ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Deqsiga 100 mg/mL solution for infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Human normal immunoglobulin (IVIg)

One mL contains:

Human normal immunoglobulin ……100 mg
(purity of at least 98 % IgG)

Each vial of 50 mL contains: 5 g of human normal immunoglobulin.
Each vial of 100 mL contains: 10 g of human normal immunoglobulin.

Distribution of IgG subclasses (approx. values):

IgG1 ≥ 56.9 %
IgG2 ≥ 26.6 %
IgG3 ≥ 3.4 %
IgG4 ≥ 0.3 %

The maximum IgA content is 2 micrograms/mL.

Produced from the plasma of human donors.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for infusion
The solution is clear or slightly opalescent and colourless or pale yellow. The solution has a pH of 4.6 – 5.1 and an osmolality of 240 – 300 mOsmol/kg.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Replacement therapy in adults, children and adolescents (0 to 18 years) in:

- Primary immunodeficiency syndromes (PID) with impaired antibody production.
- Secondary immunodeficiencies (SID) in patients who suffer from severe or recurrent infections, ineffective antimicrobial treatment and either **proven specific antibody failure (PSAF)*** or serum IgG level of < 4 g/L.

*PSAF = failure to mount at least a 2-fold rise in IgG antibody titre to pneumococcal polysaccharide and polypeptide antigen vaccines

Immunomodulation in adults, children and adolescents (0 to 18 years) in:

- Primary immune thrombocytopenia (ITP), in patients at high risk of bleeding or prior to surgery to correct the platelet count.
- Guillain Barré syndrome.
- Kawasaki disease (in conjunction with acetylsalicylic acid; see section 4.2).
- Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP).
- Multifocal Motor Neuropathy (MMN).

4.2 Posology and method of administration

IVIg therapy should be initiated and monitored under the supervision of a physician experienced in the treatment of immune system disorders.

Posology

The dose and dose regimen are dependent on the indication.

The dose may need to be individualised for each patient dependent on the clinical response. Dose based on bodyweight may require adjustment in underweight or overweight patients.

The following dose regimens are given as guidance.

Replacement therapy in primary immunodeficiency syndromes

The dose regimen should achieve a trough level of IgG (measured before the next infusion) of at least 6 g/L or within the normal reference range for the population age. 3 – 6 months are required after the initiation of therapy for equilibration (steady-state IgG levels) to occur. The recommended starting dose is 0.4 – 0.8 g/kg given once, followed by at least 0.2 g/kg given every 3 – 4 weeks.

The dose required to achieve a trough level of IgG of 6 g/L is of the order of 0.2 – 0.8 g/kg/month. The dosage interval when steady state has been reached varies from 3 – 4 weeks. IgG trough levels should be measured and assessed in conjunction with the incidence of infection. To reduce the rate of bacterial infections, it may be necessary to increase the dosage and aim for higher trough levels.

Replacement therapy in secondary immunodeficiencies (as defined in section 4.1.)

The recommended dose is 0.2 – 0.4 g/kg every 3 – 4 weeks.

IgG trough levels should be measured and assessed in conjunction with the incidence of infection. Dose should be adjusted as necessary to achieve optimal protection against infections, an increase may be necessary in patients with persisting infection; a dose decrease can be considered when the patient remains infection free.

Immunomodulation in:

Primary immune thrombocytopenia

There are two alternative treatment schedules:
- 0.8 – 1 g/kg given on day one; this dose may be repeated once within 3 days.
- 0.4 g/kg given daily for 2 – 5 days. The treatment can be repeated if relapse occurs.

Guillain Barré syndrome

0.4 g/kg/day over 5 days (possible repeat of dosing in case of relapse).

Kawasaki Disease

2 g/kg should be administered as a single dose. Patients should receive concomitant treatment with acetylsalicylic acid.

Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)

Starting dose: 2 g/kg divided over 2 – 5 consecutive days.

Maintenance doses: 1 g/kg over 1 – 2 consecutive days every 3 weeks.

The treatment effect should be evaluated after each cycle; if no treatment effect is seen after 6 months, the treatment should be discontinued.

If the treatment is effective, long-term treatment should be subject to the physician's discretion based upon the patient response and maintenance response. The dosing and intervals may have to be adapted according to the individual course of the disease.

Multifocal Motor Neuropathy (MMN)

Starting dose: 2 g/kg divided over 2 – 5 consecutive days.

Maintenance dose: 1 g/kg every 2 to 4 weeks or 2 g/kg every 4 to 8 weeks over 2 – 5 days.

The treatment effect should be evaluated after each cycle; if no treatment effect is seen after 6 months, the treatment should be discontinued.

If the treatment is effective, long-term treatment should be subject to the physician's discretion based upon the patient response and maintenance response. The dosing and intervals may have to be adapted according to the individual course of the disease. The dosage recommendations are summarised in the following table:

Table 1: The indications and dosage recommendations

Replacement therapy

Indication	Dose	Frequency of infusions
Primary immunodeficiency syndromes	starting dose: 0.4 – 0.8 g/kg maintenance dose: 0.2 – 0.8 g/kg	 every 3 – 4 weeks
Secondary immunodeficiencies (as defined in section 4.1.)	0.2 – 0.4 g/kg	every 3 – 4 weeks

Immunomodulation

Indication	Dose	Frequency of infusions
Primary immune thrombocytopenia	0.8 – 1 g/kg or 0.4 g/kg/d	on day 1, possibly repeated once within 3 days. for 2 – 5 days
Guillain Barré syndrome	0.4 g/kg/d	for 5 days

Indication	Dose	Frequency of infusions
Kawasaki disease	2 g/kg	in one dose in association with acetylsalicylic acid
Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)	starting dose: 2 g/kg maintenance dose: 1 g/kg	In divided doses over 2 – 5 consecutive days every 3 weeks in divided doses over 1 – 2 days
Multifocal Motor Neuropathy (MMN)	starting dose: 2 g/kg maintenance dose: 1 g/kg or 2 g/kg	In divided doses over 2 – 5 consecutive days. every 2 – 4 weeks or every 4 – 8 weeks in divided doses over 2 – 5 days

Paediatric population

The posology in children and adolescents (0 – 18 years) is not different to that of adults as the posology for each indication is given by body weight and must be adjusted to the clinical outcome of the above-mentioned conditions.

Hepatic impairment

No evidence is available to require a dose adjustment.

Renal impairment

No dose adjustment unless clinically warranted, see section 4.4.

Elderly

No dose adjustment in patients ≥65 years of age unless clinically warranted, see section 4.4.

Method of administration

For intravenous use.

Human normal immunoglobulin should be infused intravenously at an initial rate of 0.5 mL/kg BW/hr for 30 minutes. In case of adverse reaction, either the rate of administration must be reduced or the infusion stopped. If well tolerated, the rate of administration may gradually be increased to a maximum of 6 mL/kg BW/hr. Clinical data obtained from a limited number of patients also indicate that adult PID patients may tolerate an infusion rate of up to 8 mL/kg BW/hr. For further precautions for use see section 4.4.

If dilution prior to infusion is required, Deqsiga may be diluted with 5 % glucose solution to a final concentration of 50 mg/mL (5 % immunoglobulin). For instructions on dilution of the medicinal product before administration, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substance (human immunoglobulins) or to any of the excipients (see sections 4.4 and 6.1).

Patients with selective IgA deficiency who developed antibodies to IgA, as administering an IgA-containing product can result in anaphylaxis (see section 4.4).

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Precautions for use

Potential complications can often be avoided by ensuring that patients:

- are not sensitive to human normal immunoglobulin by initially administering the product slowly (0.5 mL/kg BW/hr).
- are carefully monitored for any symptoms throughout the infusion period. In particular, patients naive to human normal immunoglobulin, patients switched from an alternative IVIg product or when there has been a long interval since the previous infusion should be monitored during the first infusion and for the first hour after the first infusion in a controlled healthcare setting in order to detect potential adverse signs and to ensure that emergency treatment can be administered immediately should problems occur. All other patients should be observed for at least 20 minutes after administration.

In all patients, IVIg administration requires:

- adequate hydration prior to the initiation of the IVIg infusion
- monitoring of urine output
- monitoring of serum creatinine levels
- avoidance of concomitant use of loop diuretics (see section 4.5).

In case of adverse reaction, either the infusion rate must be reduced or the infusion stopped. The treatment required depends on the nature and severity of the adverse reaction.

If dilution of Deqsiga to lower concentrations is required for patients suffering from diabetes mellitus, the use of 5 % glucose solution for dilution may have to be reconsidered.

Infusion-related reaction

Certain adverse reactions (e.g., headache, flushing, chills, myalgia, wheezing, tachycardia, lower back pain, nausea, and hypotension) may be related to the rate of infusion. The recommended infusion rate given under section 4.2 must be closely followed. Patients must be closely monitored and carefully observed for any symptoms throughout the infusion period.

Adverse reactions may occur more frequently.

- in patients who receive human normal immunoglobulin for the first time or, in rare cases, when the human normal immunoglobulin product is switched or when there has been a long interval since the previous infusion.
- in patients with an active infection or underlying chronic inflammation.

Hypersensitivity

Hypersensitivity reactions are rare.

Deqsiga has a very low IgA content (not more than 2 micrograms/mL). Preparations depleted of IgA were shown to be better tolerated by some patients who reacted to IVIg preparations with higher IgA concentrations. However, the threshold IgA concentration to which the patients would be sensitive, is not clear.

Anaphylaxis can develop in any IVIg treated patients, including those
- with undetectable IgA who have anti-IgA antibodies
- who had tolerated previous treatment with human normal immunoglobulin

In case of shock, standard medical treatment for shock should be implemented.

Thromboembolism

There is clinical evidence of an association between IVIg administration and thromboembolic events such as myocardial infarction, cerebral vascular accident (including stroke), pulmonary embolism and deep vein thromboses which is assumed to be related to a relative increase in blood viscosity through the high influx of immunoglobulin in at-risk patients. Caution should be exercised in prescribing and infusing IVIg in obese patients and in patients with pre-existing risk factors for thrombotic events (such as advanced age, hypertension, diabetes mellitus and a history of vascular disease or thrombotic episodes, patients with acquired or inherited thrombophilic disorders, patients with prolonged periods of immobilisation, severely hypovolaemic patients, patients with diseases which increase blood viscosity).

In patients at risk for thromboembolic adverse reactions, IVIg products should be administered at the minimum rate of infusion and dose practicable.

Acute renal failure

Cases of acute renal failure have been reported in patients receiving IVIg therapy. In most cases, risk factors have been identified, such as pre-existing renal insufficiency, diabetes mellitus, hypovolaemia, overweight, concomitant nephrotoxic medicinal products or age over 65.

Renal parameters should be assessed prior to infusion of IVIg, particularly in patients judged to have a potential increased risk for developing acute renal failure, and again at appropriate intervals. In patients at risk for acute renal failure, IVIg products should be administered at the minimum rate of infusion and dose practicable. In case of renal impairment, IVIg discontinuation should be considered.

While reports of renal dysfunction and acute renal failure have been associated with the use of many of the licensed IVIg products containing various excipients such as sucrose, glucose and maltose, those containing sucrose as a stabiliser accounted for a disproportionate share of the total number. In patients at risk, the use of IVIg products that do not contain these excipients may be considered. Deqsiga does not contain sucrose, maltose or glucose.

Aseptic meningitis syndrome (AMS)

AMS has been reported to occur in association with IVIg treatment. The syndrome usually begins within several hours to 2 days following IVIg treatment. Cerebrospinal fluid (CSF) studies are frequently positive with pleocytosis up to several thousand cells per mm^3, predominantly from the granulocytic series, and elevated protein levels up to several hundred mg/dL. AMS may occur more frequently in association with high-dose (2 g/kg) IVIg treatment.

Patients exhibiting such signs and symptoms should receive a thorough neurological examination, including CSF studies, to rule out other causes of meningitis.

Discontinuation of IVIg treatment has resulted in remission of AMS within several days without sequelae.

Haemolytic anaemia

IVIg products can contain blood group antibodies which may act as haemolysins and induce *in vivo* coating of red blood cells (RBC) with immunoglobulin, causing a positive direct antiglobulin reaction (Coombs' test) and, rarely, haemolysis. Haemolytic anaemia can develop subsequent to IVIg therapy due to enhanced RBC sequestration. IVIg recipients should be monitored for clinical signs and symptoms of haemolysis (see section 4.8).

Neutropenia/Leukopenia

A transient decrease in neutrophil count and/or episodes of neutropenia, sometimes severe, have been reported after treatment with IVIg. This typically occurs within hours or days after IVIg administration and resolves spontaneously within 7 to 14 days.

Transfusion-related acute lung injury (TRALI)

In patients receiving IVIg, there have been reports of acute non-cardiogenic pulmonary oedema [Transfusion-related acute lung injury (TRALI)]. TRALI is characterised by severe hypoxia, dyspnoea, tachypnoea, cyanosis, fever and hypotension. Symptoms of TRALI typically develop during or within 6 hours of a transfusion, often within 1 – 2 hours. Therefore, IVIg recipients must be monitored for and IVIg infusion must be immediately stopped in case of pulmonary adverse reactions. TRALI is a potentially life-threatening condition requiring immediate intensive-care-unit management.

Interference with serological testing

After the administration of immunoglobulin the transitory rise of the various passively transferred antibodies in the patient's blood may result in misleading positive results in serological testing.

Passive transmission of antibodies to erythrocyte antigens, e.g. A, B, D, may interfere with some serological tests for red cell antibodies, for example the direct antiglobulin test (DAT), direct Coombs' test.

Administration of Deqsiga can lead to false positive readings in assays that depend on detection of beta-D-glucans for diagnosis of fungal infections. This may persist during the weeks following infusion of the product.

Transmissible agents

Deqsiga is made from human plasma. 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. Despite this, when medicinal products prepared from human blood or plasma are administered, the possibility of transmitting infectious agents cannot be totally excluded. This also applies to unknown or emerging viruses and other pathogens.

The measures taken are considered effective for enveloped viruses such as human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV), and for the non-enveloped hepatitis A and parvovirus B19 viruses.

There is reassuring clinical experience regarding the lack of hepatitis A or parvovirus B19 transmission with immunoglobulins and it is also assumed that the antibody content makes an important contribution to the viral safety.

It is strongly recommended that every time that Deqsiga is administered to a patient, the name and batch number of the product are recorded in order to maintain a link between the patient and the batch of the product.

Paediatric population

There are no paediatric specific risks about any of the above adverse events. Paediatric patients may be more susceptible to volume overload (see section 4.9).

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.
Dilution of Deqsiga with a 5 % glucose solution may result in increased blood glucose levels.

Live attenuated virus vaccines

Immunoglobulin administration may impair for a period of at least 6 weeks and up to 3 months the efficacy of live attenuated virus vaccines such as measles, rubella, mumps, and varicella. After administration of this medicinal product, an interval of 3 months should elapse before vaccination with live attenuated virus vaccines. In the case of measles, this impairment may persist for up to 1 year. Therefore, patients receiving measles vaccine should have their antibody status checked.

Loop diuretics

Avoidance of concomitant use of loop diuretics.

Paediatric population

The listed interactions apply both to adults and children.

4.6 Fertility, pregnancy and lactation

Pregnancy

The safety of this medicinal product for use in human pregnancy has not been established in controlled clinical trials and therefore should only be given with caution to pregnant women. IVIg products have been shown to cross the placenta, increasingly during the third trimester.

Clinical experience with immunoglobulins suggests that no harmful effects on the course of pregnancy, or on the foetus and the neonate are expected.

Breast-feeding

Immunoglobulins are excreted into the milk. No negative effects on the breastfed newborn/infants are anticipated.

Fertility

Clinical experience with immunoglobulins suggests that no harmful effects on fertility are to be expected.

4.7 Effects on ability to drive and use machines

Deqsiga has minor influence on the ability to drive, cycle and use machines, e.g. dizziness or nausea (see section 4.8). Patients who experience adverse reactions during treatment should wait for these to resolve before driving or operating machines.

4.8 Undesirable effects

Summary of the safety profile

Adverse reactions caused by human normal immunoglobulins (in decreasing frequency) encompass (see also section 4.4):

- chills, headache, dizziness, fever, vomiting, allergic reactions, nausea, arthralgia, low blood pressure and moderate low back pain,
- reversible haemolytic reactions; especially in those patients with blood groups A, B and AB and (rarely), haemolytic anaemia requiring transfusion,
- (rarely) a sudden fall in blood pressure and, in isolated cases, anaphylactic shock, even when the patient has shown no hypersensitivity to previous administration,
- (rarely) transient cutaneous reactions (including cutaneous lupus erythematosus – frequency unknown),
- (very rarely) thromboembolic reactions such as myocardial infarction, stroke, pulmonary embolism, deep vein thromboses,
- cases of reversible aseptic meningitis,
- cases of increased serum creatinine level and/or occurrence of acute renal failure,
- cases of Transfusion-related acute lung injury (TRALI).

Tabulated list of adverse reactions

The table presented below is according to the MedDRA system organ classification (SOC and Preferred Term Level).

Frequencies have been evaluated according to the following convention: 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 available data).

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 2: Adverse Reactions reported in clinical studies and post-marketing reports

MedDRA System Organ Class (SOC)	Adverse reaction	Frequency per patient	Frequency per infusion
Infections and Infestations	Aseptic meningitis	Uncommon	Rare
Blood and lymphatic disorders	Anaemia	Common	Uncommon
	Lymphadenopathy	Common	Rare
	Haemolysis	Not known	Not known
Immune system disorders	Hypersensitivity	Uncommon	Rare
	Anaphylactic reaction	Uncommon	Rare
	Anaphylactic shock	Not known	Not known
Metabolism and nutrition disorders	Decreased appetite	Common	Uncommon
Psychiatric disorders	Anxiety	Common	Uncommon
	Insomnia	Common	Uncommon
Nervous system disorders	Headache	Very Common	Common
	Dizziness	Common	Uncommon
	Migraine	Common	Uncommon
	Paraesthesia	Common	Rare

MedDRA System Organ Class (SOC)	Adverse reaction	Frequency per patient	Frequency per infusion
	Dysgeusia	Uncommon	Rare
	Balance disorder	Uncommon	Rare
	Dysarthria	Uncommon	Very Rare
	Amnesia	Uncommon	Very Rare
	Transient ischemic attack, cerebral vascular accident, tremor	Not known	Not known
Eye disorders	Conjunctivitis	Common	Rare
	Eye swelling	Uncommon	Rare
	Eye pain	Uncommon	Rare
Ear and labyrinth disorders	Vertigo	Uncommon	Rare
Cardiac disorders	Tachycardia (including sinus tachycardia)	Common	Uncommon
	Myocardial infarction	Not known	Not known
Vascular disorders	Hypertension (including blood pressure increased)	Very Common	Common
	Flushing (including Hot Flush)	Common	Uncommon
	Phlebitis	Uncommon	Rare
	Peripheral coldness	Uncommon	Rare
	Hypotension	Not known	Not known
	Deep vein thrombosis	Not known	Not known
Respiratory, thoracic and mediastinal disorders	Cough	Common	Uncommon
	Nasal congestion	Common	Uncommon
	Rhinorrhoea	Common	Uncommon
	Oropharyngeal pain	Common	Uncommon
	Dyspnoea	Common	Rare
	Pulmonary embolism	Uncommon	Rare
	Oropharyngeal swelling	Uncommon	Very rare
	Pulmonary oedema	Not known	Not known
Gastrointestinal disorders	Nausea	Very Common	Common
	Diarrhoea	Common	Uncommon
	Vomiting	Common	Uncommon
	Abdominal pain (including abdominal pain upper, lower and tenderness)	Common	Uncommon
	Dyspepsia	Common	Rare
	Abdominal distension	Uncommon	Rare
Skin and subcutaneous tissue disorders	Rash (including erythematous, pruritic, maculo-papular, papular)	Very Common	Uncommon
	Contusion	Common	Uncommon
	Urticaria	Common	Uncommon
	Pruritus	Common	Uncommon
	Dermatitis	Common	Rare
	Erythema	Common	Rare
	Night sweats	Uncommon	Rare
	Photosensitivity reaction	Uncommon	Rare
	Cold sweat	Uncommon	Rare
	Angioedema	Uncommon	Very Rare

MedDRA System Organ Class (SOC)	Adverse reaction	Frequency per patient	Frequency per infusion
Musculoskeletal and connective tissue disorders	Back pain	Common	Uncommon
	Arthralgia	Common	Uncommon
	Pain in extremity	Common	Uncommon
	Muscle spasms	Common	Uncommon
	Myalgia	Common	Uncommon
	Muscular weakness	Common	Uncommon
	Muscle twitching	Uncommon	Very Rare
Renal and urinary disorders	Proteinuria	Uncommon	Rare
General disorders and administration site conditions	Local reactions	Very Common	Uncommon
	• Infusion site extravasation	Common	Uncommon
	• Infusion site pain (including Discomfort)	Common	Uncommon
	• Infusion site swelling (including Local swelling, Local oedema)	Common	Rare
	• Infusion site pruritus	Uncommon	Very Rare
	Fatigue (including Lethargy)	Very Common	Common
	Pyrexia (including Body temperature increased)	Very Common	Uncommon
	Chills	Common	Uncommon
	Oedema (including peripheral, Swelling)	Common	Uncommon
	Influenza-like illness	Common	Uncommon
	Malaise	Common	Uncommon
	Chest discomfort	Common	Rare
	Chest tightness	Uncommon	Rare
	Feeling hot	Uncommon	Rare
	Burning sensation	Uncommon	Rare
Investigations	Blood urea increased	Uncommon	Rare
	White blood cell count decreased	Uncommon	Rare
	Alanine aminotransferase increased	Uncommon	Rare
	Haematocrit decreased	Uncommon	Rare
	Red blood cell count decreased	Uncommon	Rare
	Blood creatinine increased	Uncommon	Rare
	Respiratory rate increased	Uncommon	Very Rare
	Coombs direct test positive	Not known	Not known
	Oxygen saturation decreased	Not known	Not known
Injury, poisoning and procedural complications	Transfusion-related acute lung injury	Not known	Not known

Description of selected adverse reactions

Muscle twitching and weakness were reported only in patients with MMN.

Paediatric population

Frequency, type and severity of adverse reactions in children are the same as in adults.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation 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 listed in Appendix V.

For safety with respect to transmissible agents, see section 4.4.

4.9 Overdose

Overdose may lead to fluid overload and hyperviscosity, particularly in patients at risk, including infants, elderly patients or patients with cardiac or renal impairment (see section 4.4).

Paediatric population

Smaller children below the age of 5 years may be particularly susceptible to volume overload. Therefore, dosing should be carefully calculated for this population. In addition, children with Kawasaki Disease are at especially high risk due to underlying cardiac compromise so dose and rate of administration should be carefully controlled.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: immune sera and immunoglobulins, immunoglobulins, normal human, for intravascular administration, ATC code: J06BA02

Human normal immunoglobulin contains mainly immunoglobulin G (IgG) with a broad spectrum of antibodies against infectious agents.

Human normal immunoglobulin contains the IgG antibodies present in the normal population. It is usually prepared from pooled plasma from not fewer than 1 000 donations. It has a distribution of immunoglobulin G subclasses closely proportional to that in native human plasma. Adequate doses of this medicinal product may restore abnormally low immunoglobulin G levels to the normal range.

The mechanism of action in indications other than replacement therapy is not fully elucidated but includes immunomodulatory effects.

Paediatric population

There are no theoretical or observed differences in the action of immunoglobulins in children compared to adults.

5.2 Pharmacokinetic properties

Absorption

Human normal immunoglobulin is immediately and completely bioavailable in the recipient’s circulation after intravenous administration.

Distribution

It is distributed relatively rapidly between plasma and extravascular fluid, after approximately 3 – 5 days equilibrium is reached between the intra- and extravascular compartments.

Elimination

Human normal immunoglobulin has a half-life of about 32.5 days. This half-life may vary from patient to patient, in particular in primary immunodeficiency.
IgG and IgG-complexes are broken down in cells of the reticuloendothelial system.

5.3 Preclinical safety data

Immunoglobulins are normal constituents of the human body.

The safety of human normal immunoglobulin (IVIg) 10 % has been demonstrated in several non-clinical studies. Non-clinical data reveal no special risk for humans based on conventional studies of safety pharmacology and toxicity. Deqsiga revealed no increased potential to stimulate the immune system and associated risk for hypersensitivity reactions compared to human normal immunoglobulin (IVIg) 10 %.

Studies of repeated dose toxicity, genotoxicity and toxicity to reproduction in animals are impracticable due to induction of and interference by developing antibodies to heterologous proteins. Since clinical experience provides no evidence for carcinogenic potential of immunoglobulins, no experimental studies in heterogeneous species were performed.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glycine
Water for injections

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

2 years.

Chemical and physical in-use stability for the diluted product (dilution with a 5 % glucose solution to a final concentration of 50 mg/mL (5 %) immunoglobulin) has been demonstrated for 21 days at 2 °C to 8 °C as well as 28 °C to 30 °C.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8 °C, unless dilution has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

Do not store above 25 °C.
Do not freeze.
Keep the vial in the outer carton in order to protect from light.

For storage conditions after dilution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

50 mL or 100 mL of solution in a vial (Type I glass) with a stopper (bromobutyl).
Pack size: 1 vial

Not all presentations may be marketed.

6.6 Special precautions for disposal and other handling

The product should be brought to room or body temperature (20 °C – 37 °C) before use. Do not use heating devices including microwaves.

If dilution is required, 5 % glucose solution is recommended. For obtaining an immunoglobulin solution of 50 mg/mL (5 %), Deqsiga 100 mg/mL (10 %) should be diluted with an equal volume of the glucose solution. It is recommended that during dilution the risk of microbial contamination is minimised.

The product should be inspected visually for particulate matter and discolouration prior to administration The solution should be clear or slightly opalescent and colourless or pale yellow. Solutions that are cloudy or have deposits should not be used.

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

7. MARKETING AUTHORISATION HOLDER

Takeda Manufacturing Austria AG
Industriestrasse 67
1221 Vienna
Austria
medinfoEMEA@takeda.com

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/25/1919/001
EU/1/25/1919/002

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: DD Month Year

10. DATE OF REVISION OF THE TEXT

MM/YYYY

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer of the biological active substance

Baxalta Belgium Manufacturing SA
Boulevard René Branquart 80
7860 Lessines
Belgium

Name and address of the manufacturer responsible for batch release

Baxalta Belgium Manufacturing SA
Boulevard René Branquart 80
7860 Lessines
Belgium

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

- **Official batch release**

In accordance with Article 114 Directive 2001/83/EC, the official batch release will be undertaken by a state laboratory or a laboratory designated for that purpose.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (5 G/50 mL, 10 G/100 mL)

1. NAME OF THE MEDICINAL PRODUCT

Deqsiga 100 mg/mL solution for infusion
human normal immunoglobulin (IVIg)

2. STATEMENT OF ACTIVE SUBSTANCE

One mL contains 100 mg human normal immunoglobulin of which at least 98 % is IgG.

The maximum IgA content is 2 micrograms/mL.

5 g / 50 mL
10 g / 100 mL

3. LIST OF EXCIPIENTS

Glycine
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for infusion
1 vial

5. METHOD AND ROUTE OF ADMINISTRATION

Intravenous use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Do not store above 25 °C.
Do not freeze.
Keep the vial in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Takeda Manufacturing Austria AG
Industriestrasse 67
1221 Vienna
Austria

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/25/1919/001 5 g / 50 mL
EU/1/25/1919/002 10 g / 100 mL

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

DEQSIGA

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING

VIAL LABEL (5 G/50 mL, 10 G/100 mL)

NAME OF THE MEDICINAL PRODUCT

Deqsiga 100 mg/mL solution for infusion
human normal immunoglobulin (IVIg)

2. STATEMENT OF ACTIVE SUBSTANCE

One mL contains 100 mg human normal immunoglobulin of which at least 98 % is IgG.

The maximum IgA content is 2 micrograms/mL.

5 g / 50 mL
10 g / 100 mL

3. LIST OF EXCIPIENTS

Glycine
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for infusion
1 vial

5. METHOD AND ROUTE OF ADMINISTRATION

Intravenous use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Do not store above 25 °C.
Do not freeze.
Keep the vial in the outer carton in order to protect from light.

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Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Deqsiga 100 mg/mL solution for infusion
human normal immunoglobulin (IVIg)

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Deqsiga is and what it is used for

Deqsiga belongs to a class of medications called immunoglobulins. These medicines contain human antibodies, which are also present in your blood. Antibodies help your body to fight infections. Medicines like Deqsiga are used in patients who do not have enough antibodies in their blood and tend to get frequent infections. They can also be used in patients who need additional antibodies for the treatment of certain inflammatory disorders (autoimmune diseases).

Deqsiga is used for

Treatment of patients who do not have sufficient antibodies (replacement therapy). There are two groups:

1. Patients with inborn lack of antibody production (primary immunodeficiency syndromes).
2. Patients with secondary immunodeficiencies (SID) who suffer from severe or recurrent infections, ineffective antimicrobial treatment and either **proven specific antibody failure (PSAF)*** or serum IgG level of < 4 g/L.

*PSAF = failure to mount at least a 2-fold rise in IgG antibody titre to pneumococcal polysaccharide and polypeptide antigen vaccines

Treatment of patients with certain inflammatory disorders (immunomodulation). There are five groups:

1. Patients who do not have enough blood platelets (primary immune thrombocytopenia, ITP), and who are at high risk of bleeding or will have surgery soon.
2. Patients with a disease that is associated with multiple inflammations of the nerves in the whole body (Guillain Barré syndrome).
3. Patients with a disease which results in multiple inflammations of several organs of the body (Kawasaki disease).

4. Patients who suffer from a rare condition characterised by slow progressive asymmetrical weakness of limbs without sensory loss (multifocal motor neuropathy, MMN).
5. Patients who suffer from chronic inflammatory demyelinating polyradiculoneuropathy (CIDP).

2. What you need to know before you use Deqsiga

Do not use Deqsiga

- If you are allergic to human normal immunoglobulins or any of the other ingredients of this medicine (listed in section 6).
- If you have antibodies against immunoglobulin A (IgA) in your blood. Antibodies against IgA may occur if you have IgA deficiency. Since Deqsiga contains trace amounts of IgA, you might have an allergic reaction.

Warnings and precautions

➔ Talk to your doctor, pharmacist or nurse before using Deqsiga.

Which circumstances and conditions increase the risk of you having side effects?

Immunoglobulins may increase the risk of heart attack (cardiac infarction), stroke, blood clots in the lung (lung embolism) or blockage of a blood vessel in the leg (deep vein thrombosis), although only very rarely. You may be at increased risk of developing a blood clot if you are/have

- overweight,
- elderly,
- diabetes,
- bedridden for a long time,
- high blood pressure,
- low blood volume (hypovolaemia),
- problems with your blood vessels (vascular diseases),
- an increased tendency for blood clotting (thrombophilia or thrombotic episodes),
- a disease or a condition that causes your blood to thicken (hyper-viscous blood).

➔ Talk to your doctor or healthcare professional before treatment if any of the risk factors listed above apply to you.
➔ Talk to your doctor immediately if you experience signs and symptoms such as shortness of breath, chest pain, pain and swelling of a limb, weakness or numbness on one side of the body during or after receiving Deqsiga. They will carefully monitor you throughout the infusions so that any thromboembolic events can be detected and treated immediately.

Immunoglobulins may increase the risk of kidney injury which may lead to rapid loss of kidney function (acute renal failure), although only very rarely. You may be at increased risk if you have/had:

- problems with your kidneys,
- diabetes,
- low blood volume (hypovolaemia),
- overweight,
- been prescribed medicinal products that may harm your kidneys (nephrotoxic medicinal products).

➔ Talk to your doctor or healthcare professional before treatment if any of the risk factors mentioned above apply. They will decide whether to reduce the infusion rate or dose, or stop it completely.

If you have blood group A, B or AB and an underlying inflammatory condition, you may have an increased risk of breakdown of red blood cells which may lead to anaemia (haemolytic anaemia).

How long is monitoring required during the infusion

For your safety, Deqsiga treatment must be supervised by your doctor or healthcare professional. They will carefully adjust the infusion rate to suit your needs and monitor you throughout the infusion and for at least 20 minutes afterward. Additional precautions may be necessary under specific circumstances due to the increased likelihood of side effects. Examples include:

- you are receiving Deqsiga at a high infusion rate,
- you are receiving Deqsiga for the first time or after a long break in treatment (e.g., several weeks or months),
- in rare cases, when you are switching from one human normal immunoglobulin product to another,
- you have an untreated infection or an underlying chronic inflammation.

In these situations, your doctor or healthcare professional will closely observe you throughout the infusion and for at least an hour afterward.

➔ Talk to your doctor or healthcare professional immediately if you notice any side effects while receiving the Deqsiga infusion. They will decide whether to reduce the infusion rate or to stop it completely. The required action will depend on the severity and nature of the reaction.

When might slowing or stopping the infusion be required?

You may be allergic (hypersensitive) to immunoglobulins without knowing it. However, true allergic reactions are rare. They may occur even if you have previously received human immunoglobulins and have tolerated them well (see also section 4).

In very rare cases, transfusion-related acute lung injury (TRALI) can occur after receiving immunoglobulins. It will lead to a non-heart-related accumulation of fluid in the lungs' air space (non-cardiogenic pulmonary oedema). You will recognize TRALI by severe difficulty in breathing (respiratory distress), bluish skin (cyanosis), abnormally low levels of oxygen in the blood (hypoxia), decrease in blood pressure (hypotension) and increased body temperature (fever). Symptoms typically appear during or within 6 hours after receiving treatment.

➔ Tell your doctor or healthcare professional immediately if you notice such reactions during the Deqsiga infusion. They will decide whether to decrease the infusion rate or to stop the infusion completely.

Inflammation of the membranes that surround the brain and spinal cord

Inflammation of the membranes that surround the brain and spinal cord (aseptic meningitis syndrome) has been reported to occur in association with immunoglobulin treatment.

➔ Tell your doctor or healthcare professional immediately if you notice any of these signs and symptoms, including severe headache, neck stiffness, drowsiness, fever, photophobia, nausea and vomiting during or after the infusion.

Sugar content

Although Deqsiga does not contain sugar, it may be diluted with a special sugar solution (5 % glucose) which could affect your blood sugar level.

Information on the source material of Deqsiga

Deqsiga is made from human plasma (the liquid part of blood). When medicines are made from human blood or plasma, certain measures are put in place to prevent infections being passed on to patients. These include:

- careful selection of blood and plasma donors to make sure those at risk of carrying infections are excluded,
- the testing of each donation and pools of plasma for signs of virus/infections,
- the inclusion of steps in the processing of the blood or plasma that can inactivate or remove viruses.

Despite these measures, when medicines prepared from human blood or plasma are administered, the possibility of passing on infection cannot be totally excluded. This also applies to any unknown or emerging viruses or other types of infections.

The measures taken are considered effective for enveloped viruses such as human immunodeficiency virus (HIV), hepatitis B virus and hepatitis C virus, and for the non-enveloped hepatitis A and parvovirus B19 viruses.

Immunoglobulins have not been associated with hepatitis A or parvovirus B19 infections possibly because the antibodies against these infections, which are contained in the product, are protective.

It is strongly recommended that every time you receive a dose of Deqsiga, the name and batch number of the medicine are recorded in order to maintain a record of the batches used.

Children and adolescents

There are no specific or additional warnings or precautions applicable for children and adolescents.

Other medicines and Deqsiga

➔ Tell your doctor or healthcare professional if you are taking, have recently taken or might take any other medicines.

The concomitant use of medicines that increase the excretion of water from your body (loop diuretics) should be avoided during treatment with Deqsiga. Your doctor will decide whether you should use or continue treatment with loop diuretics.

The infusion of Deqsiga may impair the effect of some live virus vaccines such as measles, rubella, mumps, and chicken pox. Therefore, after receiving immunoglobulins, you may have to wait up to 3 months before receiving your live-attenuated vaccine. You may have to wait for up to 1 year after receiving Deqsiga before you receive your measles vaccine.

➔ Tell your vaccinating doctor prior to a vaccination about your treatment with Deqsiga.

Deqsiga effects on blood tests

Deqsiga contains a wide variety of different antibodies, some of which can affect blood tests. Treatment with Deqsiga may interfere with the results of specific blood tests (serological tests).

➔ Tell your doctor or healthcare professional that you have been given this medicine, if you have a blood test after receiving Deqsiga.

Pregnancy, breast-feeding and fertility

- If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.
- No clinical trials have been performed with Deqsiga in pregnant or breast-feeding women. However, clinical experience with immunoglobulins suggests that no harmful effects on the course of pregnancy, or on the foetus and the neonate are expected. If you are breast-feeding and receive Deqsiga, the antibodies of the medicine can also be found in the breast milk. No negative effects on the breastfed newborn/infants are anticipated.
- Clinical experience with immunoglobulins suggests that no harmful effects on fertility are expected.

Driving and using machines

Patients may experience side effects such as dizziness or nausea during treatment with Deqsiga that could impact their ability to drive, cycle or operate machinery. If these reactions occur, you or your child should wait until they have ended before restarting these activities. Consult your doctor about any side effects you or your child may experience.

3. How to use Deqsiga

Deqsiga is intended for intravenous administration (infusion into a vein). It is given to you by your doctor or nurse. Dose and frequency of the infusion will vary depending on your condition and your body weight.

At the beginning of your infusion, you will receive Deqsiga at a slow rate. Dependent on how comfortable you are, your doctor may then gradually increase the infusion rate.

Use in children and adolescents

The same indications, dose, and frequency of infusion as for adults apply for children and adolescents (age 0 to 18).

If you use more Deqsiga than you should

If you get more Deqsiga than you should, your blood may become too thick (hyperviscous). This could particularly happen when you are a patient at risk, e.g., an elderly patient or a patient having problems with your kidneys.

➔ Be sure that you take adequate fluids, so you are not dehydrated and notify your doctor or healthcare professional if you are known to have any medical problems prior to infusion.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Certain side effects, e.g., headache or flushing, may be reduced by slowing the infusion rate.

In rare and isolated cases, the following serious side effects have been reported with immunoglobulin preparations:

- severe hypersensitivity reactions such as a sudden drop in blood pressure or anaphylactic shock (e.g., you may feel light-headed or dizzy, wheezing, swelling of the throat, lips, or tongue, skin

rash, abnormal heartbeat or chest pain, or have blurred vision), even when you have shown no hypersensitivity on previous infusions.
- heart attack (e.g. when you have sudden chest pain or shortness of breath)
- stroke (e.g., when you have a sudden onset of muscle weakness, have a loss of sensation and/or balance, decreased alertness or difficulty in speaking)
- blood clots in the arteries of the lungs (e.g., when you have chest pain, difficulty in breathing or are coughing up blood)
- blood clot (e.g. when you have redness, pain and swelling of one or both legs)
- transfusion-related acute lung injury (TRALI) (e.g., you may feel chest pain, chest discomfort, difficulty in breathing).
- temporary non-infective meningitis (e.g., you may experience severe headaches, nausea, vomiting, a stiff neck, fever and sensitivity to light).
- Reversible haemolytic anaemia/haemolysis (e.g. you may feel light-headed, weakness, be abnormally pale, dark-coloured urine).
- Severe kidney injury (e.g. when you have low back pain, fatigue, difficulty in passing urine).

➔ Seek medical care with no delay if any of the above symptom**s** happen during or after the infusion**.**

Side effects observed in controlled clinical studies and in post-marketing experience are presented in order of decreased frequency:

Very common (may affect more than 1 in 10 people):
Headache, high blood pressure, feeling sick, rash, local reactions (e.g., pain and swelling or other reactions at the infusion site), fever, tiredness.

Common (may affect up to 1 in 10 people):
Low red blood cell count, swollen lymph glands, decreased appetite, difficulty in sleeping, anxiety, dizziness, migraine, numbness or tingling of the skin or of a limb, redness and discomfort in the eye, rapid heartbeat, reddening of the skin, cough, runny nose, blocked nose, pain of mouth and throat, difficulty breathing, diarrhoea, vomiting, abdominal pain, indigestion, bruising, itchy rash, itching, inflammation of the skin, ~~reddening of the skin,~~ back pain, joint pain, pain in your arms or legs, muscle pain, muscle cramps, muscular weakness, chills, accumulation of fluid under the skin, Influenza-like illness, feeling generally unwell, discomfort in the chest.

Uncommon (may affect up to 1 in 100 people):
Inflammation of the membranes that surround the brain and spinal cord, allergic reactions, sudden, severe allergic reactions, taste disturbance, memory loss, difficulty speaking, impaired balance, eye pain or swelling, a spinning sensation, peripheral coldness, inflammation of a vein, clot in a blood vessel in the lungs, swelling of mouth and throat, abdominal swelling, cold sweat, sunburn-like reactions (following exposure to light), sweating during sleep, muscle twitching, excess protein in the urine, chest tightness, feeling hot, burning sensation, rapid swelling under the skin, changes to blood test results (i.e., increased kidney and liver function tests, and decreased white blood cell and red blood cell counts).

Frequency not known (cannot be estimated from available data):
Destruction of red blood cells, transient stroke, stroke, shaking, low blood pressure, heart attack, blood clot in a deep vein (usually in the leg), accumulation of fluid in the lung, positive result of Coombs' test, decreased oxygen saturation in blood, transfusion related acute lung injury.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Deqsiga

- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date which is stated on the label and carton after EXP. The expiry date refers to the last day of that month.
- Do not use this medicine if you notice particles in the vial or discolouration of the liquid.
- Do not store above 25 °C.
- Do not freeze.
- Keep the vial in the outer carton in order to protect from light.

6. Contents of the pack and other information

What Deqsiga contains

- The active substance of Deqsiga is human normal immunoglobulin.
- 1 mL of Deqsiga contains 100 mg of human protein of which at least 98 % is immunoglobulin G (IgG).
- The other ingredients (excipients) are glycine and water for injections.

What Deqsiga looks like and contents of the pack

Deqsiga is a solution for infusion in vials of 50 mL or100 mL. The solution is clear or slightly opalescent and colourless or pale-yellow.

Not all presentations may be marketed.

Marketing Authorisation Holder

Takeda Manufacturing Austria AG
Industriestrasse 67
1221 Vienna
Austria

Manufacturer

Baxalta Belgium Manufacturing
SA Boulevard René Branquart 80
7860 Lessines
Belgium

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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This leaflet was last revised in MM/YYYY.

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu

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The following information is intended for healthcare professionals only:

Method of administration

- Deqsiga must only be administered intravenously. Other routes of administration have not been evaluated.
- Deqsiga should be infused intravenously at an initial rate of 0.5 mL/kg BW/hour for 30 minutes. In case of adverse reaction, either the rate of administration must be reduced or the infusion stopped. If well tolerated, the rate of administration may gradually be increased to a maximum of 6 mL/kg BW/hour. Clinical data obtained from a limited number of patients also indicate that adult PID patients may tolerate an infusion rate of up to 8 mL/kg BW/hr.
- If dilution to lower concentrations is required prior to infusion, Deqsiga may be diluted with 5 % glucose solution to a final concentration of 50 mg/mL (5 % immunoglobulin).
- Any infusion-related adverse events should be treated by lowering infusion rates or by stopping the infusion.

Incompatibilities

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

Special precautions for storage

Chemical and physical in-use stability for the diluted product (dilution with a 5 % glucose solution to a final concentration of 50 mg/mL (5 %) immunoglobulin) has been demonstrated for 21 days at 2 °C to 8 °C as well as at 28 °C to 30 °C.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8 °C, unless dilution has taken place in controlled and validated aseptic conditions.

Instructions for handling and disposal

- The product must be brought to room or body temperature (20 °C – 37 °C) before use. Do not use heating devices including microwaves.
- Deqsiga should be inspected visually for particulate matter and discolouration prior to administration. Only clear to slightly opalescent and colourless to pale yellow solutions are to be administered. Do not use if particulate matter or discolouration is observed.
- If dilution is required, 5 % glucose solution is recommended. To obtain an immunoglobulin solution of 50 mg/mL (5 %), Deqsiga 100 mg/mL (10 %) should be diluted with an equal volume of the glucose solution. It is recommended that during dilution, the risk of microbial contamination is minimised.
- Any unused product or waste material should be disposed of in accordance with local requirements.

Dose recommendations

Replacement therapy

Indication	Dose	Frequency of infusions
Primary immunodeficiency syndromes	starting dose: 0.4 – 0.8 g/kg maintenance dose: 0.2 – 0.8 g/kg	 every 3 – 4 weeks
Secondary immunodeficiencies (as defined in section 4.1 of the SmPC)	0.2 – 0.4 g/kg	every 3 – 4 weeks

Immunomodulation

Indication	Dose	Frequency of infusions
Primary immune thrombocytopenia	0.8 – 1 g/kg or 0.4 g/kg/d	on day 1, possibly repeated once within 3 days. for 2 – 5 days
Guillain Barré syndrome	0.4 g/kg/d	for 5 days
Kawasaki disease	2 g/kg	in one dose in association with acetylsalicylic acid
Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)	starting dose: 2 g/kg maintenance dose: 1 g/kg	in divided doses over 2 – 5 consecutive days every 3 weeks in divided doses over 1 – 2 days

Indication	Dose	Frequency of infusions
Multifocal Motor Neuropathy (MMN)	starting dose: 2 g/kg maintenance dose: 1 g/kg or 2 g/kg	in divided doses over 2 – 5 consecutive days. every 2 – 4 weeks or every 4 – 8 weeks in divided doses over 2 – 5 days