjects Responders (n=29)
Median and range	2 (1 to 4)	14 (1 to 20)
Mean ± standard deviation	1.8 ± 0.8	12.4 ± 5.8

In 18 of the 23 subjects (78%) who had bleeding at baseline, the hemorrhages had completely resolved by Day 7.

Assessment of Bleeding at Day 7 in Subjects with Baseline Bleeding

Number of Subjects with Baseline Bleeding	Severity at Day 7			
	None	Minor	Mild	Missing
ITP (n=23)	18 (78%)	2 (9%)	1 (4%)	2 (9%)

The response rate according to the primary measure of efficacy was 81% (95% CI: 64%–92%). According to an alternative definition of response that required the increase in platelet count to be confirmed on at least 2 separate occasions at least 7 days apart and absence of bleeding, the response rate was 50% (95% CI: 32%-68%).

Treatment of Guillain-Barré Syndrome (GBS) in Adults

Support for the use of *Panzyga*® in the treatment of moderate to severe cases of GBS in adults when used in the first two weeks of disease onset, comes from a systematic review of clinical trials providing moderate quality of evidence[1].

Treatment of Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) in Adults

In this prospective, double-blind, randomized, multicenter Phase III study, overall 142 patients with CIDP aged between 18 and 83 years (median: 59 years) were enrolled. Of these 59% were male and 41% were female.
After a Wash-out Phase, during which the current medication (immunoglobulins or corticosteroids) was reduced stepwise until the patient deteriorated, patients were randomized 1:2:1 to receive first a loading dose of 2 g/kg and then either 0.5 g/kg, 1.0 g/kg or 2.0 g/kg *Panzyga*® for 7 maintenance infusions at 3-week intervals during the 24-week Dose-evaluation Phase. 123 patients completed the study.
The primary efficacy parameter of the study was the proportion of responders in the 1.0 g/kg *Panzyga*® arm at Week 24 relative to Baseline (Week 0). A responder was defined as a patient in the 1.0 g/kg group with a decrease of at least 1 point in the adjusted INCAT disability score relative to Baseline. Results are presented in the Table below.

Responder rates for Adjusted INCAT Disability Score

	0.5 g/kg N=34	1.0 g/kg N=69	2.0 g/kg N=36	Total All Patients N=139
Adjusted INCAT Disability Score				
Number (%) of responders	22 (64.71%)	55 (79.71%)	33 (91.67%)	110 (79.14%)
95% CI	47.9; 78.5	68.8; 87.5	78.2; 97.1	71.6; 85.1

Secondary efficacy endpoints included: Proportion of responders in the 0.5 g/kg and 2.0 g/kg *Panzyga*® arms at Week 24 relative to Baseline compared to the 1.0 g/kg arm, based on: the adjusted INCAT disability score; the grip strength (Martin Vigorimeter) using the previously published minimum clinically important difference (MCID) cut-off of 8 kPa; and, the Inflammatory Rasch-built Overall Disability Scale (I-RODS) scores using the MCID concept related to the varying standard errors (MCID-SE).

The results from the analyses of the secondary efficacy endpoints consistently supported the primary analysis.

17 NON-CLINICAL TOXICOLOGY

Animal Toxicity Studies

Acute toxicity was tested in mice and rats. Local tolerance was investigated in rabbits.

The further preclinical evaluation of *Panzyga*® focused on the evaluation of its safety with respect to impurities that are derived from the manufacturing process. The level of impurities is controlled by the manufacturing process specifications on raw materials, by in-process controls, and by the final product specification. A program of studies has been carried out to assess the toxicological effects of TNBP and Octoxynol (Triton X-100). Based on the results of these studies and on previous experience with Octapharma IgG products, the levels of TNBP and Octoxynol (Triton X-100) present in the final formulation are not of clinical concern.

Single Dose Toxicity

Two GLP-compliant single dose toxicity studies were performed with *Panzyga*® in high doses of 2 000 mg IgG/kg b.w. in rats and up to 10 000 mg IgG/kg b.w. in mice. In both studies no mortality, no test item-related clinical signs and no macroscopic findings were observed.

Repeated Dose Toxicity

Repeated dose toxicity testing in animals with human immunoglobulin preparations is impracticable due to the induction of, and the interference with antibodies. Therefore no studies were conducted with *Panzyga*®.

Reproductive Toxicity

Due to the induction of and the interference with antibodies no studies were conducted with *Panzyga*®. To date, IgG has not been reported to be associated with embryo-foetal developmental and reproductive toxicity, respectively.

Local Tolerance

The local tolerance of *Panzyga*® was tested in two studies after intravenous, intra-arterial and paravenous administration to rabbits. The animals were observed for 72 and/or 96 hours and then sacrificed for histological evaluation of the injection sites.
Panzyga® was well tolerated, no general or relevant local changes, and no histological noticeable findings were observed.

Mutagenicity and Carcinogenicity

Clinical experience with IgG products does not provide any evidence of mutagenic or tumorigenic effects of IgG. Therefore no studies on mutagenicity/genotoxicity were conducted. No studies were conducted regarding carcinogenicity since the metabolization of *Panzyga*® does not lead to any degradation of the product that could cause carcinogenicity.

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PATIENT MEDICATION INFORMATION

PANZYGA®
Immunoglobulin Intravenous (Human)

Read this carefully before you start taking *Panzyga*® and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about *Panzyga*®.

Serious Warnings and Precautions

- Thromboembolic events such as heart attack, stroke, and obstructions of a deep vein e.g. in the calves or of a blood vessel in the lung (pulmonary embolism) may occur with administration of human immunoglobulin intravenous (IVIG) products.
- Thromboembolic events occur more commonly in patients with pre-existing risk factors for thromboembolism receiving IVIG products.
- In general the risk factors for thromboembolic events include: obesity; advance age; hypertension; diabetes mellitus; previous events of heart attack, stroke, and obstructions of a deep vein etc.; prolonged periods of immobilisation; intake of certain hormones (e.g. the pill).
- Thrombosis may occur even in the absence of known risk factors.

What is *Panzyga*® used for?

1) *Panzyga*® is used to treat adults and children:
- Who are either born with (PID) or develop (SID) not enough protective proteins (Immunoglobulins) in their blood to defend against infections.

2) *Panzyga*® is used to treat adults:
- Who do not have enough blood platelets and who are at high risk of bleeding (immune thrombocytopenic purpura, ITP).
- Who suffer from moderate to severe Guillain-Barré Syndrome (GBS).
- Who suffer from chronic inflammatory demyelinating polyneuropathy (CIDP) which is a chronic disease and is characterized by inflammation of peripheral nerves which may lead to muscle weakness/numbness mainly in the limbs.

How does *Panzyga*® work?
Panzyga® is used as antibody replacement therapy, in people who have low levels of these infection-fighting proteins. By replacing these important antibodies, *Panzyga*® helps make people better able to avoid infections and fight them when they do occur.
How *Panzyga*® works in immune thrombocytopenic purpura is unknown, but it is believed to block platelet removal from the bloodstream. The mechanism of action in GBS and CIDP is not fully understood, but includes modulatory effects of the immune system which consequently helps improve function of muscles and nerves.

What are the ingredients in *Panzyga*®?
Medicinal ingredients: Immunoglobulin Intravenous (Human)
Non-medicinal ingredients: Glycine, Water for Injections

***Panzyga*® comes in the following dosage forms:**
Panzyga® is a 100 mg/mL solution for intravenous infusion and comes in the following dosage forms:

Fill Size	**Grams IgG**
10 mL	1 g
25 mL	2.5 g
50 mL	5 g
100 mL	10 g
200 mL	20 g
300 mL	30 g

Do not use *Panzyga*® if:
- You have a history of severe allergic reactions to immunoglobulin/antibody treatment.
- You have a condition known as selective IgA deficiency.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take *Panzyga*®. Talk about any health conditions or problems you may have, including if you:
- Have a history of allergic or other reactions to immunoglobulins or to any of the ingredients.
- Have a history of heart disease, problems with your circulation or have had blood clots.
- Have a history of migraine.
- Have a history of kidney disease or diabetes.
- Are pregnant or think that you are pregnant or if you are nursing.
- Have recently been vaccinated.

Other warnings you should know about:

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with *Panzyga*®:
- *Panzyga*® may reduce the effect of certain virus vaccines, such as measles, mumps and rubella. Inform the immunizing physician of recent treatments with *Panzyga*® so appropriate precautions can be taken.
- *Panzyga*® should not be mixed with other products.
- In order to infuse any product that may remain in the infusion tubing at the end of the infusion the tubing may be flushed with either 0.9% (9 mg/ml) saline or 5% (50 mg/ml) dextrose solution.

How to take *Panzyga*®:
Panzyga® is injected into a vein. It should not be used if it looks cloudy or is leaking. It should be warmed up to room or body temperature before use. Discard any remaining contents after use. Do not use the product after its expiry date (printed on the bottle).
Usual dose:
Your doctor will determine the dose(s) of *Panzyga*®.

- The usual dose of *Panzyga*® for patients with Primary or Secondary Immune Deficiency is 200 to 800 mg/kg body weight, every 3 to 4 weeks. Doses may be adjusted over time to achieve the desired clinical response and serum IgG levels.
- The usual dose for patients with Immune Thrombocytopenic Purpura is 1g/kg body weight for 2 consecutive days.
- The usual starting dose of *Panzyga*® for patients with Guillain-Barré Syndrome is 2 g/kg body weight given in divided doses over 2 to 5 consecutive days.
- The usual starting dose of *Panzyga*® for patients with Chronic Inflammatory Demyelinating Polyneuropathy is 2 g/kg bodyweight, best given divided in 2 equal doses on 2 consecutive days. For maintenance treatment the usual dose is 1-2 g/kg body weight given every 3 weeks.

In case of measles exposure your dose might need to be adjusted. Please consult your doctor or healthcare professional, if you have been exposed to measles.

Overdose:

If you think you have taken too much *Panzyga*®, contact your healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

Overdose may lead to fluid overload, particularly in the elderly and in patients with kidney problems.

Missed Dose:
A missed dose should be given as soon as possible.

What are possible side effects from using *Panzyga*®?

These are not all the possible side effects you may feel when taking *Panzyga*®. If you experience any side effects not listed here, contact your healthcare professional.

The following symptoms are common:

- Headache
- Nausea
- Fever
- Skin inflammation (dermatitis)

The following symptoms are uncommonly or rarely observed:

- Dizziness
- Chills
- Drowsiness
- Reduced sense of touch
- Shivering
- Anxiety
- Eye itching
- Ear pain
- Fast heart rate
- Increase in blood pressure

- Cough
- Vomiting
- Belly pain or discomfort
- Diarrhoea
- Rash
- Hives
- Itching
- Redness of the skin
- Flu-like symptoms
- Joint or muscle pain
- Pain in a limb or the neck
- Chest pain
- Feeling cold
- Physical weakness
- Fatigue
- Changes in liver function parameters (lab test)
- Drop in white or red blood cells (lab test)
- Abnormally low levels of specific white blood cells called neutrophils (decreased neutrophils counts)

If any of the above listed symptoms occur, are severe or if they worry you, talk to your doctor or pharmacist.

In rare cases, treatment with IVIG can also result in the following rare but serious symptoms. Tell your doctor right away if you have any of the following symptoms.

- Severe headache with nausea, vomiting, neck stiffness, fever, and sensitivity to light. These could be signs of a temporary and reversible, non-infectious swelling of the membranes surrounding the brain and spinal cord (aseptic meningitis).
- Pain, swelling, warmth, redness, or a lump in your legs or arms, unexplained shortness of breath, chest pain or discomfort that worsens on deep breathing, unexplained rapid pulse, numbness or weakness on one side of the body, sudden confusion, or trouble speaking. These could be signs of a blood clot.
- Hives, swelling of the lips, tongue or throat, difficulty breathing, faintness, nausea, vomiting. These could be signs of an allergic reaction. Allergic reactions are rare, but can induce an anaphylactic shock, even in patients who had tolerated the previous treatments.
- Fatigue, weakness, dizziness, headache, dark urine, jaundice and/or paleness. These may be symptoms of hemolytic anemia, a condition where you have not enough red blood cells.
- Severe difficulty in breathing, chest pain, chest discomfort, painful respiration typically appearing within 1 to 6 hours after receiving treatment. These could be signs of a reaction called Transfusion-related Acute Lung Injury (TRALI).
- Lower back pain, fatigue, decrease in the amount of urine, in patients with kidney problems these could be signs of acute renal failure.

Panzyga® has been manufactured with specific steps to reduce the risk of complications due to formation of blood clots. However, patients with known risk factors should be well hydrated by taking adequate fluids and *Panzyga*® may be injected at a slower speed.

This is not a complete list of side effects. For any unexpected effects while taking *Panzyga*®, contact your doctor or pharmacist.
If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:
Store refrigerated (+2 °C to +8 °C) for up to 36 months. Within this shelf-life the product may be stored up to 12 months at ≤ 25°C. After the storage at ≤ 25°C the product must be used or discarded.
Warm up to room or body temperature before use. Do not freeze. Protect from light. Discard any remaining contents after use. Do not use after expiry date.

Keep out of reach and sight of children.

If you want more information about *Panzyga*®:
- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website; the manufacturer's website http://www.octapharma.ca, or by calling 1-888-438-0488.

This leaflet was prepared by Octapharma Pharmazeutika Produktionsges.m.b.H

Last Revised: May 19, 2021