ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

KIOVIG 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 10 ml contains: 1 g of human normal immunoglobulin
Each vial of 25 ml contains: 2.5 g of human normal immunoglobulin
Each vial of 50 ml contains: 5 g of human normal immunoglobulin
Each vial of 100 ml contains: 10 g of human normal immunoglobulin
Each vial of 200 ml contains: 20 g of human normal immunoglobulin
Each vial of 300 ml contains: 30 g of human normal immunoglobulin

Distribution of IgG subclasses (approx. values):

IgG1 ≥56.9%
IgG2 ≥26.6%
IgG3 ≥3.4%
IgG4 ≥1.7%

The maximum IgA content is 140 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.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

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

- Primary immunodeficiency syndromes with impaired antibody production (see section 4.4).
- Hypogammaglobulinaemia and recurrent bacterial infections in patients with chronic lymphocytic leukaemia, in whom prophylactic antibiotics have failed.
- Hypogammaglobulinaemia and recurrent bacterial infections in plateau phase multiple myeloma patients who have failed to respond to pneumococcal immunisation.
- Hypogammaglobulinaemia in patients after allogeneic haematopoietic stem cell transplantation (HSCT).
- Congenital AIDS and recurrent bacterial infections.

Immunomodulation in adults, and children and adolescents (0-18 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.
- Multifocal Motor Neuropathy (MMN).

4.2 Posology and method of administration

Replacement therapy should be initiated and monitored under the supervision of a physician experienced in the treatment of immunodeficiency.

Posology

The dose and dose regimen is dependent on the indication.

In replacement therapy the dose may need to be individualised for each patient dependent on the pharmacokinetic and clinical response. The following dose regimens are given as a guideline.

Replacement therapy in primary immunodeficiency syndromes

The dose regimen should achieve a trough level of IgG (measured before the next infusion) of at least 5 to 6 g/l. Three to six months are required after the initiation of therapy for equilibration 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 three to four weeks.

The dose required to achieve a trough level of 5-6 g/l is of the order of 0.2-0.8 g/kg/month. The dose interval when steady state has been reached varies from 3-4 weeks.

Trough levels should be measured and assessed in conjunction with the incidence of infection. To reduce the rate of infection, it may be necessary to increase the dose and aim for higher trough levels.

Hypogammaglobulinaemia and recurrent bacterial infections in patients with chronic lymphocytic leukaemia, in whom prophylactic antibiotics have failed; hypogammaglobulinaemia and recurrent bacterial infections in plateau phase multiple myeloma patients who have failed to respond to pneumococcal immunisation; congenital AIDS and recurrent bacterial infections

The recommended dose is 0.2-0.4 g/kg every three to four weeks.

Hypogammaglobulinaemia in patients after allogeneic haematopoietic stem cell transplantation

The recommended dose is 0.2-0.4 g/kg every three to four weeks. The trough levels should be maintained above 5g/l.

Primary immune thrombocytopenia

There are two alternative treatment schedules:
- 0.8-1g/kg given on day one; this dose may be repeated once within 3 days
- 0.4 g/kg given daily for two to five days.

The treatment can be repeated if relapse occurs.

Guillain Barré syndrome

0.4 g/kg/day over 5 days.

Kawasaki Disease

1.6-2 g/kg should be administered in divided doses over two to five days or 2.0 g/kg as a single dose. Patients should receive concomitant treatment with acetylsalicylic acid.

Multifocal Motor Neuropathy (MMN)

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

The dose recommendations are summarised in the following table:

Indication	Dose	Frequency of injections
Replacement therapy in primary immunodeficiency	starting dose: 0.4-0.8 g/kg thereafter: 0.2-0.8 g/kg	every 3-4 weeks to obtain IgG trough level of at least 5-6 g/l
Replacement therapy in secondary immunodeficiency	0.2-0.4 g/kg	every 3-4 weeks to obtain IgG trough level of at least 5-6 g/l
Congenital AIDS	0.2-0.4 g/kg	every 3-4 weeks
Hypogammaglobulinaemia (<4 g/l) in patients after allogeneic haematopoietic stem cell transplantation	0.2-0.4 g/kg	every 3-4 weeks to obtain IgG trough level above 5g/l
Immunomodulation:		
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	1.6-2 g/kg or 2 g/kg	in divided doses for 2-5 days in association with acetylsalicylic acid in one dose in association with acetylsalicylic acid
Multifocal Motor Neuropathy (MMN)	starting dose: 2 g/kg maintenance dose: 1 g/kg or 2 g/kg	given over 2-5 days every 2-4 weeks or every 4-8 weeks

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 adjusted to the clinical outcome of the above mentioned conditions.

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. If well tolerated (see section 4.4), 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, KIOVIG 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.

Any infusion-related adverse events should be treated by lowering infusion rates or by stopping the infusion.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
Hypersensitivity to human immunoglobulins, especially in patients with antibodies against IgA.

4.4 Special warnings and precautions for use

Certain severe adverse reactions 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.
Certain adverse reactions may occur more frequently

- in case of high rate of infusion
- 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.

Potential complications can often be avoided by ensuring that patients:

- are not sensitive to human normal immunoglobulin by initially injecting 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 order to detect potential adverse signs. All other patients should be observed for at least 20 minutes after administration.

In case of adverse reaction, either the rate of administration must be reduced or the infusion stopped. The treatment required depends on the nature and severity of the adverse reaction.
In case of shock, standard medical treatment for shock should be implemented.

In all patients, IVIg administration requires:

- adequate hydration prior to the initiation of the infusion of IVIg
- monitoring of urine output
- monitoring of serum creatinine levels
- monitoring for signs and symptoms of thrombosis
- assessment of blood vicosity in patients at risk for hyperviscosity
- avoidance of concomitant use of loop diuretics.

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

Hypersensitivity

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.

Rarely, human normal immunoglobulin can induce a fall in blood pressure with anaphylactic reaction, even in patients who had tolerated previous treatment with human normal immunoglobulin.

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 thrombosis 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 infusion of IVIg in obese patients and in patients with pre-existing risk factors for thrombotic events (such as a history of atherosclerosis, multiple cardiovascular risk factors, advanced age, impaired cardiac output, hypertension, use of estrogens, diabetes mellitus and a history of vascular disease or thrombotic episodes, patients with acquired or inherited thrombophilic disorders, hypercoagulable disorders, patients with prolonged periods of immobilisation, severely hypovolemic patients, patients with diseases which increase blood viscosity, patients with indwelling vascular catheters and patients with high dose and rapid infusion).

Hyperproteinemia, increased serum viscosity and subsequent relative pseudohyponatremia may occur in patients receiving IVIg therapy. This should be taken into account by physicians, since initiation of treatment for true hyponatremia (i.e. decreasing serum free water) in these patients may lead to a further increase in serum viscosity and a possible predisposition to thromboembolic events.

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. These include acute renal failure, acute tubular necrosis, proximal tubular nephropathy and osmotic nephrosis. In most cases, risk factors have been identified, such as pre-existing renal insufficiency, diabetes mellitus, hypovolemia, overweight, concomitant nephrotoxic medicinal products, age over 65, sepsis, hyperviscosity or paraproteinemia.

In case of renal impairment, IVIg discontinuation should be considered. While these 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 stabilizer 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. KIOVIG does not contain sucrose, maltose or glucose.

In patients at risk for acute renal failure, IVIg products should be administered at the minimum rate of infusion and dose practicable.

Transfusion Related Acute Lung Injury (TRALI)

There have been reports of noncardiogenic pulmonary edema (Transfusion Related Acute Lung Injury, TRALI) in patients administered IVIg (including KIOVIG).

Aseptic meningitis syndrome (AMS)

Aseptic meningitis syndrome has been reported to occur in association with IVIg treatment. Discontinuation of IVIg treatment has resulted in remission of AMS within several days without sequelae. The syndrome usually begins within several hours to 2 days following IVIg treatment. Cerebrospinal fluid 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.
From post-marketing data with KIOVIG no clear correlation of AMS to higher doses was observed. Higher incidences of AMS were seen in women.

Haemolytic anaemia

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

Interference with serological testing

After infusion 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 KIOVIG 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

KIOVIG 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 HIV, HBV and HCV, and for the non-enveloped viruses HAV and parvovirus B19.

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 KIOVIG 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 with regard to any of the above adverse events. Paediatric patients may be more susceptible to volume overload (see Section 4.9).

4.5 Interactions with other medicinal products and other forms of interactions

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 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.

Dilution of KIOVIG with a 5% glucose solution may result in increased blood glucose levels.

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 it should only be given with caution to pregnant women and breast-feeding mothers. 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 to be expected.

Breast-feeding

Immunoglobulins are excreted into the milk and may contribute to protecting the neonate from pathogens which have a mucosal portal of entry.

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

The ability to drive and operate machines may be impaired by some adverse reactions associated with KIOVIG. 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 such as chills, headache, dizziness, fever, vomiting, allergic reactions, nausea, arthralgia, low blood pressure and moderate low back pain may occur occasionally.

Rarely human normal immunoglobulins may cause a sudden fall in blood pressure and, in isolated cases, anaphylactic shock, even when the patient has shown no hypersensitivity to previous administration.

Cases of reversible aseptic meningitis and rare cases of transient cutaneous reactions have been observed with human normal immunoglobulin. Reversible haemolytic reactions have been observed in patients, especially those with blood groups A, B, and AB. Rarely, haemolytic anaemia requiring transfusion may develop after high dose IVIg treatment (see also Section 4.4).

Increase in serum creatinine level and/or acute renal failure have been observed.

Very rarely: Thromboembolic reactions such as myocardial infarction, stroke, pulmonary embolism, and deep vein thromboses.

Tabulated list of adverse reactions

The tables presented below are according to the MedDRA system organ classification (SOC and Preferred Term Level). Table 1 shows the adverse reactions from clinical trials and Table 2 shows the post-marketing ARs.

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 1
Frequency of Adverse Reactions (ADRs) in clinical studies with KIOVIG

MedDRA System Organ Class (SOC)	Adverse reaction	Frequency
Infections and infestations	Bronchitis, nasopharyngitis	Common
	Chronic sinusitis, fungal infection, infection, kidney infection, sinusitis, upper respiratory tract infection, urinary tract infection, bacterial urinary tract infection, meningitis aseptic	Uncommon
Blood and lymphatic system disorders	Anaemia, lymphadenopathy	Common
Immune system disorders	Hypersensitivity, anaphylactic reaction	Uncommon
Endocrine disorders	Thyroid disorder	Uncommon
Metabolism and nutrition disorders	Decreased appetite	Common
Psychiatric disorders	Insomnia, anxiety	Common
	Irritability	Uncommon
Nervous system disorders	Headache	Very common
	Dizziness, migraine, paresthesia, hypoesthesia	Common
	Amnesia, dysarthria, dysgeusia, balance disorder, tremor	Uncommon
Eye disorders	Conjunctivitis	Common
	Eye pain, eye swelling	Uncommon
Ear and labyrinth disorders	Vertigo, fluid in middle ear	Uncommon
Cardiac disorders	Tachycardia	Common
Vascular disorders	Hypertension	Very common
	Flushing	Common
	Peripheral coldness, phlebitis	Uncommon

Table 1 Frequency of Adverse Reactions (ADRs) in clinical studies with KIOVIG		
MedDRA System Organ Class (SOC)	**Adverse reaction**	**Frequency**
Respiratory, thoracic and mediastinal disorders	Cough, rhinorrhoea, asthma, nasal congestion, oropharyngeal pain, dyspnea	Common
	Oropharyngeal swelling	Uncommon
Gastrointestinal disorders	Nausea	Very common
	Diarrhoea, vomiting, abdominal pain, dyspepsia	Common
	Abdominal distension	Uncommon
Skin and subcutaneous tissue disorders	Rash	Very common
	Contusion, pruritus, urticaria, dermatitis, erythema	Common
	Angioedema, acute urticaria, cold sweat, photosensitivity reaction, night sweats, hyperhidrosis	Uncommon
Musculoskeletal and connective tissue disorders	Back pain, arthralgia, pain in extremity, myalgia, muscle spasms, muscular weakness	Common
	Muscle twitching	Uncommon
Renal and urinary disorders	Proteinuria	Uncommon
General disorders and administration site conditions	Local reactions (e.g. infusion site pain/swelling/reaction/pruritus), pyrexia, fatigue	Very common
	Chills, edema, influenza-like illness, chest discomfort, chest pain, asthenia, malaise, rigors	Common
	Chest tightness, feeling hot, burning sensation, swelling	Uncommon
Investigations	Blood cholesterol increased, blood creatinine increased, blood urea increased, white blood cell count decreased, alanine aminotransferase increased, haematocrit decreased, red blood cell count decreased, respiratory rate increased	Uncommon

Table 2 Post-Marketing Adverse Reactions (ARs)		
MedDRA System Organ Class (SOC)	**Adverse reaction**	**Frequency**
Blood and lymphatic system disorders	Hemolysis	Not known
Immune system disorders	Anaphylactic shock	Not known
Nervous system disorders	Transient ischemic attack, cerebral vascular accident	Not known
Cardiac disorders	Myocardial infarction	Not known
Vascular disorders	Hypotension, deep vein thrombosis	Not known
Respiratory, thoracic and mediastinal disorders	Pulmonary embolism, pulmonary edema	Not known
Investigations	Coombs direct test positive, oxygen saturation decreased	Not known
Injury, poisoning and procedural complications	Transfusion-related acute lung injury	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 elderly patients or patients with cardiac or renal impairment.

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 1000 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

Human normal immunoglobulin is immediately and completely bioavailable in the recipient's circulation after intravenous administration. It is distributed relatively rapidly between plasma and extravascular fluid; after approximately 3 to 5 days equilibrium is reached between the intra- and extravascular compartments.
Pharmacokinetic parameters for KIOVIG were determined in the two clinical studies in PID patients performed in Europe and the US. In these studies, a total of 83 subjects at least 2 years of age were treated with doses of 300 to 600 mg/kg body weight every 21 to 28 days for 6 to 12 months. The median IgG half-life after administration of KIOVIG was 32.5 days. This half-life may vary from patient to patient, in particular in primary immunodeficiency. Pharmacokinetic parameters for the product are summarized in the table below. All parameters were analysed separately for three age groups, children (below 12 years, n=5), adolescents (13 to 17 years, n=10), and adults (above 18 years of age, n=64). The values obtained in the studies are comparable to parameters reported for other human immunoglobulins.

Summary of KIOVIG pharmacokinetic parameters						
Parameter	**Children (12 years or below)**		**Adolescents (13 to 17 years)**		**Adults (18 years or above)**	
	Median	**95% CI***	**Median**	**95% CI**	**Median**	**95% CI**
Terminal half-life (days)	41.3	20.2 to 86.8	45.1	27.3 to 89.3	31.9	29.6 to 36.1
C_{min} (mg/dl)/(mg/kg) (trough level)	2.28	1.72 to 2.74	2.25	1.98 to 2.64	2.24	1.92 to 2.43
C_{max} (mg/dl)/(mg/kg) (peak level)	4.44	3.30 to 4.90	4.43	3.78 to 5.16	4.50	3.99 to 4.78
In-vivo recovery (%)	121	87 to 137	99	75 to 121	104	96 to 114
Incremental recovery (mg/dl)/(mg/kg)	2.26	1.70 to 2.60	2.09	1.78 to 2.65	2.17	1.99 to 2.44
$AUC_{0\text{-}21d}$ (g·h/dl) (area under the curve)	1.49	1.34 to 1.81	1.67	1.45 to 2.19	1.62	1.50 to 1.78

*CI – Confidence Interval

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 KIOVIG 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.

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.

If dilution to lower concentrations is required, immediate use after dilution is recommended.
The in-use stability of KIOVIG after 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; however, these studies did not include the microbial contamination and safety aspect.

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

10, 25, 50, 100, 200 or 300 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 before use.

If dilution is required, 5% glucose solution is recommended. For obtaining an immunoglobulin solution of 50 mg/ml (5%), KIOVIG 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.

KIOVIG should only be administered intravenously. Other routes of administration have not been evaluated.

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

7. MARKETING AUTHORISATION HOLDER

Baxter AG
Industriestrasse 67
A-1221 Vienna, Austria

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/05/329/001
EU/1/05/329/002
EU/1/05/329/003
EU/1/05/329/004
EU/1/05/329/005
EU/1/05/329/006

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorization: 19 January 2006
Date of latest renewal: 06 December 2010

10. DATE OF REVISION OF THE TEXT

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

ANNEX II

A. MANUFACTURERS 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

E. SPECIFIC OBLIGATION TO COMPLETE POST-AUTHORISATION MEASURES FOR THE CONDITIONAL MARKETING AUTHORISATION/THE MARKETING AUTHORISATION UNDER EXCEPTIONAL CIRCUMSTANCES

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

Name and address of the manufacturers of the biological active substance

Baxalta Belgium Manufacturing SA
Boulevard René Branquart 80
B-7860 Lessines
Belgium

Name and address of the manufacturers responsible for batch release

Baxalta Belgium Manufacturing SA
Boulevard René Branquart 80
B-7860 Lessines
Belgium

Baxter SA
Boulevard René Branquart 80
B-7860 Lessines
Belgium

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

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**

The requirements for submission of periodic safety update reports 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 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.

- **Additional risk minimisation measures**

Not applicable.

- **Obligation to conduct post-authorisation measures**

Not applicable.

E. SPECIFIC OBLIGATION TO COMPLETE POST-AUTHORISATION MEASURES FOR THE CONDITIONAL MARKETING AUTHORISATION/THE MARKETING AUTHORISATION UNDER EXCEPTIONAL CIRCUMSTANCES

Not applicable.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (1G, 2.5G, 5G, 10G, 20G AND 30G)

1. NAME OF THE MEDICINAL PRODUCT

KIOVIG 100 mg/ml solution for infusion
Human normal immunoglobulin

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Human protein, 100 mg/ml, at least 98% is IgG.

Maximum immunoglobulin A (IgA) content: 140 micrograms/ml.
1 g / 10 ml
2.5 g / 25 ml
5 g / 50 ml
10 g / 100 ml
20 g / 200 ml
30 g / 300 ml

3. LIST OF EXCIPIENTS

Glycine
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for infusion (10%)
1 vial

5. METHOD AND ROUTE(S) 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 container 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

Baxter AG
Industriestrasse 67
A-1221 Vienna
Austria

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/05/329/001 1 g / 10 ml
EU/1/05/329/002 2.5 g / 25 ml
EU/1/05/329/003 5 g / 50 ml
EU/1/05/329/004 10 g / 100 ml
EU/1/05/329/005 20 g / 200 ml
EU/1/05/329/006 30 g / 300 ml

13. BATCH NUMBER

Lot:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

KIOVIG

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING

VIAL LABEL (5G, 10G, 20G AND 30G)

1. NAME OF THE MEDICINAL PRODUCT

KIOVIG 100 mg/ml solution for infusion
Human normal immunoglobulin

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Human protein, 100 mg/ml, at least 98% is IgG.

Maximum immunoglobulin A (IgA) content: 140 micrograms/ml.

5 g / 50 ml
10 g / 100 ml
20 g / 200 ml
30 g / 300 ml

3. LIST OF EXCIPIENTS

Glycine
Water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for infusion (10%)
1 vial

5. METHOD AND ROUTE(S) 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 container 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

Baxter AG
Industriestrasse 67
A-1221 Vienna
Austria

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/05/329/003 5 g / 50 ml
EU/1/05/329/004 10 g / 100 ml
EU/1/05/329/005 20 g / 200 ml
EU/1/05/329/006 30 g / 300 ml

13. BATCH NUMBER

Lot:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL (1G)

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

KIOVIG 100 mg/ml solution for infusion
Human Normal Immunoglobulin
Intravenous use.

2. METHOD OF ADMINISTRATION

Read the package leaflet before use.

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 g / 10 ml

6. OTHER

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL (2.5G)

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

KIOVIG 100 mg/ml solution for infusion
Human Normal Immunoglobulin
Intravenous use.

2. METHOD OF ADMINISTRATION

Read the package leaflet before use.

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

Lot:

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

2.5 g / 25 ml

6. OTHER

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

B. PACKAGE LEAFLET

Package leaflet: Information for the user

KIOVIG 100 mg/ml solution for infusion
Human normal immunoglobulin

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.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- 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 KIOVIG is and what it is used for

KIOVIG 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 KIOVIG 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 cure of certain inflammatory disorders (autoimmune diseases).

KIOVIG is used for

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

1. Patients with inborn lack of antibody production (primary immunodeficiency syndromes).
2. Patients with a cancer of the blood (chronic lymphocytic leukaemia) that leads to a lack of antibody production and recurrent infections when preventative antibiotics have failed.
3. Patients with cancer of the bone marrow (multiple myeloma) and lack of antibody production with recurrent infections who have failed to respond to a vaccine against certain bacteria (pneumococci).
4. Children and adolescents (age 0 to 18) with AIDS from birth and recurrent bacterial infections.
5. Patients with low antibody production following transplantation of bone marrow cells from another person.

Treatment of patients with certain inflammatory disorders (immunomodulation). There are four 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 in the near future.
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 characterized by slow progressive asymmetrical weakness of limbs without sensory loss (multifocal motor neuropathy, MMN).

2. What you need to know before you use KIOVIG

Do not use KIOVIG:

if you are allergic to immunoglobulins or to any other ingredients of this medicine (listed in section 6).

For example, if you have an immunoglobulin A deficiency, you may have antibodies against immunoglobulin A in your blood. Since KIOVIG contains trace amounts of immunoglobulin A (less than 0.14 mg/ml), you might get an allergic reaction.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using KIOVIG.

How long monitoring is required during the infusion

- You will be carefully observed during the infusion period with KIOVIG to make sure that you do not suffer a reaction. Your doctor will make sure that the rate at which KIOVIG is infused is suitable for you.
- If KIOVIG is administered at a high rate, if you suffer from a condition with low antibody levels in your blood (hypo- or agammaglobulinemia), if you have not received this medicine before or if there has been a long interval (e.g. several weeks) since you last received it, there may be a higher risk of side effects. In such cases, you will be closely monitored during your infusion and for an hour after your infusion has stopped.
- If you have already received KIOVIG previously and received the last treatment recently, then you will only be observed during the infusion and for at least 20 minutes after your infusion.

When slowing or stopping the infusion may be required

In rare cases your body may have previously reacted to specific antibodies and therefore will be sensitive to medicines containing antibodies. This may happen particularly if you suffer from immunoglobulin A deficiency. In these rare cases, you may get allergic reactions such as a sudden fall in blood pressure or shock even if you have already received treatment with medicines containing antibodies in the past.

If you experience a reaction during the infusion of KIOVIG, tell your doctor immediately. Depending on your doctor’s decision the rate of infusion can be slowed or the infusion can be stopped altogether.

Special patient groups

- Your doctor will take special care if you are overweight, elderly, diabetic, or if you suffer from high blood pressure, low blood volume (hypovolaemia), or problems with your blood vessels (vascular diseases). In these conditions, immunoglobulins may increase the risk of cardiac infarction, stroke, lung embolism, or deep vein thrombosis, although only in very rare cases. Tell your doctor if you are diabetic. Although KIOVIG does not contain sugar, it may be diluted with a special sugar solution (5% glucose), which could affect your blood sugar level.
- Your doctor will also take special care if you have or had previously problems with your kidneys, or if you receive medicinal products that may harm your kidney (nephrotoxic medicinal products), as there is a very rare chance of acute kidney failure.
  Please tell your doctor if you have a kidney disorder. Your doctor will choose the appropriate intravenous immunoglobulin for you.

Information on the source material of KIOVIG

KIOVIG is made from human plasma (the liquid part of blood). When medicines are made from human blood or plasma, a number of 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, and the testing of each donation and pools of plasma for signs of virus/infections. Manufacturers of these products also include 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 for the manufacture of KIOVIG 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 virus and parvovirus B19. KIOVIG also contains certain antibodies that can prevent an infection with hepatitis A virus and parvovirus B19.

Other medicines and KIOVIG

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

If you have received a vaccination during the last six weeks and up to three months, the infusion of immunoglobulins like KIOVIG 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 immunoglobulins before you receive your measles vaccine.

Effects on blood tests

KIOVIG contains a wide variety of different antibodies, some of which can affect blood tests. If you have a blood test after receiving KIOVIG, please inform the person taking your blood or your doctor that you have received the medication.

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 made with KIOVIG in pregnant or breast-feeding women. However, medicines that contain antibodies have been used in pregnant or breast-feeding women, and it has been shown that there are no harmful effects on the course of pregnancy or the baby to be expected.
- If you are breast-feeding and receive KIOVIG, the antibodies of the medicine can also be found in the breast milk. Therefore, your baby may be protected from certain infections.

Driving and using machines

Patients may experience reactions (for example dizziness or nausea) during the treatment with KIOVIG, which might affect the ability to drive and use machines. If this happens, you should wait until the reactions have disappeared.

3. How to use KIOVIG

KIOVIG 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 KIOVIG 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 KIOVIG than you should

If you get more KIOVIG 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 physician if you are known to have medical problems.

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.

Below is a list of side effects reported with KIOVIG:

- Very common side effects (may affect more than 1 in 10 people):
  Headache, high blood pressure, nausea, rash, local reactions (e.g. pain and swelling or other reactions at the infusion site), fever, tiredness.
- Common side effects (may affect up to 1 in 10 people):
  Bronchitis, common cold, 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, reduced sense of touch, eye inflammation, rapid heartbeat, flushing, cough, runny nose, chronic cough or wheezing (asthma), stuffy nose, sore throat, shortness of breath, diarrhoea, vomiting, abdominal pain, indigestion, contusion, itchingand hives, dermatitis, reddened skin, pain in your back, pain in your joints, pain in your arms or legs, muscle pain, muscle cramps, muscular weakness, chills, accumulation of fluid under the skin, influenza-like illness, pain or discomfort in the chest, lack of strength or feeling of weakness, indisposition, shaking chills.
- Uncommon side effects (may affect up to 1 in 100 people):
  Chronic infection of the nose, fungal infections, various infections (of the nose and throat, kidney or bladder), sterile inflammation of the layers lining the brain, serious allergic reactions, disorder of the thyroid, excessive response to stimuli, memory impairment, difficulty in speaking, unusual taste in the mouth, impaired balance, involuntary trembling, eye pain or swelling, vertigo, fluid in middle ear, peripheral coldness, vein inflammation, ear and throat swelling, abdominal distension, rapid swelling of the skin, acute inflammation of the skin, cold sweat, increased reaction of the skin to sunlight, excessive sweating also during sleep, muscle twitching, excess of serum protein in the urine, chest tightness, feeling hot, burning sensation, swelling, increased rate of breathing, changes to blood test results.
- Frequency not known (cannot be estimated from available data):
  Destruction of red blood cells, life-threatening allergic shock, transient stroke, stroke, low blood pressure, heart attack, blood clot in a major vein, blood clot in the main artery of the lung, 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 KIOVIG

- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date which is printed 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 particulate matter or discolouration.
- Do not store above 25°C.
- Do not freeze.
- Keep the container in the outer carton in order to protect from light.

6. Contents of the pack and other information

What KIOVIG contains

- The active substance of KIOVIG is human normal immunoglobulin.
- 1 ml of KIOVIG 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 KIOVIG looks like and contents of the pack

KIOVIG is a solution for infusion in vials of 10, 25, 50, 100, 200 or 300 ml. The solution is clear or slightly opalescent and colourless or pale-yellow.
Not all presentations may be marketed.

Marketing Authorisation Holder
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Industriestrasse 67
A-1221 Vienna
Austria

Manufacturer
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B-7860 Lessines
Belgium

Baxter SA
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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

Other sources of information

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

The following information is intended for healthcare professionals only:

Method of administration

- KIOVIG must only be administered intravenously. Other routes of administration have not been evaluated.
- KIOVIG should be infused intravenously at an initial rate of 0.5 ml/kg bodyweight/hour for 30 minutes. If well tolerated, the rate of administration may gradually be increased to a maximum of 6 ml/kg bodyweight/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, KIOVIG 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.

Special precautions

- Any infusion-related adverse events should be treated by lowering the infusion rate or by stopping the infusion.
- It is recommended that every time KIOVIG is administered, the name and batch number of the product is recorded.

Incompatibilities

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

Special precautions for storage

- After dilution to lower concentrations, immediate use is recommended. The in-use stability of KIOVIG after 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; however, these studies did not include the microbial contamination and safety aspects.

Instructions for handling and disposal

- The product must be brought to room or body temperature before use.
- KIOVIG should be inspected visually for particulate matter and discoloration 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. For obtaining an immunoglobulin solution of 50 mg/ml (5%), KIOVIG 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

Indication	Dose	Frequency of injections
Replacement therapy in primary immunodeficiency	starting dose: 0.4-0.8 g/kg thereafter: 0.2-0.8 g/kg	every 3-4 weeks to obtain IgG trough level of at least 5-6 g/l
Replacement therapy in secondary immunodeficiency	0.2-0.4 g/kg	every 3-4 weeks to obtain IgG trough level of at least 5-6 g/l
Congenital AIDS	0.2-0.4 g/kg	every 3-4 weeks
Hypogammaglobulinaemia (<4 g/l) in patients after allogeneic haematopoietic stem cell transplantation	0.2-0.4 g/kg	every 3-4 weeks to obtain IgG trough level above 5g/l
Immunomodulation:		
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	1.6-2 g/kg or 2 g/kg	in divided doses for 2-5 days in association with acetylsalicylic acid in one dose in association with acetylsalicylic acid
Multifocal Motor Neuropathy (MMN)	starting dose: 2 g/kg maintenance dose: 1 g/kg or 2 g/kg	given over 2-5 days every 2-4 weeks or every 4-8 weeks

d = day