European Medicines Agency
Human Medicines Evaluation Unit

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COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE (CHMP)

GUIDELINE ON THE CORE SPC FOR HUMAN PLASMA DERIVED HEPATITIS-B IMMUNOGLOBULIN FOR INTRAMUSCULAR USE (CPMP/BPWG/4222/02)

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CORE SPC
FOR
HUMAN PLASMA DERIVED HEPATITIS B IMMUNOGLOBULIN
FOR INTRAMUSCULAR USE

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.*
*In addition, for the content of sections 4.4 and 4.8 concerning transmissible agents, refer to the current version of the "Note for Guidance on the Warning on Transmissible Agents in SPCs and Package Leaflets for plasma-derived medicinal products" (CPMP/BPWG/BWP/561/03).****

This core SPC covers human hepatitis B immunoglobulin for intramuscular administration defined by European Pharmacopoeia monograph 0722

* *http://www.emea.eu.int/htms/human/qrd/qrdplt/AnnotatedTemplate-H.pdf*
** *http://www.emea.eu.int/htms/human/qrd/qrdplt/qrdconvention.pdf*
*** *http://www.emea.eu.int/pdfs/human/bpwg/056103en.pdf*

1. NAME OF THE MEDICINAL PRODUCT

{(Invented) name, strength, pharmaceutical form}.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Human hepatitis B immunoglobulin

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

For excipients, see section 6.1.

3. PHARMACEUTICAL FORM

[Product specific]

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Immunoprophylaxis of hepatitis B

- In case of accidental exposure in non-immunised subjects (including persons whose vaccination is incomplete or status unknown).
- In haemodialysed patients, until vaccination has become effective.
- In the newborn of a hepatitis B virus carrier-mother.
- In subjects who did not show an immune response (no measurable hepatitis B antibodies) after vaccination and for whom a continuous prevention is necessary due to the continuous risk of being infected with hepatitis B.

<Consideration should also be given to other official guidance on the appropriate use of human hepatitis B immunoglobulin for intramuscular use.>

4.2 Posology and method of administration

Posology

- Prevention of hepatitis B in case of accidental exposure in non-immunised subjects:
  At least 500 IU, depending on the intensity of exposure, as soon as possible after exposure, and preferably within 24 - 72 hours.
- Immunoprophylaxis of hepatitis B in haemodialysed patients:
  8-12 IU/kg with a maximum of 500 IU, every 2 months until seroconversion following vaccination.
- Prevention of hepatitis B in the newborn, of a hepatitis B virus carrier-mother, at birth or as soon as possible after birth:
  30-100 IU/kg. The hepatitis B immunoglobulin administration may need to be repeated until seroconversion following vaccination.

In all these situations, vaccination against hepatitis B virus is highly recommended. The first vaccine dose can be injected the same day as human hepatitis B immunoglobulin, however in different sites.

In subjects who did not show an immune response (no measurable hepatitis B antibodies) after vaccination, and for whom continuous prevention is necessary, administration of 500 IU to adults and 8 IU/kg to children every 2 months can be considered; a minimum protective antibody titre is considered to be 10 mIU/mL.

<Consideration should also be given to dose and dose schedules for human hepatitis B immunoglobulin for intramuscular use recommended in other official guidance.>

Method of administration

{(Invented) name of product} should be administered via the intramuscular route.

If a large volume (>2 ml for children or >5 ml for adults) is required, it is recommended to administer this in divided doses at different sites.

When simultaneous vaccination is necessary, the immunoglobulin and the vaccine should be administered at two different sites.

If intramuscular administration is contraindicated (bleeding disorders), the injection can be administered subcutaneously if no intravenous product is available. [*Product specific*] <However, it should be noted that there are no clinical efficacy data to support administration by the subcutaneous route.>

4.3 Contraindications

Hypersensitivity to any of the components.

Hypersensitivity to human immunoglobulins.

4.4 Special warnings and precautions for use

Ensure that {(Invented) name of product} is not administered into a blood vessel, because of the risk of shock.

If the recipient is a carrier of HBsAg, there is no benefit in administering this product.

True hypersensitivity reactions are rare.

[*Product specific*]

<{(Invented) name of the product} contains a small quantity of IgA. Individuals who are deficient in IgA have the potential for developing IgA antibodies and may have anaphylactic reactions after administration of blood components containing IgA. The physician must therefore weigh the benefit of treatment with {(invented) name of product} against the potential risk of hypersensitivity reactions.>

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

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

[The text to be inserted here for transmissible agents should be in accordance with the current version of the guideline on the Warning on Transmissible Agents in SPCs and Package Leaflets for plasma-derived medicinal products (CPMP/BPWG/BWP/561/03).]

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

Live attenuated virus vaccines

Immunoglobulin administration may interfere with the development of an immune response to live attenuated virus vaccines such as rubella, mumps, measles and varicella for a period of 3 months. After administration of this product, an interval of at least 3 months should elapse before vaccination with live attenuated virus vaccines.

Human hepatitis B immunoglobulin should be administrated three to four weeks after vaccination with such a live attenuated vaccine; in case administration of human hepatitis B immunoglobulin is essential within three to four weeks after vaccination, then revaccination should be performed three months after the administration of human hepatitis B immunoglobulin.

Interference with serological testing

After injection 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 antiglobulin test (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. 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

<There are no robust data on the frequency of undesirable effects from clinical trials. The following undesirable effects have been reported: >

<The following undesirable effects have been reported <from {x} patients in clinical studies> <and from post-marketing experience> >

[If there are robust data on the frequency of undesirable effects from clinical trials the section should be prepared in line with the general provisions of the SPC guideline.]

MedDRA Standard System Organ Class	**Undesirable effects**	**<Frequency>**
Immune system disorders	Hypersensitivity, anaphylactic shock	
Nervous system disorders	Headache	
Cardiac disorders	Tachycardia	
Vascular disorders	Hypotension	
Gastrointestinal disorders	Nausea, vomiting	
Skin and subcutaneous tissue disorders	Skin reaction, erythema, itching, pruritus	
Musculoskeletal, connective tissue and bone disorders	Arthralgia	
General disorders and administration site conditions	Fever, malaise, chill At injection site: swelling, pain, erythema, induration, warmth, pruritus, rash, itching	

[The text to be inserted here for transmissible agents should be in accordance with the current version of the guideline on the Warning on Transmissible Agents in SPCs and Package Leaflets for plasma-derived medicinal products (CPMP/BPWG/BWP/561/03).]

4.9 Overdose

Consequences of an overdose are not known.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: immune sera and immunoglobulins

- Hepatitis B immunoglobulin ATC code: J06BB04

Human hepatitis B immunoglobulin contains mainly immunoglobulin G (IgG) with a specifically high content of antibodies against hepatitis B virus surface antigen (HBs).

5.2 Pharmacokinetic properties

Human hepatitis B immunoglobulin for intramuscular use is bioavailable in the recipient's circulation after a delay of 2-3 days.

Human hepatitis B immunoglobulin has a half-life of about 3-4 weeks. This half-life may vary from patient to patient.

IgG and IgG-complexes are broken down in 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]

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

<Total reconstitution should be obtained within *[product specific time]*.>

The colour can vary from colourless to pale-yellow up to light brown. 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]