

**SUMMARY OF PRODUCT CHARACTERISTICS,
LABELLING AND PACKAGE LEAFLET**

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

SUBCUVIA 160 g/l Solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Human Normal Immunoglobulin (SC/IMiG)

1 l solution contains:

human protein 160 g

(of which at least 95% are immunoglobulin)

Distribution of IgG subclasses: IgG1 45-75%

IgG2 20-45%

IgG3 3-10%

IgG4 2-8%

Maximum IgA content: 4.8 g/l

1 vial of 5 ml contains 0.8 g human protein (of which at least 95 % are immunoglobulin).

1 vial of 10 ml contains 1.6 g human protein (of which at least 95 % are immunoglobulin).

For a full list of excipients, see section 6.1.

This medicinal product contains 1.2 mg sodium per ml.

3. PHARMACEUTICAL FORM

Solution for injection

The product is a clear or slightly opalescent, colourless to pale yellow solution.

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 hypogammaglobulinaemia and recurrent infections.

4.2 Posology and method of administration

Replacement therapy

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 should be adjusted to maintain an approximate level of at least 4-6 g/L of circulating IgG.

The dosage regimen using the subcutaneous route should achieve a sustained level of IgG (measured before the next infusion). A loading dose of at least 0.2-0.5 g/kg given during the course of one week (0.1 – 0.15 g/kg bodyweight at any given day) 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.

The subcutaneous route is the method of choice for the SUBCUVIA administration.

SUBCUVIA may also be injected by the intramuscular route. In such cases, the cumulative monthly dose should be divided up into weekly, or bi-weekly applications, in order to keep the injected volume low. To further minimize the discomfort for the patient, each single dosage may need to be injected at different anatomic sites.

Method of administration

Human normal immunoglobulin is administered via the subcutaneous or intramuscular route.

SUBCUVIA should be administered via the subcutaneous route. In exceptional cases, where the subcutaneous administration is not possible, SUBCUVIA can be given intramuscularly.

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

It is recommended to use an initial administration speed of 10 ml/h/pump.

The infusion speed can be enhanced for 1ml/h/pump every subsequent infusion. The recommended maximum speed is 20 ml/h/pump. More than one pump can be used simultaneously. The infusion site should be changed every 5-15 ml.

Intramuscular injection must be given by a physician or nurse.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients.

SUBCUVIA must not be given intravascularly.

SUBCUVIA must not be administered intramuscularly in cases of severe thrombocytopenia and in other disorders of haemostasis.

4.4 Special warnings and precautions for use

If SUBCUVIA is accidentally administered into a blood vessel, patients could develop shock. Therefore, it must be ensured that SUBCUVIA is not administered into a blood vessel.

The recommended infusion rate stated under 4.2. Method of administration should be adhered to. Patients should be closely monitored and carefully be observed for any adverse events throughout the infusion period. Patients on self-home treatment and/or their guardian must be trained to detect the early signs of hypotensive reactions that may seldom occur. Suspicion of allergic or anaphylactic type reactions requires immediate discontinuation of the injection. If severe anaphylactoid reactions do occur, standard medical treatment should be implemented and the patient or guardian should contact a doctor immediately.

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 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 implemented.

SUBCUVIA 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 infective 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.

The measures taken may be of limited value against non-enveloped viruses such as 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 SUBCUVIA 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.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

Following interactions could be observed:

Live attenuated virus vaccines

Immunoglobulin administration may impair the efficacy of live attenuated virus vaccines such as measles, rubella, mumps and varicella for a period of at least 6 weeks and up to 3 months. 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 in 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 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 studies on the effects on the ability to drive and use machines have been performed.

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

4.8 Undesirable effects

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

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.

Adverse reactions such as chills, headache, fever, vomiting, allergic reactions, nausea, dizziness, hyperhidrosis, pallor, paraesthesia, tachycardia, arthralgia, low blood pressure and moderate low back pain may occur occasionally.

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

In very rare cases anaphylactic/anaphylactoid reactions, such as dyspnoea, chest tightness, flushing of the face and skin, feeling of heat, and urticaria, may occur.

The adverse reactions reported per treatment in the listing hereafter are based on reports from clinical trials and on post-marketing experience for this type of product. Their frequency has been evaluated by using the following criteria: very common ($\geq 1/10$), common ($\geq 1/100 - < 1/10$), uncommon ($\geq 1/1000 - < 1/100$), rare ($\geq 1/10.000 - < 1/1000$) and very rare ($< 1/10.000$).

1) Clinical trials

The incident rate is $\geq 1/100 - < 1/10$, i.e. common for all Adverse Events reported below.

General disorders and administration site conditions

- Swelling
- Local pain

2) Post-Marketing Experience

The incident rate for the Adverse Events reported below is $\geq 1/1000$ – $< 1/100$, i.e. uncommon.

General disorders and administration site conditions

- Redness
- Induration
- Itching

The incident rate for the Adverse Events reported below is $\geq 1/10\ 000$ - $< 1/1000$, i.e. rare.

General disorders and administration site conditions

- Fever
- Swelling
- Local heat
- Fatigue
- Malaise

Immune system disorders

- Urticaria

Nervous system disorders

- Tremor
- Paraesthesia

Skin and Subcutaneous tissue disorders

- Pruritus
- Hyperhidrosis
- Pallor

The undesirable effects below listed reflect the type of undesirable effects that may be reported with SUBCUVIA.

Cardiac disorders

- Tachycardia

Gastrointestinal disorders

- Nausea
- Vomiting

General disorders and administration site conditions

- Chills
- Soreness
- Local pain
- Bruising
- Rash
- Chest tightness
- Feeling of heat

Immune system disorders

- Allergic reactions
- Anaphylactic shock
- Anaphylactic/anaphylactoid reactions

Investigations

- Fall in blood pressure

Musculoskeletal and connective tissue disorders

- Arthralgia
- Moderate low back pain

Nervous system disorders

- Headache
- Dizziness

Respiratory, thoracic and mediastinal disorders

- Dyspnoea

Vascular disorders

- Flushing of the face and skin
- Low blood pressure

For safety with respect to transmissible agents, see 4.4.

4.9 Overdose

No case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: immune sera and immunoglobulins: immunoglobulins, normal human, for extravascular administration. ATC code: J06BA01

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 about 4 days.

Data from clinical trials show that trough levels of 7,24-7,86 g/l can be maintained by dosing regimens of 1,25 ml (0,2 g)/kg bw administered at intervals of 2 weeks.

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

Single dose toxicity studies demonstrate that the doses several times higher than the maximum recommended human dose had no toxic effects on laboratory animals.

Repeated dose toxicity testing in animals is impracticable due to interference with developing antibodies to heterologous protein.

Reproductive and developmental toxicity studies were not performed with this product.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glycine

Sodium chloride

Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

30 months.

Once opened: use immediately.

6.4 Special precautions for storage

Store in a refrigerator (2°C - 8°C).

During the shelf life, the product may be stored at room temperature (not more than 25°C) for up to 6 weeks. The date of transfer to room temperature and the end of the 6-week period should be recorded on the outer carton. Once the product is stored at room temperature it must not be returned to the refrigerator and must be discarded, if not used by the end of the 6-week period.

Do not freeze.

Keep the container in the outer carton in order to protect from light.

6.5 Nature and contents of container

5 ml of solution in a vial (Type I glass) with a stopper (halogenobutyl rubber)

– pack size of 1 or 20

10 ml of solution in a vial (Type I glass) with a stopper (halogenobutyl rubber)

– pack size of 1 or 20

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

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

The liquid preparation is clear and pale yellow to light brown; during storage it may show formation of slight turbidity or a small amount of particulate matter.

Do not use solutions that are more than just slightly turbid.

Entered vials must not be reused.

After opening of the vial the product must be used immediately.

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

7. MARKETING AUTHORISATION HOLDER

To be completed nationally

8. MARKETING AUTHORISATION NUMBER(S)

To be completed nationally

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

To be completed nationally

10. DATE OF REVISION OF THE TEXT

To be completed nationally

<11. DOSIMETRY>

n.a.

<12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS>

n.a.

LABELLING

PARTICULARS TO APPEAR ON THE OUTER IMMEDIATE PACKAGING

Carton box for vials of 0.8 g/5 ml

1. NAME OF THE MEDICINAL PRODUCT

SUBCUVIA 160 g/l Solution for Injection
Human Normal Immunoglobulin

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Human protein (at least 95% Human Normal Immunoglobulin) 160 g/l

3. LIST OF EXCIPIENTS

Glycine
Sodium chloride
Water for Injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection 0.8 g/5 ml

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous or intramuscular use.
Read the package leaflet before use.

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

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Do not use solution that are more than just slightly turbid.

8. EXPIRY DATE

[For terms on Batch number and Expiry date see Appendix IV]

EXP.

Date removed from refrigerator: __/__/____

End of 6-week period at room temperature: __/__/____

Do not use after this date.

9. SPECIAL STORAGE CONDITIONS

[For storage conditions statements see Appendix III]

Store in a refrigerator.

SUBCUVIA may be stored at room temperature (not more than 25°C) for up to 6 weeks within the shelf life.

Do not freeze.

Store in the original 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**

To be completed nationally

12. MARKETING AUTHORISATION NUMBER(S)

To be completed nationally

13. BATCH NUMBER

[For terms on Batch number and Expiry date see Appendix IV]

Lot:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

To be completed nationally

16. INFORMATION IN BRAILLE

SUBCUVIA

PARTICULARS TO APPEAR ON THE OUTER IMMEDIATE PACKAGING

Carton box for vials of 1.6 g /10 ml

1. NAME OF THE MEDICINAL PRODUCT

SUBCUVIA 160 g/l Solution for Injection
Human Normal Immunoglobulin

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Human protein (at least 95% Human Normal Immunoglobulin) 160 g/l

3. LIST OF EXCIPIENTS

Glycine
Sodium chloride
Water for Injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
1.6 g/10 ml

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous or intramuscular use.
Read the package leaflet before use.

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

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Do not use solution that are more than just slightly turbid.

8. EXPIRY DATE

[For terms on Batch number and Expiry date see Appendix IV]

EXP.

Date removed from refrigerator: __/__/____

End of 6-week period at room temperature: __/__/____

Do not use after this date.

9. SPECIAL STORAGE CONDITIONS

[For storage conditions statements see Appendix III]

Store in a refrigerator.

SUBCUVIA may be stored at room temperature (not more than 25°C) for up to 6 weeks within the shelf life.

Do not freeze.

Store in the original 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**

To be completed nationally

12. MARKETING AUTHORISATION NUMBER(S)

To be completed nationally

13. BATCH NUMBER

[For terms on Batch number and Expiry date see Appendix IV]

Lot:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

To be completed nationally

16. INFORMATION IN BRAILLE

SUBCUVIA

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Vial label 0.8 g/5 ml

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

SUBCUVIA 160 g/l Solution for injection
Human Normal Immunoglobulin

s.c. or i.m. use

2. METHOD OF ADMINISTRATION

Read the package leaflet before use.

3. EXPIRY DATE

[For terms on Batch number and Expiry date see Appendix IV]

EXP:

4. BATCH NUMBER

[For terms on Batch number and Expiry date see Appendix IV]

Lot:

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.8 g/5 ml

6. OTHER

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Vial label 1.6 g/10 ml

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

SUBCUVIA 160 g/l Solution for injection
Human Normal Immunoglobulin

s.c. or i.m. use

2. METHOD OF ADMINISTRATION

Read the package leaflet before use.

3. EXPIRY DATE

[For terms on Batch number and Expiry date see Appendix IV]

EXP:

4. BATCH NUMBER

[For terms on Batch number and Expiry date see Appendix IV]

Lot:

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1.6 g/10 ml

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

Outer carton for pack sizes containing 20 vials of 0.8 g/5ml

1. NAME OF THE MEDICINAL PRODUCT

SUBCUVIA 160 g/l Solution for Injection
Human Normal Immunoglobulin

20 x 0.8 g/5 ml

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Human protein (at least 95% Human Normal Immunoglobulin) 160 g/l

3. LIST OF EXCIPIENTS

Glycine
Sodium chloride
Water for Injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
0.8 g/ 5 ml

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous or intramuscular use.
Read the package leaflet before use.

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

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Do not use solution that are more than just slightly turbid.

8. EXPIRY DATE

[For terms on Batch number and Expiry date see Appendix IV]

EXP.

Date removed from refrigerator: __/__/____

End of 6-week period at room temperature: __/__/____

Do not use after this date.

9. SPECIAL STORAGE CONDITIONS

[For storage conditions statements see Appendix III]

Store in a refrigerator.

SUBCUVIA may be stored at room temperature (not more than 25°C) for up to 6 weeks within the shelf life.

Do not freeze.

Store in the original 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**

To be completed nationally

12. MARKETING AUTHORISATION NUMBER(S)

To be completed nationally

13. BATCH NUMBER

[For terms on Batch number and Expiry date see Appendix IV]

Lot:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

To be completed nationally

16. INFORMATION IN BRAILLE

SUBCUVIA

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

Outer carton for pack sizes containing 20 vials of 1.6 g/10 ml

1. NAME OF THE MEDICINAL PRODUCT

SUBCUVIA 160 g/l Solution for Injection
Human Normal Immunoglobulin

20 x 1.6 g/10 ml

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Human protein (at least 95% Human Normal Immunoglobulin) 160 g/l

3. LIST OF EXCIPIENTS

Glycine
Sodium chloride
Water for Injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
1.6 g/10 ml

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous or intramuscular use.
Read the package leaflet before use.

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

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Do not use solution that are more than just slightly turbid.

8. EXPIRY DATE

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9. SPECIAL STORAGE CONDITIONS

[For storage conditions statements see Appendix III]

Store in a refrigerator.

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Do not freeze.

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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**

To be completed nationally

12. MARKETING AUTHORISATION NUMBER(S)

To be completed nationally

13. BATCH NUMBER

[For terms on Batch number and Expiry date see Appendix IV]

Lot:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

To be completed nationally

16. INFORMATION IN BRAILLE

SUBCUVIA

PACKAGE LEAFLET

PACKAGE LEAFLET: INFORMATION FOR THE USER

SUBCUVIA 160 g/l Solution for Injection

Active substance: Human Normal Immunoglobulin

Read all of this leaflet carefully before you start using this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What SUBCUVIA is and what it is used for
2. Before you use SUBCUVIA
3. How to use SUBCUVIA
4. Possible side effects
5. How to store SUBCUVIA
6. Further information

1. WHAT SUBCUVIA IS AND WHAT IT IS USED FOR

SUBCUVIA belongs to a class of medicines called immunoglobulins. These medicines contain antibodies which are normally found in your blood. Antibodies are proteins that help you to fight infection by neutralising bacteria, viruses, and other foreign bodies. SUBCUVIA is used in the treatment of certain diseases that are caused by a lack of antibodies in your blood. These types of diseases are called antibody deficiency syndromes. If you do not have enough antibodies, you become vulnerable to frequent infections. Regular and sufficient doses of SUBCUVIA can correct this lack of antibodies.

Adults and children can be prescribed SUBCUVIA as antibody replacement therapy. The most common reasons for people being prescribed antibody replacement therapy are:

- People who are born with an inability to make their own immune antibodies (congenital agammaglobulinaemia),
- People who cannot make enough own immune antibodies (hypogammaglobulinaemia)
- People who have a mixed group of reasons for not making enough own immune antibodies (common variable immunodeficiency)
- People whose blood and other body systems are unable to make sufficient antibodies (severe combined immunodeficiency)
- People who cannot make a particular class of antibody (IgG subclass deficiencies) with recurrent infections

In addition, SUBCUVIA is used for antibody replacement therapy with certain severe blood diseases, such as cancers of the bone marrow:

- myeloma
- chronic lymphatic leukaemia

These cancers can lead to severe secondary (acquired) antibody deficiencies and recurrent infections.

2. BEFORE YOU USE SUBCUVIA

Do NOT use SUBCUVIA

You MUST NOT use SUBCUVIA

- if you are allergic (hypersensitive) to immunoglobulins or any of the other ingredients of SUBCUVIA (see Section 6 – “What SUBCUVIA contains”)
- you must not inject SUBCUVIA into a blood vessel (intravascularly)
- you must not inject SUBCUVIA into a muscle (intramuscularly) if you have severe platelet deficiency (low platelets) or other blood clotting disorders.

Take special care with SUBCUVIA

The following is very important and should be considered before you receive or use SUBCUVIA:

- Infusion speed: the correct infusion speed is important (see Section 3, HOW TO USE SUBCUVIA). You are more likely to get side effects if the infusion is too fast.
- Side effects are more frequent if you
 - are using SUBCUVIA for the first time.
 - have received another immunoglobulin and have been switched to SUBCUVIA
 - have not used SUBCUVIA treatment for more than 8 weeks.
- Immunoglobulin A (IgA) deficiency: if you suffer from a deficiency with anti-IgA antibodies. There is an increased risk of allergic reactions.
- Severe allergic reactions (anaphylaxis). You may experience severe allergic reactions with a fall in blood pressure. These reactions are rare but they can occur even if you have not previously had problems with similar treatments.

Home treatment

Before you start home treatment you should assign a guardian person. This guardian should help you keep an eye on potential side effects. During the infusion you must look out for first signs of side effects (for further details see section 3. “HOW TO USE SUBCUVIA”). If you experience any, you or your guardian must stop the infusion immediately and contact a doctor. If you experience a severe side effect, you must seek emergency treatment immediately.

Viral Safety

When medicines are made from human blood or plasma, certain measures are put in place to prevent the spread of infection. These measures include careful selection of blood and plasma donors to make sure that people who are at risk of carrying infections are not donors. Donated blood and plasma is tested for viruses and other infections. The blood and plasma is also treated to inactivate or remove viruses. However, it cannot be guaranteed that infection will not be transmitted. This also applies to any unknown or emerging viruses or other types of infections. The measures taken are considered effective for some viruses such as human immunodeficiency virus (HIV), hepatitis B virus and hepatitis C virus. However, they may not be effective against other viruses such as hepatitis A virus and parvovirus B19 although immunoglobulins have not been associated with these particular infections.

It is strongly recommended that you keep a record of the batch number and expiry date every time you receive a dose of SUBCUVIA.

Taking other medicines

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines. This includes medicines obtained without a prescription, or if you have received a vaccination in the last 6 weeks.

- SUBCUVIA may reduce the effect of some live virus vaccines such as measles, rubella, mumps and chicken pox. Therefore, after receiving SUBCUVIA, you may have to wait for up to 3 months before receiving certain vaccines. You may have to wait for up to 1 year after receiving SUBCUVIA before you can receive a measles vaccine.
- Please tell your doctor when you have a blood test that you have been using SUBCUVIA. This is because it may affect the results of the test.
- Do not mix SUBCUVIA with other medicinal products.

Pregnancy and breast-feeding

Please tell your doctor if you are pregnant or breast-feeding. Your doctor will decide if SUBCUVIA may be used during pregnancy or breast-feeding.
Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines

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

3. HOW TO USE SUBCUVIA

Starting of treatment

Your treatment will be started by your doctor. At first, SUBCUVIA will be injected slowly. You will then be watched carefully for at least 20 minutes to see if you have any side effects. Once the doctor has found the right dose for you, you may be allowed to give the treatment to yourself at home.

Home treatment

Your doctor will show you how to use the syringe driver, and the infusion techniques. Your doctor will also teach you how to recognize severe adverse effects and what to do if these occur. You will also be shown how to keep the treatment diary. You will be allowed to start home treatment as soon as you show that you can give yourself the treatment. You may start home treatment as long as you do not have any severe side effects.

Preparations

- Always use SUBCUVIA exactly as your doctor has instructed you. You should check with your doctor if you are unsure.
- Assign a guardian person who can watch you for potential side effects during the infusion and for at least 20 minutes after you received SUBCUVIA. These side effects could be a low blood pressure or allergic reaction. Your doctor will give you and your guardian detailed instructions. These include information to recognize an allergic reaction as soon as possible. Early symptoms of an allergic reaction include:
 - fall in blood pressure (hypotension)
 - increased pulse rate
 - vomiting (being sick)
 - cold sweat
 - chills
 - sensation of heat
 - hives
 - itching
 - difficulty in breathing.

During the infusion you must look out for first signs of allergic reactions. If you experience any of the above symptoms you or your guardian must stop the infusion immediately and contact a doctor. If you have severe symptoms, you must seek emergency treatment immediately.

- You should bring the solution to room temperature (25°C) or body temperature (37°C) before use.
- Do not use solutions that are more than just slightly cloudy. The solution will be clear and pale yellow to light brown. During storage it may show formation of slight turbidity or a small amount of particulate matter.
- Do not reuse a vial once the stopper has been punctured.

Infusion

1. The infusion sites are the abdomen, the thighs or the buttocks. You should position the needle at an angle of 45 to 90 degrees.

2. Infuse SUBCUVIA subcutaneously (under the skin). You must make sure that SUBCUVIA is not infused into a blood vessel because this can lead to shock (See Section 2 - Take special care with SUBCUVIA).
3. Please keep strictly to the dosage and the infusion speed your doctor instructed you to use. The usual starting speed is 10 ml/h/pump. The infusion speed can be increased by 1 ml/h/pump after each new infusion up to a maximum of 20 ml/h/pump. You can use more than one pump at the same time.
4. Change the infusion site every 5-15 ml.
5. Use each syringe only once.
6. Sometimes it is not possible to give SUBCUVIA subcutaneously (under the skin). When this happens, SUBCUVIA may be given to you intramuscularly (into a muscle). Intramuscular administration must be given by your doctor or nurse.
7. Keep a full record of SUBCUVIA dosing by attaching the self-adhesive label into your dosing diary.

Disposal

Dispose of any unused product or waste material as instructed by your doctor or pharmacist. Do not put the cover back on used needles. Put used needles, syringes and vials into the puncture-proof container and keep it out of the reach and sight of children. Dispose of the full puncture-proof container as instructed by your doctor. Never put the unused needles and syringes into your household waste bin.

If you use more SUBCUVIA than you should

You should strictly keep to the dosage and infusion speed your doctor instructed you to use. Please tell your doctor if you accidentally use more SUBCUVIA than instructed.

There are no known symptoms of an overdose.

If you forget to use SUBCUVIA

Do not infuse a double dose to make up for a forgotten dose. Just infuse your next dose as usual and make a note in your diary that you missed a dose.

If you stop using SUBCUVIA

Tell your doctor if you decide to stop treatment and the reasons why.

If you have any more questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, SUBCUVIA can cause side effects, although not everybody gets them.

Common (in less than 1 in 10, but more than 1 in 100 patients treated)

- Reactions at the infusion site
 - Swelling
 - Pain

Uncommon (in less than 1 in 100, but more than 1 in 1,000 patient treated)

- Reactions at the infusion site
 - Redness
 - Induration (hardness)
 - Itching

Rare (in less than 1 in 1,000, but more than 1 in 10,000 patients treated)

- Fever
- Feeling of heat
- Fatigue (tiredness)
- Malaise (generally feeling unwell)

- Urticaria (itching skin rash)
- Tremor (shaking)
- Pruritus (itching)
- Excessive transpiration
- Looking pale
- Tingling of the skin (“pin and needles”)

Occasionally, the following side effects have occurred:

- Tachycardia (increased pulse rate)
- Nausea (feeling sick)
- Vomiting (being sick)
- Chills
- Soreness
- Bruising
- Rash
- Chest tightness
- Allergic reactions
- Anaphylactic shock (including fainting, unconsciousness and death)
- Anaphylactic/anaphylactoid (life threatening allergic) reactions
- Sudden fall in blood pressure
- Joint pain (arthralgia)
- Moderate low back pain
- Headache
- Dizziness
- Dyspnoea (difficulty breathing)
- Flushing of the face and skin
- Low blood pressure

If any of the side effects becomes serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE SUBCUVIA

- Keep out of the reach and sight of children.
- Do not use SUBCUVIA after the expiry date which is stated on the label and carton after EXP. The expiry date refers to the last day of that month.
- Store at 2°C-8°C (in a refrigerator).
- Do not freeze.
- SUBCUVIA may be stored at room temperature (not more than 25°C) for up to 6 weeks. Record the date of transfer to room temperature and the end of the 6-week period on the outer carton. Once SUBCUVIA has been stored at room temperature, it must not be returned to the refrigerator. It must be discarded if not used by the end of the 6-week period.
- Keep the vial in the outer carton to protect it from light.
- Do not use SUBCUVIA if the solution appears foggy or milky. It should be clear or slightly cloudy.
- Once a vial has been opened, the product must be used immediately.
- Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What SUBCUVIA contains

The active substance is human normal immunoglobulin.

It contains 16% (160 g/l) of human protein of which at least 95% is immunoglobulin G (IgG). The IgG subclass contents are:

- IgG1 45-75%
- IgG2 20-45%
- IgG3 3-10%
- IgG4 2-8%

Maximum IgA content 4.8 g/l

The other ingredients are glycine, sodium chloride and water for injections.

SUBCUVIA contains 1,2 mg sodium per ml.

What SUBCUVIA looks like and contents of the pack

SUBCUVIA is a solution for injection in a vial (0.8 g/5 ml or 1.6 g/10 ml; pack sizes of 1 vial or 20 vials).

The liquid preparation is clear and pale yellow to light brown. Slight cloudiness or a small number of visible particles may form during storage. Do not use if the solution is more than just slightly cloudy.

Marketing Authorisation Holder

<[To be completed nationally]>

Manufacturer

BAXTER AG
Industriestrasse 67
A – 1220 Vienna

This medicinal product is authorised in the Member States of the EEA under the following names:

SUBCUVIA

This leaflet was last approved in {MM/YYYY}.

<[To be completed nationally]>

Detailed information on this medicine is available on the web site of {MA/Agency}

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The following information is intended for medical or healthcare professionals only:

Posology and method of administration

Posology

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 should be adjusted to maintain an approximate level of 4-6 g/L of circulating IgG. The dosage regimen using the subcutaneous route should achieve a sustained level of IgG (measured before the next infusion). A loading dose of at least 0.2-0.5 g/kg given during the course of one week (0.1 – 0.15 g/kg bodyweight at any given day) 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.

The subcutaneous route is the method of choice for the SUBCUVIA administration.

SUBCUVIA may also be injected by the intramuscular route. In such cases, the cumulative monthly dose should be divided up into weekly, or bi-weekly applications, in order to keep the injected volume low. To further minimize the discomfort for the patient, each single dosage may need to be injected at different anatomic sites.

Method of administration

Human normal immunoglobulin is administered via the subcutaneous or intramuscular route.

SUBCUVIA should be administered via the subcutaneous route. In exceptional cases, where the subcutaneous administration is not possible, SUBCUVIA can be given intramuscularly.

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

Subcutaneous infusion

for home treatment should be initiated by a physician experienced in the guidance of patients for home treatment. The patient must be instructed in the use of a syringe driver, the infusion techniques, the keeping of treatment diary, recognition of and measures to be taken in case of severe adverse events. It is recommended to use an initial administration speed of 10 ml/h/pump.

The infusion speed can be enhanced for 1ml/h/pump every subsequent infusion. The recommended maximum speed is 20 ml/h/pump. More than one pump can be used simultaneously. The infusion site should be changed every 5-15 ml.

Potential complications can often be avoided by ensuring that:

- patients are not sensitive to human normal immunoglobulin by first injecting the product slowly.
- 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.

Intramuscular injection must be given by a physician or by a nurse.

Incompatibilities

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

SUBCUVIA is a trademark of Baxter International Inc./Baxter Healthcare S.A.
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