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Human Medicines Evaluation Unit

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COMMITTEE FOR PROPRIETARY MEDICINAL PRODUCTS (CPMP)

CORE SPC FOR HUMAN NORMAL IMMUNOGLOBULIN FOR SUBCUTANEOUS AND INTRAMUSCULAR USE (CPMP/BPWG/282/00)

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7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 74 18 85 45
E-mail: mail@emea.eu.int http://www.emea.eu.int

CORE SPC
FOR
HUMAN NORMAL IMMUNOGLOBULIN FOR SUBCUTANEOUS AND INTRAMUSCULAR USE
(SC/IMIg)

The QRD Product Information template with explanatory notes and the convention to be followed for QRD templates** provide general guidance on format and text and should be read in conjunction with the core SPC and the Guideline on Summary of Product Characteristics.*

This core SPC covers human normal immunoglobulin for intramuscular administration defined by the European Pharmacopoeia monograph 0338, as well as human normal immunoglobulin for subcutaneous administration.

* *(http://www.emea.eu.int/htms/human/qrd/qrdplt/01aspc52exp.pdf)*
** *(http://www.emea.eu.int/htms/human/qrd/qrdplt/qrdconventionv5.pdf)*

1. NAME OF THE MEDICINAL PRODUCT

{(Invented) name of product <strength> <pharmaceutical form>}

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Human normal immunoglobulin (<IMIg><SC/IMIg>)

[Product specific information on quantitative composition. Include: IgG subclasses, human protein content and minimum content of IgG (e.g. human protein x g/l of which at least y% is IgG), maximum IgA content.]

<Hepatitis A antibody titre at least 100 IU/ml>

For excipients, see 6.1.

3. PHARMACEUTICAL FORM

[Product specific]

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Replacement therapy in adults <and children> in primary immunodeficiency syndromes such as:

- congenital agammaglobulinaemia and hypogammaglobulinaemia
- common variable immunodeficiency
- severe combined immunodeficiency
- IgG subclass deficiencies with recurrent infections

Replacement therapy in myeloma or chronic lymphatic leukaemia with severe secondary hypogammaglobulinemia and recurrent infections

[Product specific for SC/IMIG with a minimum antibody content for HAV of 100 IU/ml:]

<- Hepatitis A prophylaxis in travellers who present less than 2 weeks before possible exposure, preferably in combination with vaccination.

  For long term hepatitis A prophylaxis, active immunisation is recommended.

- Hepatitis A prophylaxis in persons exposed less than 2 weeks previously.>

4.2 Posology and method of administration

Posology

The dose and dosage regimen is dependent on the indication.

Replacement therapy

The product should be administered via the subcutaneous route.

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

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

The dosage regimen using the subcutaneous route should achieve a sustained level of IgG. A loading dose of at least 0.2-0.5 g/kg may be required. After steady state IgG levels have been attained, maintenance doses are administered at repeated intervals to reach a cumulative monthly dose of the order of 0.4-0.8 g/kg.

Trough levels should be measured in order to adjust the dose and dosage interval.

[Product specific, IMIG with a minimum antibody content for HAV of 100 IU/ml:]

<**Hepatitis A prophylaxis**

The product should be administered via the intramuscular route.

- **Short term Hepatitis A prophylaxis** in travellers who present less than 14 days before possible exposure.

  For stays in endemic areas of less than 3 months a dose of 0.003-0.004 g/kg (0.02 ml/kg) body weight administered intramuscularly is recommended. IMIG with a minimum antibody content for HAV of 100 IU/m can be given in combination with Hepatitis A vaccine.

- **Hepatitis A prophylaxis** in persons exposed less than 2 weeks previously: 0.003-0.004 g/kg (0.02 ml/kg) body weight administered intramuscularly.>

Method of administration

Depending on the indication, human normal immunoglobulin should be administered via the subcutaneous or intramuscular route.

Subcutaneous infusion for home treatment should be initiated by a physician experienced in the guidance of patients for home treatment. The patient will be instructed in the use of a syringe driver, infusion techniques, the keeping of a treatment diary and measures to be taken in case of severe adverse events.

[Product specific, details on infusion rate]

Intramuscular injection must be given by a physician or nurse.

4.3 Contraindications

Hypersensitivity to any of the components.

{(Invented) name of product}] must not be given intravenously.

{(Invented) name of product} must not be administered intramuscularly in cases of severe thrombocytopenia and in other disorders of haemostasis.

4.4 Special warnings and special precautions for use

If {(invented) name of product} is accidentally administered into a blood vessel, patients could develop shock.

The recommended infusion rate stated under "4.2 Method of administration" should be adhered to. Patients should be closely monitored and carefully observed for any adverse events throughout the infusion period.

Certain 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 treatment has been stopped for more than eight weeks.

True hypersensitivity reactions are rare. They can particularly occur in the very rare cases of IgA deficiency with anti-IgA antibodies and these patients should be treated with caution.

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.

Potential complications can often be avoided by ensuring that:

- patients are not sensitive to human normal immunoglobulin, by first injecting the product slowly (see 4.2);
- patients are carefully monitored for any symptoms throughout the infusion period. In particular, patients naïve to human normal immunoglobulin, patients switched from an alternative 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.

Suspicion of allergic or anaphylactic type reactions requires immediate discontinuation of the injection. In case of shock, standard medical treatment should be administered.

[The choice of text indicated between <> depends on whether inactivation/removal procedures in the production process are effective for the specified virus.]

When medicinal products prepared from human blood or plasma are administered, infectious diseases due to transmission of infective agents cannot be totally excluded. This also applies to pathogens of unknown nature. The risk of transmission of infective agents is however reduced by:

- selection of donors by a medical interview and screening of individual donations and plasma pools for HBsAg and antibodies to HIV and HCV,
- testing of plasma pools for HCV genomic material;
- inactivation/removal procedures included in the production process that have been validated using model viruses. These procedures are considered effective for HIV, HCV, HBV <, HAV> <and> <, parvovirus B19>.

Human normal immunoglobulin for intramuscular use has a reassuring viral safety record. <Although the viral inactivation/removal procedures used may be of limited value against non-enveloped viruses,> the hepatitis A and parvovirus B19 antibody content makes an important contribution to the viral safety.

It is strongly recommended that every time that {(invented) name of product} is administered, the name and batch number of the product are recorded.

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.

Interference with serological testing

After injection of immunoglobulin the transitory rise of the various passively transferred antibodies in the patients 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 (reticulocyte count, haptoglobin and Coombs test).

4.6 Pregnancy and lactation

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 and breast-feeding mothers. 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.

4.7 Effects on ability to drive and use machines

No effects on ability to drive and use machines have been observed.

4.8 Undesirable effects

Adverse reactions such as chills, headache, 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.

Local reactions at infusion sites: swelling, soreness, redness, induration, local heat, itching, bruising and rash.

With intramuscular administration, local pain and tenderness can be observed at the injection site.

For information on viral safety see 4.4

4.9 Overdose

Consequences of an overdose are not known.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: immune sera and immunoglobulins: immunoglobulins, normal human, for extravascular 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.

5.2 Pharmacokinetic properties

With subcutaneous administration of human normal immunoglobulin, peak levels are achieved in the recipient's circulation after a delay of {x} days.

Data from clinical trials show that trough levels of {insert product specific} can be maintained by dosing regimens of {insert product specific- dose and intervals}.

With intramuscular administration, human normal immunoglobulin is bioavailable in the recipient's circulation after a delay of 2-3 days.

IgG and IgG-complexes are broken down in cells of the reticuloendothelial system.

5.3 Preclinical safety data

[Product specific]

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

[Product specific.]

6.2 Incompatibilities

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

[Product specific]

6.3 Shelf-life

[Product specific]

6.4 Special precautions for storage

[Product specific]

6.5 Nature and contents of container

[Product specific]

6.6 Instructions for use and handling and disposal

[Product specific, detailed infusion technique]

The product should be brought to room or body temperature before use.

<Total reconstitution should be obtained within {product specific time}.>

The solution should be clear or slightly opalescent. Do not use solutions that are cloudy or have deposits. <Reconstituted products should be inspected visually for particulate matter and discoloration prior to administration.>

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

7. MARKETING AUTHORISATION HOLDER

{Name and address}

8. MARKETING AUTHORISATION NUMBER(S)

[Product specific]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

[Product specific]

10. DATE OF REVISION OF THE TEXT

[Product specific]