DIVIZJONI TAS-SAHHA

Palazzo Castellania, 15, Triq il-Merkanti,
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Malta

HEALTH DIVISION

Palazzo Castellania, 15 Merchants Street,
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DH Circular No 50/2007

6th March 2007

Attention all Consultants
Medical Officers
Pharmacists
Nurses

Re: Properties of the Anti-D Immunoglobulin Preparation currently available

The preparation, volume, posology and method of administration of the Anti-D immunoglobulin which is currently available are different from the previous one.

Each vial contains 1500IU Human Anti-D immunoglobulin. The volume of the solution that needs to be administered to give the correct dose is stated on the label. The volume can vary depending on the batch available as stated on the relevant Patient Information Leaflet (PIL).

The posology and doses required are specified in the annexed table and Summary of Product Characteristics (SPCs).

For your attention please,

Dr R Busuttil
Director General Health

D-GAM®, Human Anti-D Immunoglobulin now has three separate Summary of Product Characteristics – one for each dose strength.

Annex 1

Bio Products Laboratory

SDS3A

SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of Product: **D-GAM®, Human Anti-D Immunoglobulin**

2. Qualitative and Quantitative Composition:

Human Anti-D Immunoglobulin Ph.Eur.*
Each vial contains: 5 - 50 mg/L protein (250 and 500 iu vials) or 20 - 180 mg/L protein (1,500 and 2,500 iu vials) of which at least 95% is gammaglobulin (IgG). The product contains less than 0.02% w/w of IgA. For excipients see 6.1.
The product is prepared from plasma from RhD-negative screened donors who have been immunised against RhD antigen and contains specific antibodies against erythrocyte RhD antigen. Donors are selected from the USA.
*The product is presented in three different concentrations but the highest concentration is filled in different volumes to achieve two dose presentations. The product is therefore available in four nominal doses, namely 250 iu per vial, 500 iu per vial, 1,500 iu per vial and 2,500 iu per vial.

3. Pharmaceutical Form: A solution for injection.

4. Clinical Particulars:

4.1 Therapeutic indications

Prevention of RhD immunisation in RhD negative women:

i. Pregnancy/delivery of a RhD positive baby.
ii. Abortion/threatened abortion, ectopic pregnancy or hydatidiform mole.
iii. After ante-partum haemorrhage (APH), amniocentesis, chorionic biopsy or obstetric manipulative procedure e.g. external version, or abdominal trauma, which may cause transplacental haemorrhage (TPH).

Treatment of RhD negative patients after incompatible transfusions of RhD positive blood or other products containing red blood cells (*e.g.* platelets).

4.2 Posology and method of administration

Posology

a) Post-Natal Dosage
The recommended dose is 500 iu.
For postnatal use, the product should be administered as soon as possible within 72 hours of delivery.
If a large fetomaternal haemorrhage is suspected, its extent should be determined by a suitable method and additional doses of anti-D should be administered as indicated.

b) Ante-Natal Prophylaxis
500 iu given at both 28 and 34 weeks of gestation.

c) Following a Potentially Sensitising Event During Pregnancy
D-GAM® should be administered as soon as possible and no later than 72 hours after the event.
Up to 20 weeks gestation: recommended dose is 250 iu per incident.
After 20 weeks gestation: recommended dose is 500 iu per incident. A test for the size of the FMH should be performed when anti-D is given after 20 weeks and additional doses of anti-D should be administered as indicated.

d) Prevention of Immunisation in RhD Negative Patients Given Blood Components Containing RhD Positive Cells
Recommended doses: 125 iu per ml of transfused RhD positive red cells; 250 iu per three adult doses of platelets.

Method of administration
For intramuscular use (preferably into the deltoid muscle).
D-GAM® is for single injection only.
In the case of haemorrhagic disorders, where intramuscular injections are contra-indicated, Anti-D immunoglobulin may be administered subcutaneously. Careful manual pressure with a compress should be applied to the site after injection.
If large total doses (>5 ml) are required, it is advisable to administer them in divided doses at different sites.

4.3 Contraindications

Hypersensitivity to any of the components.

4.4 Special warnings and special precautions for use

Do not administer this product intravenously (risk of shock).
In the case of post-partum use, the product is intended for maternal administration. It should not be given to the newborn infant.
The product is not intended for use in RhD positive individuals.
Patients should be observed for at least 20 minutes after administration.
If symptoms of allergic or anaphylactic type reactions occur, immediate discontinuation of the administration is required.
True hypersensitivity reactions are rare but allergic type responses to Anti-D immunoglobulin may occur. Patients should be informed of the early signs of hypersensitivity reactions including hives, generalised urticaria, tightness of the chest, wheezing, hypotension and anaphylaxis. The treatment required depends on the nature and severity of the side effect. In case of shock, the current medical standards for shock treatment should be observed.
D-GAM® contains a small quantity of IgA. Although anti-D immunoglobulin has been used successfully to treat selected IgA deficient individuals, the attending physician must weigh the benefit against the potential risks of hypersensitivity reactions. Individuals deficient in IgA have a potential for development of IgA antibodies and anaphylactic reactions after administration of blood components containing IgA.
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 hitherto unknown nature. The risk of transmission of infective agents is however reduced by:

(i) Selection of donors by a medical interview and screening of individual donations and plasma pools for HBsAg and antibodies to HIV and HCV.
(ii) Testing of plasma pools for HCV genomic material.
(iii) Inactivation/removal procedures included in the production process that have been validated using model viruses. These procedures are considered effective for HIV, HCV and HBV. The specific virus inactivation process used is solvent/detergent treatment.

The viral removal/inactivation procedures may be of limited value against non-enveloped viruses such as hepatitis A virus or parvovirus B19.
In the interest of patients, it is recommended that, whenever possible, every time that D-GAM® is administered to them, the name and batch number of the product is registered.

4.5 Interactions with other medicaments and other forms of interactions

Active immunisation with live virus vaccines (e.g. measles, mumps or rubella) should be postponed until 3 months after the administration of Anti-D immunoglobulin, as the efficacy of the live virus vaccine may be impaired. If Anti-D immunoglobulin needs to be administered within 2-4 weeks of a live virus vaccination, then the efficacy of such a vaccination may be impaired.
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.
The results of blood typing and antibody testing, including the Coombs' or antiglobulin test, are significantly affected by the administration of anti-D immunoglobulin.

4.6 Pregnancy and lactation
This medicinal product is used in pregnancy.

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
Local pain and tenderness can be observed at the injection site; this can be prevented by dividing larger doses over several injection sites.
Occasionally fever, malaise, headache, cutaneous reactions and chills occur.
In rare cases: nausea, vomiting, hypotension, tachycardia and allergic or anaphylactic type reactions, including dyspnoea and shock, are reported, even when the patient has shown no hypersensitivity to previous administration.
For information on viral safety see 4.4.

4.9 Overdose
No data are available on overdosage. Patients with incompatible transfusion who receive a large dose of anti-D immunoglobulin should be monitored clinically and by biological parameters, because of the risk of haemolytic reaction.
In other RhD negative individuals, overdosage should not lead to more frequent or more severe undesirable effects than the normal dose.

5. Pharmacological Properties:

5.1 Pharmacodynamic properties
Pharmacotherapeutic group: immune sera and immunoglobulins: Anti-D (Rh) immunoglobulin. ATC code: J06BB01.
Anti-D immunoglobulin contains specific antibodies (IgG) against the RhD antigen of human erythrocytes.

5.2 Pharmacokinetic properties
Measurable levels of antibodies are obtained approximately 8 hours after intramuscular injection. Peak serum levels are usually achieved 2 to 3 days later.
The half-life in the circulation of individuals with normal IgG levels is 3 to 4 weeks.
IgG and IgG-complexes are broken down in cells of the reticuloendothelial system.

5.3 Preclinical safety data
D-GAM® is a preparation of human plasma proteins, so safety testing in animals is not particularly relevant to the safety of use in man. Acute toxicity studies in rat and mouse showed species specific reactions, which bear no relevance to administration in humans.
Repeated dose safety testing is impracticable due to the induction of and interference with antibodies to human protein. Clinical experience provides no sign of tumourigenic and mutagenic effects.

6. Pharmaceutical Particulars:

6.1 List of excipients
Sodium chloride
Glycine
Sodium acetate trihydrate
Sodium hydroxide

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

6.3 Shelf-life
Stored at 2° - 8°C: 2 years.
Stored at 25°C: 1 week.

6.4 Special precautions for storage

D-GAM® should be stored in the original container at 2°C to 8°C. Storage for up to one week at ambient temperatures (25°C) in the original container is not detrimental. DO NOT FREEZE.

The condition of date-expired, or incorrectly stored product cannot be guaranteed. Such product may be unsafe, and should not be used.

6.5 Nature and contents of container

Neutral borosilicate glass vial (Type I Ph.Eur.) with overseal consisting of a halobutyl rubber wad (Type I Ph.Eur.), clear lacquered aluminium skirt and flip-off polypropylene cap.

6.6 Instruction for use and handling and disposal

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

The solution should be clear or slightly opalescent. Do not use solutions which are cloudy or have deposits.

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

7. Holder of Marketing Authorisation:

Bio Products Laboratory
Dagger Lane
Elstree
Hertfordshire
WD6 3BX
United Kingdom.

8. Marketing Authorisation Number:

PL 08801/0047 - 250 iu dose size. POM

9. Date of First Authorisation/Renewal of Authorisation:

31 July 2000

10. Date of (Partial) Revision of the Text:

November 2004 Version code: SDS3A

Bio Products Laboratory

SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of Product: # D-GAM®, Human Anti-D Immunoglobulin

2. Qualitative and Quantitative Composition:

Human Anti-D Immunoglobulin Ph.Eur.*
Each vial contains: 5 - 50 mg/L protein (250 and 500 iu vials) or 20 - 180 mg/L protein (1,500 and 2,500 iu vials) of which at least 95% is gammaglobulin (IgG). The product contains less than 0.02% w/w of IgA. For excipients see 6.1.
The product is prepared from plasma from RhD-negative screened donors who have been immunised against RhD antigen and contains specific antibodies against erythrocyte RhD antigen. Donors are selected from the USA.
*The product is presented in three different concentrations but the highest concentration is filled in different volumes to achieve two dose presentations. The product is therefore available in four nominal doses, namely 250 iu per vial, 500 iu per vial, 1,500 iu per vial and 2,500 iu per vial.

3. Pharmaceutical Form: A solution for injection.

4. Clinical Particulars:

4.1 Therapeutic indications

Prevention of RhD immunisation in RhD negative women:
i. Pregnancy/delivery of a RhD positive baby.
ii. Abortion/threatened abortion, ectopic pregnancy or hydatidiform mole.
iii. After ante-partum haemorrhage (APH), amniocentesis, chorionic biopsy or obstetric manipulative procedure e.g. external version, or abdominal trauma, which may cause transplacental haemorrhage (TPH).
Treatment of RhD negative patients after incompatible transfusions of RhD positive blood or other products containing red blood cells (e.g. platelets).

4.2 Posology and method of administration

Posology
a) Post-Natal Dosage
The recommended dose is 500 iu.
For postnatal use, the product should be administered as soon as possible within 72 hours of delivery.
If a large fetomaternal haemorrhage is suspected, its extent should be determined by a suitable method and additional doses of anti-D should be administered as indicated.
b) Ante-Natal Prophylaxis
500 iu given at both 28 and 34 weeks of gestation.
c) Following a Potentially Sensitising Event During Pregnancy
D-GAM® should be administered as soon as possible and no later than 72 hours after the event.
Up to 20 weeks gestation: recommended dose is 250 iu per incident.
After 20 weeks gestation: recommended dose is 500 iu per incident. A test for the size of the FMH should be performed when anti-D is given after 20 weeks and additional doses of anti-D should be administered as indicated.
d) Prevention of Immunisation in RhD Negative Patients Given Blood Components Containing RhD Positive Cells
Recommended doses: 125 iu per ml of transfused RhD positive red cells; 250 iu per three adult doses of platelets.

Method of administration
For intramuscular use (preferably into the deltoid muscle).
D-GAM® is for single injection only.
In the case of haemorrhagic disorders, where intramuscular injections are contra-indicated, Anti-D immunoglobulin may be administered subcutaneously. Careful manual pressure with a compress should be applied to the site after injection.
If large total doses (>5 ml) are required, it is advisable to administer them in divided doses at different sites.

4.3 Contraindications
Hypersensitivity to any of the components.

4.4 Special warnings and special precautions for use
Do not administer this product intravenously (risk of shock).
In the case of post-partum use, the product is intended for maternal administration. It should not be given to the newborn infant.
The product is not intended for use in RhD positive individuals.
Patients should be observed for at least 20 minutes after administration.
If symptoms of allergic or anaphylactic type reactions occur, immediate discontinuation of the administration is required.
True hypersensitivity reactions are rare but allergic type responses to Anti-D immunoglobulin may occur. Patients should be informed of the early signs of hypersensitivity reactions including hives, generalised urticaria, tightness of the chest, wheezing, hypotension and anaphylaxis. The treatment required depends on the nature and severity of the side effect. In case of shock, the current medical standards for shock treatment should be observed.
D-GAM® contains a small quantity of IgA. Although anti-D immunoglobulin has been used successfully to treat selected IgA deficient individuals, the attending physician must weigh the benefit against the potential risks of hypersensitivity reactions. Individuals deficient in IgA have a potential for development of IgA antibodies and anaphylactic reactions after administration of blood components containing IgA.
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 hitherto unknown nature. The risk of transmission of infective agents is however reduced by:
(i) Selection of donors by a medical interview and screening of individual donations and plasma pools for HBsAg and antibodies to HIV and HCV.
(ii) Testing of plasma pools for HCV genomic material.
(iii) Inactivation/removal procedures included in the production process that have been validated using model viruses. These procedures are considered effective for HIV, HCV and HBV. The specific virus inactivation process used is solvent/detergent treatment.

The viral removal/inactivation procedures may be of limited value against non-enveloped viruses such as hepatitis A virus or parvovirus B19.
In the interest of patients, it is recommended that, whenever possible, every time that D-GAM® is administered to them, the name and batch number of the product is registered.

4.5 Interactions with other medicaments and other forms of interactions
Active immunisation with live virus vaccines (e.g. measles, mumps or rubella) should be postponed until 3 months after the administration of Anti-D immunoglobulin, as the efficacy of the live virus vaccine may be impaired. If Anti-D immunoglobulin needs to be administered within 2-4 weeks of a live virus vaccination, then the efficacy of such a vaccination may be impaired.
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.
The results of blood typing and antibody testing, including the Coombs' or antiglobulin test, are significantly affected by the administration of anti-D immunoglobulin.

4.6 Pregnancy and lactation
This medicinal product is used in pregnancy.

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
Local pain and tenderness can be observed at the injection site; this can be prevented by dividing larger doses over several injection sites.
Occasionally fever, malaise, headache, cutaneous reactions and chills occur.
In rare cases: nausea, vomiting, hypotension, tachycardia and allergic or anaphylactic type reactions, including dyspnoea and shock, are reported, even when the patient has shown no hypersensitivity to previous administration.
For information on viral safety see 4.4.

4.9 Overdose
No data are available on overdosage. Patients with incompatible transfusion who receive a large dose of anti-D immunoglobulin should be monitored clinically and by biological parameters, because of the risk of haemolytic reaction.
In other RhD negative individuals, overdosage should not lead to more frequent or more severe undesirable effects than the normal dose.

5. Pharmacological Properties:

5.1 Pharmacodynamic properties
Pharmacotherapeutic group: immune sera and immunoglobulins: Anti-D (Rh) immunoglobulin. ATC code: J06BB01.
Anti-D immunoglobulin contains specific antibodies (IgG) against the RhD antigen of human erythrocytes.

5.2 Pharmacokinetic properties
Measurable levels of antibodies are obtained approximately 8 hours after intramuscular injection. Peak serum levels are usually achieved 2 to 3 days later.
The half-life in the circulation of individuals with normal IgG levels is 3 to 4 weeks.
IgG and IgG-complexes are broken down in cells of the reticuloendothelial system.

5.3 Preclinical safety data
D-GAM® is a preparation of human plasma proteins, so safety testing in animals is not particularly relevant to the safety of use in man. Acute toxicity studies in rat and mouse showed species specific reactions, which bear no relevance to administration in humans.
Repeated dose safety testing is impracticable due to the induction of and interference with antibodies to human protein. Clinical experience provides no sign of tumourigenic and mutagenic effects.

6. Pharmaceutical Particulars:

6.1 List of excipients
Sodium chloride
Glycine
Sodium acetate trihydrate
Sodium hydroxide

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

6.3 Shelf-life
Stored at 2° - 8°C: 2 years.
Stored at 25°C: 1 week.

6.4 Special precautions for storage

D-GAM® should be stored in the original container at 2°C to 8ºC. Storage for up to one week at ambient temperatures (25ºC) in the original container is not detrimental. DO NOT FREEZE.

The condition of date-expired, or incorrectly stored product cannot be guaranteed. Such product may be unsafe, and should not be used.

6.5 Nature and contents of container

Neutral borosilicate glass vial (Type I Ph.Eur.) with overseal consisting of a halobutyl rubber wad (Type I Ph.Eur.), clear lacquered aluminium skirt and flip-off polypropylene cap.

6.6 Instruction for use and handling and disposal

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

The solution should be clear or slightly opalescent. Do not use solutions which are cloudy or have deposits.

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

7. Holder of Marketing Authorisation:

Bio Products Laboratory
Dagger Lane
Elstree
Hertfordshire
WD6 3BX
United Kingdom.

8. Marketing Authorisation Number:

PL 08801/0048 - 500 iu dose size. POM

9. Date of First Authorisation/Renewal of Authorisation:

31 July 2000

10. Date of (Partial) Revision of the Text:

November 2004 Version code: SDS3B

Bio Products Laboratory

SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of Product: **D-GAM®, Human Anti-D Immunoglobulin**

2. Qualitative and Quantitative Composition:

Human Anti-D Immunoglobulin Ph.Eur.*
Each vial contains: 5 - 50 mg/L protein (250 and 500 iu vials) or 20 – 180 mg/L protein (1,500 and 2,500 iu vials) of which at least 95% is gammaglobulin (IgG). The product contains less than 0.02% w/w of IgA. For excipients see 6.1.
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3. Pharmaceutical Form: A solution for injection.

4. Clinical Particulars:

4.1 Therapeutic indications

Prevention of RhD immunisation in RhD negative women:

i. Pregnancy/delivery of a RhD positive baby.
ii. Abortion/threatened abortion, ectopic pregnancy or hydatidiform mole.
iii. After ante-partum haemorrhage (APH), amniocentesis, chorionic biopsy or obstetric manipulative procedure e.g. external version, or abdominal trauma, which may cause transplacental haemorrhage (TPH).

Treatment of RhD negative patients after incompatible transfusions of RhD positive blood or other products containing red blood cells (e.g. platelets).

4.2 Posology and method of administration

Posology

a) Post-Natal Dosage
The recommended dose is 500 iu.
For postnatal use, the product should be administered as soon as possible within 72 hours of delivery.
If a large fetomaternal haemorrhage is suspected, its extent should be determined by a suitable method and additional doses of anti-D should be administered as indicated.

b) Ante-Natal Prophylaxis
500 iu given at both 28 and 34 weeks of gestation.

c) Following a Potentially Sensitising Event During Pregnancy
D-GAM® should be administered as soon as possible and no later than 72 hours after the event.
Up to 20 weeks gestation: recommended dose is 250 iu per incident.
After 20 weeks gestation: recommended dose is 500 iu per incident. A test for the size of the FMH should be performed when anti-D is given after 20 weeks and additional doses of anti-D should be administered as indicated.

d) Prevention of Immunisation in RhD Negative Patients Given Blood Components Containing RhD Positive Cells
Recommended doses: 125 iu per ml of transfused RhD positive red cells; 250 iu per three adult doses of platelets.

Method of administration
For intramuscular use (preferably into the deltoid muscle).
D-GAM® is for single injection only.
In the case of haemorrhagic disorders, where intramuscular injections are contra-indicated, Anti-D immunoglobulin may be administered subcutaneously. Careful manual pressure with a compress should be applied to the site after injection.
If large total doses (>5 ml) are required, it is advisable to administer them in divided doses at different sites.

4.3 Contraindications
Hypersensitivity to any of the components.

4.4 Special warnings and special precautions for use
Do not administer this product intravenously (risk of shock).
In the case of post-partum use, the product is intended for maternal administration. It should not be given to the newborn infant.
The product is not intended for use in RhD positive individuals.
Patients should be observed for at least 20 minutes after administration.
If symptoms of allergic or anaphylactic type reactions occur, immediate discontinuation of the administration is required.
True hypersensitivity reactions are rare but allergic type responses to Anti-D immunoglobulin may occur. Patients should be informed of the early signs of hypersensitivity reactions including hives, generalised urticaria, tightness of the chest, wheezing, hypotension and anaphylaxis. The treatment required depends on the nature and severity of the side effect. In case of shock, the current medical standards for shock treatment should be observed.
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(ii) Testing of plasma pools for HCV genomic material.
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In the interest of patients, it is recommended that, whenever possible, every time that D-GAM® is administered to them, the name and batch number of the product is registered.

4.5 Interactions with other medicaments and other forms of interactions
Active immunisation with live virus vaccines (e.g. measles, mumps or rubella) should be postponed until 3 months after the administration of Anti-D immunoglobulin, as the efficacy of the live virus vaccine may be impaired. If Anti-D immunoglobulin needs to be administered within 2-4 weeks of a live virus vaccination, then the efficacy of such a vaccination may be impaired.
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.
The results of blood typing and antibody testing, including the Coombs' or antiglobulin test, are significantly affected by the administration of anti-D immunoglobulin.

4.6 Pregnancy and lactation
This medicinal product is used in pregnancy.

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
Local pain and tenderness can be observed at the injection site; this can be prevented by dividing larger doses over several injection sites.
Occasionally fever, malaise, headache, cutaneous reactions and chills occur.
In rare cases: nausea, vomiting, hypotension, tachycardia and allergic or anaphylactic type reactions, including dyspnoea and shock, are reported, even when the patient has shown no hypersensitivity to previous administration.
For information on viral safety see 4.4.

4.9 Overdose
No data are available on overdosage. Patients with incompatible transfusion who receive a large dose of anti-D immunoglobulin should be monitored clinically and by biological parameters, because of the risk of haemolytic reaction.
In other RhD negative individuals, overdosage should not lead to more frequent or more severe undesirable effects than the normal dose.

5. Pharmacological Properties:

5.1 Pharmacodynamic properties
Pharmacotherapeutic group: immune sera and immunoglobulins: Anti-D (Rh) immunoglobulin. ATC code: J06BB01.
Anti-D immunoglobulin contains specific antibodies (IgG) against the RhD antigen of human erythrocytes.

5.2 Pharmacokinetic properties
Measurable levels of antibodies are obtained approximately 8 hours after intramuscular injection. Peak serum levels are usually achieved 2 to 3 days later.
The half-life in the circulation of individuals with normal IgG levels is 3 to 4 weeks.
IgG and IgG-complexes are broken down in cells of the reticuloendothelial system.

5.3 Preclinical safety data
D-GAM® is a preparation of human plasma proteins, so safety testing in animals is not particularly relevant to the safety of use in man. Acute toxicity studies in rat and mouse showed species specific reactions, which bear no relevance to administration in humans.
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6. Pharmaceutical Particulars:

6.1 List of excipients
Sodium chloride
Glycine
Sodium acetate trihydrate
Sodium hydroxide

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

6.3 Shelf-life
Stored at 2° - 8°C: 2 years.
Stored at 25°C: 1 week.

6.4 Special precautions for storage

D-GAM® should be stored in the original container at 2°C to 8°C. Storage for up to one week at ambient temperatures (25°C) in the original container is not detrimental. DO NOT FREEZE.

The condition of date-expired, or incorrectly stored product cannot be guaranteed. Such product may be unsafe, and should not be used.

6.5 Nature and contents of container

Neutral borosilicate glass vial (Type I Ph.Eur.) with overseal consisting of a halobutyl rubber wad (Type I Ph.Eur.), clear lacquered aluminium skirt and flip-off polypropylene cap.

6.6 Instruction for use and handling and disposal

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

The solution should be clear or slightly opalescent. Do not use solutions which are cloudy or have deposits.

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

7. Holder of Marketing Authorisation:

Bio Products Laboratory
Dagger Lane
Elstree
Hertfordshire
WD6 3BX
United Kingdom.

8. Marketing Authorisation Number:

PL 08801/0049 - 1,500 iu and 2,500 iu dose sizes. POM

9. Date of First Authorisation/Renewal of Authorisation:

31 July 2000

10. Date of (Partial) Revision of the Text:

November 2004 Version code: SDS3C

	D-GAM® Human Anti-D Immunoglobulin (1,2)
Production Company	BPL
Qualitative and Quantitative composition	1500 IU Human Anti-D Immunoglobulin Ph Eur. 20-180 mg/L protein of which at least 95% is IgG
Presentation and Volume	Vial containing single dose of 1500 IU Volume to give correct dose as stated on the vial label.
Posology and Method of Adminsitration	**Postpartum prophylaxis (within 72 hours of delivery) standard recommended doses**
	500 IU
	Antepartum prophylaxis
	500 IU at 28 weeks and 34 weeks of gestation
	Following a potential sensitising event during pregnancy
	Up to 20 weeks gestation
	250 IU per incident
	After 20 weeks gestation
	500 IU per incident *A test for the size of the fetomaternal haemorrhage should be performed when Anti-D given after 20 weeks gestation and additional doses of anti-D should be administered as indicated*
	Prevention of Immunisation in RhD Negative Patients Given Blood Components Containing RhD Positive Cells
	125 IU per ml of transfused RhD positive red cells
	250 IU per three adult doses of platelets

References: (1) BPL UK (2004) D-GAM, Human Anti-D Immunoglobulin SPC. Available at http://www.bpl.co.uk. Last accessed 2nd March, 2007; (2) BPL UK (2003) D-GAM, Human Anti-D Immunoglobulin PIL Version SDL2 Available at http://www.bpl.co.uk. Last accessed 2nd March, 2007.

D-GAM®
HUMAN ANTI-D IMMUNOGLOBULIN

Please read this carefully before using this medicine. If you do not follow the advice you may come to harm. This leaflet tells you how to use this product. If you have any questions, ask your doctor or the manufacturer.

WHAT IS YOUR MEDICINE?
The product is called D-GAM®. It is a solution for injection containing gammaglobulin (antibodies which can protect against certain infections or conditions), with an increased level of Anti-D antibody. It is obtained from blood plasma from screened donors. These donors are selected from the USA. The product is for intramuscular injection (only to be injected into muscles), and is only available on a doctor's prescription.

This product comes in a vial as a 5-180 mg/ml solution of human plasma protein (depending on the dose) of which not less than 95% is IgG (immunoglobulin G, or gammaglobulin, the antibody-containing part of human plasma). The product also contains sodium chloride at the same strength as is normally found in your body, glycine to enhance stability and sodium acetate with a small quantity of sodium hydroxide to control acidity/alkalinity during manufacture. The product is available in four dose sizes of 250 iu, 500 iu, 1,500 iu and 2,500 iu. The volume of the solution that needs to be administered to give the correct dose is stated on the label.

The product is manufactured and marketed by BPL, Bio Products Laboratory, Dagger Lane, Elstree, Herts., WD6 3BX, U.K.

WHAT IS YOUR MEDICINE USED FOR?
This medicine is used to prevent women of a certain blood type (Rh(D) negative), and of child-bearing age, becoming sensitised (reactive) to Rh(D) positive red blood cells.

The prevention of sensitisation, in these situations, has been shown to prevent destruction of the baby's red blood cells if Rh(D) positive (either in the current pregnancy or, more particularly, in future pregnancies).

It should be used:

1. Soon after giving birth to a baby whose red blood cells are Rh(D) positive, irrespective of the ABO blood group of the mother;
2. Soon after an abortion when sensitisation is possible;
3. Soon after any incident or intervention during pregnancy which might lead to bleeding across the placenta;
4. As a routine preventative measure during pregnancy (usually at 28 and 34 weeks);
5. Soon after blood components containing Rh(D) positive red blood cells have been given, for any reason.

Your doctor or midwife will tell you if it is advisable for you to have this medicine.

WHEN SHOULD YOU NOT USE THIS MEDICINE?
If you suffer from any blood disorders, which interfere with clotting or if you think you might be allergic to this product, you must tell your doctor before this product is injected.

WHEN YOU SHOULD BE CAREFUL ABOUT USING THIS MEDICINE
This product must <u>not</u> be injected intravenously (into veins), since it may cause a severe reaction if given in this way. Injections must be intramuscular, and care should be taken to draw back the plunger of the syringe before injection in order to be sure that the needle is not in a blood vessel. If large total doses over 5 ml need to be given, it is advisable to split the dose and give the injections into different sites of the body.

This medicine is <u>not</u> for injection into the newborn baby.

True allergic reactions to this product are rare, when it is injected intramuscularly as directed. In the case of shock, urgent medical advice is needed.

If you start to feel unwell when this medicine is being injected, then the injection must be stopped immediately. You should remain with another person for at least twenty minutes after injection.

You should tell your doctor of any vaccinations you have recently had or are about to have.

Besides Anti-D, this product provides you with a range of antibodies. These antibodies will interfere with the response to some vaccines, especially MMR (measles, mumps and rubella) and varicella (chickenpox) vaccines. Such vaccinations should be given at least three weeks before D-GAM® or not until three months after. D-GAM® is unlikely to contain an antibody to yellow fever; so this vaccine can be given whenever needed.

This product will raise the level of various antibodies in your blood for several weeks. If you require a blood test during this period, tell your doctor when you last had this product injected, as misleading positive results may occur with certain tests.

This medicine has been widely used for many years in pregnant women without any harmful effects. There are no known effects on the ability to drive or operate machinery after injection of this product.

HOW MUCH OF YOUR MEDICINE TO TAKE?
DO NOT EXCEED RECOMMENDED DOSE.

Following Birth:
The usual dose is 500 iu, this may be increased in certain circumstances dependent on the results of a particular blood test (e.g. Kleihauer).

Preventative Measures Before Birth:
500 iu given at both 28 and 34 weeks.

Following An Incident or Intervention During Pregnancy:
Up to 20 weeks, the recommended dose is 250 iu; after 20 weeks the recommended dose is 500 iu.

Prevention of Immunisation (Protection) in Patients Given Blood Components Containing Red Cells of a Certain Blood Type (Rh(D) positive):
The recommended dose is 125 iu per ml of red cells which have been injected or 250 iu for every 3 adult doses of platelets from Rh(D) positive donors which have been given.

Your doctor or midwife will tell you if it is advisable for you to have this medicine.

INJECTION OF THE MEDICINE
This product must be given by slow injection into a large muscle. It should not be injected intravenously.

This medicine should be injected as soon as it is convenient after delivery, but within 72 hours whenever possible to have the best effect. Injection of this medicine, due to an incident or intervention during pregnancy, should be as close to the time of the incident as possible.

This product is for single injection only. Safely throw away any used material and unused solution. You should ask your doctor for a special container for this purpose.

No other medicines or fluids should be added to this product as their effects on the product have not been established.

If you suffer from certain blood disorders your doctor or nurse may inject this product just under the skin.

Solutions which are cloudy or have deposits should not be used.

POSSIBLE SIDE EFFECTS OF USING THIS MEDICINE
As with all intramuscular injections, there may be some short-term discomfort at the site of injection. Very rarely, a hardened area may develop where the injection was given. The following have been reported after injection: headache, feeling cold, feeling or being sick, chest pain, shortness of breath, shaking, dizziness, swelling of the face, coating of the tongue, mouth ulcers and joint pains. If you have any of these or continuous pain, itching, rash or any other unusual reaction or are just feeling unwell, you must tell your doctor.

When medicinal products prepared from human blood or plasma are given to patients, the risk of infectious diseases by certain germs cannot be totally ruled out, including some which may not have yet been discovered.

To reduce the risk from such germs, strict controls are applied to the selection of blood donors and donations. All such donations have been found negative by certain tests for AIDS and liver disease viruses (hepatitis B surface antigen, antibodies to HIV-1, HIV-2 and HCV) and plasma pools are also tested negative for these same viral markers and additionally for HCV-RNA. In addition, virus removal and/or inactivation procedures are included in the production process. The specific virus inactivation process used in the production of BPL's D-GAM® is solvent/detergent treatment.

The current procedures (including solvent/detergent treatment) applied in the manufacture of medicinal products derived from human blood or plasma are effective against enveloped viruses such as HIV, hepatitis B and hepatitis C viruses, but are of limited value against non-enveloped viruses such as hepatitis A virus.

WHAT TO DO IN CASE YOU ARE GIVEN TOO MUCH
If too much of this product is given, there is no cause for alarm. If you feel unwell afterwards or have any discomfort, tell your doctor.

STORAGE OF THE MEDICINE
D-GAM® should be stored in the original container at 2-8°C but DO NOT FREEZE. The expiry date is printed on the label. Do not use the product after this date. If necessary, the product can be kept at room temperature (25°C) for a short period (up to one week). The condition of date-expired or incorrectly stored product cannot be guaranteed.

FURTHER INFORMATION
Product Licence Numbers:

PL 08801/0047 - 250 iu dose size

PL 08801/0048 - 500 iu dose size

PL 08801/0049 - 1,500 and 2,500 iu dose size

BPL welcomes comments regarding the use and form of this product. Any comments should be directed to the Marketing Department at the address below.

MANUFACTURED AND MARKETED BY:

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Package Insert Revised: January 2003 Version SDL2