Package leaflet: Information for the user

CUTAQUIG, 165 mg/ml, solution for injection
Human normal immunoglobulin (SCIg)

This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet
1. What Cutaquig is and what it is used for
2. What you need to know before you use Cutaquig
3. How to use Cutaquig
4. Possible side effects
5. How to store Cutaquig
6. Contents of the pack and other information

1. What Cutaquig is and what it is used for

What Cutaquig is
Cutaquig belongs to a class of medicines called “human normal immunoglobulins”. Immunoglobulins are also known as antibodies and are proteins found in healthy people’s blood. Antibodies are part of the immune system (the body’s natural defense) and help your body to fight infections.

How Cutaquig works
Cutaquig contains immunoglobulins that have been prepared from the blood of healthy people. The medicine works in exactly the same way as the immunoglobulins naturally present in your blood.

What Cutaquig is used for
Cutaquig is used in patients who do not have enough antibodies to fight off infections and therefore tend to have frequent infections. Regular administration of sufficient doses of Cutaquig can raise abnormally low immunoglobulin levels in your blood to normal levels (replacement therapy).

Cutaquig is prescribed to adults and children (aged 0-18 years) in the following situations:

Treatment of patients who are born with a reduced ability or inability to produce antibodies (primary immunodeficiency syndromes). These include but are not limited to conditions such as:
- low antibody levels (hypogammaglobulinaemia) or absence of antibodies (agammaglobulinaemia) in the blood
- combination of low antibody levels, frequent infections and inability to produce adequate amounts of antibodies after vaccination (common variable immunodeficiency)
- combination of low level or absence of antibodies and absence or nonfunctional immune cells (severe combined immunodeficiency)
- lack of certain antibody (immunoglobulin G) subclasses causing recurrent infections.

Treatment of patients with a certain type of blood cancer (chronic lymphocytic leukaemia), and recurrent infections where prophylactic antibiotics have failed or are contra-indicated.
Treatment of patients with cancer of the bone marrow (multiple myeloma), and recurrent infections.

Treatment of low antibody levels in patients before and after transplantation of bone marrow cells from another person (allogeneic haematopoietic stem cell transplantation – HSCT)

2. What you need to know before you use Cutaquig

Do NOT use Cutaquig:
- if you are allergic to human normal immunoglobulin, or any of the other ingredients of this medicine (listed in section 6).

Do NOT inject Cutaquig into a blood vessel.

Warnings and precautions:
Talk to your doctor or pharmacist before using Cutaquig.

You may be allergic (hypersensitive) to immunoglobulins without knowing it.
True allergic reactions such as sudden fall in blood pressure or anaphylactic shock (a sharp fall in blood pressure with other symptoms such as swelling of the throat, breathing difficulties and skin rash) are rare but they may occur occasionally even if you received human immunoglobulins previously and tolerated them well. It may happen particularly if you do not have enough of the immunoglobulin type A (IgA) in your blood (IgA deficiency) and have antibodies against IgA.

- Tell your doctor or healthcare professional prior to treatment if you have an immunoglobulin type A (IgA) deficiency. Cutaquig contains residual amounts of IgA that might cause an allergic reaction.
  In these rare cases, allergic reactions such as a sudden fall in blood pressure or shock may occur (see also section 4).
  Signs and symptoms of these rare allergic reactions include
  - Feeling light headed, dizzy or faint
  - Skin rash and itchiness, swelling in the mouth or throat, difficulty breathing, wheezing
  - Abnormal heart rate, chest pain, blueness of lips or fingers and toes
  - Blurred vision
  If you notice such signs during the infusion of Cutaquig, tell your doctor immediately.
  He or she will decide whether to slow down the infusion rate or whether to stop the infusion completely.

- Tell your doctor if you have a history of heart or blood vessel disease or blood clots, have thick blood, or have been immobile for some time. These things may increase your risk of having a blood clot after using Cutaquig. Also, tell your doctor what drugs you are using, as some drugs, such as those that contain the hormone oestrogen (for example, birth control pills), may increase your risk of developing a blood clot. Contact your doctor immediately if you experience signs and symptoms such as shortness of breath, chest pain, pain and swelling of a limb, weakness or numbness on one side of the body after receiving Cutaquig.

- Contact your doctor if you experience the following signs and symptoms: severe headache, neck stiffness, drowsiness, fever, photophobia, nausea, and vomiting after receiving Cutaquig. Your doctor will decide if further tests are necessary and whether Cutaquig should be continued.

- Cutaquig contains blood group antibodies that may cause destruction of red blood cells and therefore anaemia (low number of red blood cells).

Your healthcare professional will avoid potential complications by ensuring:
- that you are not sensitive to human normal immunoglobulin
  The medicine must be infused slowly at first. The recommended infusion rate given under
section 3 must be closely followed.

- that you are carefully monitored for any symptoms throughout the infusion period, especially if:
  - You receive human normal immunoglobulin for the first time
  - You have switched from a different medicine to Cutaquig
  - There has been a long interval (more than eight weeks) since the last infusion.

In these cases, it is recommended that you are monitored during the first infusion and for an hour afterwards. If the points above do not apply for you, it is recommended that you are observed for at least 20 min after administration.

**Children and adolescents**
The listed warnings and precautions apply both to adults and to children.

**Other medicines and Cutaquig**
- Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines.
- You must not mix Cutaquig with any other medicines.
- Tell your vaccinating doctor prior to a vaccination about your treatment with Cutaquig. Cutaquig (as all human normal immunoglobulin solutions) may interfere with the effect of some live virus vaccines such as measles, rubella, mumps or chicken pox. Therefore, after receiving Cutaquig you may have to wait up to 3 months before receiving your live-attenuated vaccine. In the case of measles vaccination the impairment may persist for up to one year.

- **Blood Glucose Testing**
  Some types of blood glucose testing systems (so called glucometers) falsely interpret the maltose contained in Cutaquig as glucose. This may result in falsely elevated glucose readings during an infusion and for a period of about 15 hours after the end of the infusion and, consequently, in the inappropriate administration of insulin, resulting in life-threatening hypoglycaemia (i.e. a decreased blood sugar level). Also, cases of true hypoglycaemia may go untreated if the hypoglycaemic state is masked by falsely elevated glucose readings.

Accordingly, when administering Cutaquig or other maltose-containing products, the measurement of blood glucose must be done with a test-system using a glucose-specific method. Systems based on the glucose dehydrogenase pyrroloquinolinequinone (GDH PQQ) or glucose-dye-oxidoreductase methods should not be used.

Review carefully the product information of the blood glucose testing system, including that of the test strips, to determine if the system is appropriate for use with maltose-containing parenteral products. If any uncertainty exists, please ask your treating physician to determine if the glucose testing system you are using is appropriate for use with maltose-containing parenteral products.

**Cutaquig with food, drink and alcohol**
No effects have been observed.

**Pregnancy, breast-feeding and fertility**
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine. This product should only be used during pregnancy or breast-feeding after consultation with your doctor or pharmacist.

No clinical studies have been performed with Cutaquig in pregnant women. However, medicines that contain immunoglobulins have been used in pregnant and breast-feeding women for years, and no harmful effects on the course of pregnancy or on the baby have been observed.

If you are breast-feeding and receive Cutaquig, the immunoglobulins of the medicine can also be found in the breast milk. Therefore, your baby may be protected from certain infections.
Experience with immunoglobulins suggests that no harmful effects on fertility are to be expected.

**Driving and using machines**
The ability to drive and operate machines may be impaired by some adverse reactions associated with Cutaquig. Patients who experience adverse reactions during treatment should wait for these to resolve before driving or operating machines.

**Cutaquig contains Sodium**
This medicinal product contains 33.1 mg sodium per vial of 48 ml and 13.8 mg per vial of 20 ml, equivalent to 1.7% and 0.7% respectively of the WHO recommended maximum daily intake of 2 g sodium for an adult.

**Information on what Cutaquig is made of**
Cutaquig is made from human blood plasma (this is the liquid part of the blood). When medicines are made from human blood or plasma, certain measures are put in place to prevent infections being passed on to patients. These include:
- careful selection of blood and plasma donors to make sure those at risk of carrying infections are excluded,
- the testing of each donation and pools of plasma for signs of virus/infections,
- the inclusion of steps in the processing of the blood or plasma that can inactivate or remove viruses.

Despite these measures, when medicines prepared from human blood or plasma are administered, the possibility of passing on infection cannot be totally excluded. This also applies to any unknown or emerging viruses or other types of infections.

The measures taken are considered effective for enveloped viruses such as human immunodeficiency virus (HIV – the AIDS causing virus), hepatitis B virus and hepatitis C virus.
The measures taken may be of limited value against non-enveloped viruses such as hepatitis A Virus and parvovirus B19.

Immunoglobulins have not been associated with hepatitis A or parvovirus B19 infections possibly because the antibodies against these infections, which are contained in the product, are protective.

It is strongly recommended that every time you receive a dose of Cutaquig the name and batch number of the medicine are recorded in order to maintain a record of the batches used (see also Annex I: Administration Guidance).

### 3. How to use Cutaquig

Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Cutaquig has to be infused under the skin (subcutaneous or SC administration).

The treatment will be started off by your doctor or nurse experienced in treating patients with a weak immune system.

Once the doctor/nurse has found the right dose and infusion rate for you and once you have received the first few infusions under supervision, you may be allowed to administer the treatment yourself at home or receive it at home by your (trained) caregiver. Your doctor or nurse experienced in guiding patients to home treatment will ensure that you or your caregiver receive training and precise information on
- germ free (aseptic) infusion technique
- the use of the infusion device (if necessary)
• keeping a treatment diary
• what action to take in the event of serious side effects (see also section 4).

As soon as you are able to treat yourself, and if no side effects have arisen during treatment, your
doctor may allow you to continue treatment at home.

Dosage
Your individual dosage and infusion rate will be determined by your doctor, who will adapt the dose especially for you, taking into account your weight, any previous treatment you may have received and your response to treatment. Always follow your doctor’s instructions.

Your doctor will determine whether you need a loading dose (for adults and children) of at least 1.2 to 3.0 ml/kg of body weight divided over several days. Following this, you will receive Cutaquig on a regular basis from daily to once every 2 weeks. The cumulative dose per month will be about 2.4 to 4.8 ml/kg of body weight. Your healthcare professional may adjust your dose depending on your response to the treatment.

Do not change the dose or dosing interval without contacting your doctor. If you think you should receive Cutaquig more or less frequently, please speak to your doctor. If you think you missed a dose, please speak to your doctor as soon as possible.

Method and route of administration
Selection of infusion site(s):
Suggested areas for subcutaneous infusion of Cutaquig are abdomen, thighs, upper arms, or upper leg/hip area. Multiple subcutaneous infusion sites can be used at the same time. The number of infusion sites is unlimited, but infusion sites should be at least 5 cm apart. Rotate sites with each administration as advised by your doctor or nurse.

The amount infused per site varies but it is recommended to divide large infusion volumes (> 30 ml) and infuse into several infusion sites. In infants and children infusion sites may be changed every 5-15 ml.

Infusion rate:
The recommended initial infusion speed is 15 ml/h/site. If well-tolerated, you may gradually increase the infusion rate to 25 ml/h/site.

Recommended infusion speed for all sites combined:
30 ml/h for the first 6 infusions, then gradually increase to 50 ml/h and if well tolerated to 80 ml/h.

Detailed instructions for use are provided below.

Cutaquig is for subcutaneous (under the skin) administration only. Do not inject into a blood vessel.

Only use Cutaquig at home once you have been properly instructed and trained by your healthcare professional.

Follow the administration guidance at the end of the packaging leaflet (Annex I) step by step and use aseptic/sterile technique when administering Cutaquig.

Use gloves if you have been told to do so when preparing the infusion.

Use in children and adolescents
The same indications, dose and frequency of infusion as for adults apply for children and adolescents (age 0 to 18 years).

If you use more Cutaquig than you should
If you think, you have infused too much Cutaquig, contact your healthcare professional as soon as possible.

If you forget to use Cutaquig
Inform your doctor or healthcare professional as soon as possible if you missed a dose. Do not infuse a double dose of Cutaquig to make up for a missed dose.

4. Possible side effects

Like all medicines, this medicine can cause side effects, such as chills, headache, dizziness, fever, vomiting, allergic reactions, nausea, joint pain, low blood pressure and moderate low back pain, although not everybody gets them.

Certain side effects such as headache, chills, or body aches, may be reduced by slowing the infusion rate.

No related serious adverse drug reactions were observed in subjects treated with Cutaquig during the clinical studies evaluating its safety.

You may be allergic (hypersensitive) to immunoglobulins and allergic reactions such as a sudden fall in blood pressure and in isolated cases, shock may occur. Doctors are aware of these possible side effects and will monitor you during and after the initial infusions.

Tell your doctor immediately if you notice any of the following:

- Feeling light-headed, dizzy or faint,
- Skin rash and itchiness, swelling of the mouth or throat, difficulty breathing, wheezing,
- Abnormal heart rates, chest pain, blueness of lips or fingers and toes,
- Blurred vision.

When using Cutaquig at home, you may perform the infusion in the presence of your caregiver who will help you watch out for signs of an allergic reaction. In case of any symptoms for an allergic reaction, stop the infusion, and get help if necessary.

Please also see section 2 of this leaflet about the risk of allergic reactions.

The following side effects are very common (may affect more than 1 in 10 infusions):

- Reactions at the injection site such as redness, swelling, itching, and discomfort.

The following side effects are rare (may affect more than 1 in 10,000 infusions):

- Headache
- Abdominal pain
- Abdominal distension
- Vomiting
- Muscle pain
- Fever
- Positive blood test for antibodies
- Irregular blood test results showing destruction of red blood cells

Side effects seen with similar medicines

The following side effects have been observed with infusion of human normal immunoglobulin. Although these side effects have so far not been seen with Cutaquig, it is possible that someone using Cutaquig may get them.

- Tingling, tickling, prickling, burning sensation
- trembling
- tiredness
- restlessness
- shivering
migraine
loss of consciousness
epileptic fits
diarrhoea
itching and rash
pain
oedema at the site of infusion
pain related to the musculature and bones (musculoskeletal pain)
feeling cold, low body temperature (hypothermia)
high blood pressure
flu-like symptoms
fast heart beat
abnormal heart beats
suspension of heart beating
shortness of breath
(acute) breathing problems
bluish skin
decreased oxygen in the blood
accumulating fluid in the lung
asthma like symptoms
cough, wheezing
suspension of breathing
abnormal liver function
rash, hives
irritation of the skin, inflammation of the skin, severe manifestations of the skin, hair loss
sudden swelling of skin areas or mucosal tissue
facial swelling
kidney problems
chest pain, chest discomfort, hot flush, increased sweating,
results of blood tests suggesting impaired liver or kidney function
decreased number of blood cells
decreased number of red blood cells due to destruction of these cells
weight loss

Tell your doctor right away if you have any of the following symptoms. They could be signs of a serious problem.

- Severe headache with nausea, vomiting, neck stiffness, fever, and sensitivity to light. These could be signs of a temporary and reversible, non-infectious swelling of the membranes surrounding the brain and spinal cord (meningitis).
- Pain, swelling, warmth, redness, or a lump in your legs or arms, unexplained shortness of breath, chest pain or discomfort that worsens on deep breathing, unexplained rapid pulse, numbness or weakness on one side of the body, sudden confusion, or trouble speaking. These could be signs of a blood clot.

Side effects such as these may occur even when you have previously received human immunoglobulin and tolerated them well.
Please also refer to section 2 for additional details on circumstances which increase the risk if side effects.

**Reporting of side effects**
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system:

HPRA Pharmacovigilance
Earlsfort Terrace
IRL – Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: [www.hpra.ie](http://www.hpra.ie)
e-mail: medsafety@hpра.ie

By reporting side effects you can help provide more information on the safety of this medicine.

5. **How to store Cutaquig**

Keep this medicine out of the sight and reach of children.

Do not use this medicine 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 in a refrigerator (2 °C – 8 °C). Do not freeze. Keep the vial in the outer carton in order to protect it from light.

Within its shelf-life, the product may be stored at room temperature (do not store above 25 °C) for up to 6 months without being refrigerated again during this period, and must be discarded if not used after this.

After first opening, the product should be used immediately.

Do not use Cutaquig if the solution is cloudy or contains particles.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. **Contents of the pack and other information**

**What Cutaquig contains**
The active substance is human normal immunoglobulin 165 mg/ml (at least 95% is immunoglobulin G)

- IgG1 .......... 71%
- IgG2 .......... 25%
- IgG3 .......... 3%
- IgG4 .......... 2%

The other excipients are Maltose, Polysorbate 80 and water for injections.
The maximum IgA content is 600 micrograms/ml
Cutaquig contains ≤ 30 mmol/l Sodium

**What Cutaquig looks like and contents of the pack**
Cutaquig is a solution for injection.
The solution is clear and colourless.
During storage the solution may turn to slightly opalescent and pale-yellow.

Cutaquig is available as:
6, 10, 12, 20, 24 or 48 ml of solution in a vial (Type I glass) with a bromobutyl rubber stopper - pack size of 1, 10 or 20.
Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
Marketing Authorisation Holder:
Octapharma (IP) SPRL
Researchdreef 65
1070 Anderlecht
Belgium

Manufacturer:
Octapharma Pharmazeutika Produktionsges.m.b.H.
Oberlaaer Strasse 235
1100 Vienna
Austria

This medicinal product is authorised in the Member States of the EEA under the following names:
Austria, Belgium, Bulgaria, Croatia, Czech Republic, Denmark
Estonia, Finland, France, Germany, Hungary, Iceland, Ireland,
Italy, Latvia, Lithuania, Luxembourg, Malta, The Netherlands,
Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain,
Sweden, United Kingdom:

This leaflet was last revised in 06/2019.
Annex I – Administration guidance

1. Prepare the necessary number of Cutaquig vials
   - If stored in the fridge put the vials at room temperature at least 90 minutes prior to infusion.
   - Do not heat the vials or put them into the microwave.
   - Do not shake the vials to avoid foaming.

2. Getting ready for infusion
   - Choose and prepare a clean work area using antiseptic wipes or disinfecting solution (Figure 1).
     
     ![Figure 1](image1.png)

   - Gather your infusion equipment:
     - Infusion pump (optional) & compatible syringe(s)
     - Needle (for drawing up product from the vial)
     - Infusion set
     - Infusion tubing and Y-connector (if required)
     - Alcohol & alcohol wipes/antiseptic wipes
     - Gauze or transparent dressing and tape
     - Sharps container
     - Treatment diary and pen
   - Wash your hands thoroughly and let them dry (Figure 2). Use disinfectant gel as has been shown to you during training.
     
     ![Figure 2](image2.png)

   - If necessary program the pump according to the user manual and as you have been shown during the training by your healthcare professional.

3. Checking & opening the vials
   - Inspect each vial carefully for:
     - Correct labelled dose based on your prescription,
     - Check the appearance of the solution (it should be clear and colourless to pale yellow or light brown),
- Make sure the protective cap has not been broken or is missing.
- Check the expiry date and batch number.
- Do not use the solution if it is cloudy or contains particles.
- Remove the protective cap.
- Disinfect the rubber stopper by using an antiseptic wipe and allow it to dry (Figure 3).

![Figure 3](image)

Figure 3

4. **Preparing and filling the syringe**

- Open sterile syringe and needle.
- Attach the needle to the syringe with a screw action.
- Draw back on the plunger to fill the syringe with air which should be roughly equal to the amount of solution needed from the vial.
- Insert the needle into the vial and turn the vial upside down. Inject air - ensuring the tip of the needle is not in the solution to avoid foaming.
- Next, making sure the needle remains always in the solution, slowly draw up the Cutaquig (Figure 4).

![Figure 4](image)

Figure 4

- Withdraw the needle from the vial.
- This procedure might need to be repeated if you need multiple vials for the calculated dose.
- When finished remove the needle and dispose it into the sharps bin.
- Immediately proceed to the next step as the IgG solution should be used promptly.

5. **Preparing the infusion pump and tubing (optional)**

- Follow the manufacturer’s instructions for preparing the infusion pump.
- To prime the administration tubing attach filled syringe to the infusion tubing and gently push the plunger to fill the tubing with Cutaquig and to remove all air. (Figure 5).
6. Deciding on infusion sites and inserting the infusion needle(s)

- Cutaquig can be infused in the following areas: abdomen, thigh, upper arm, and/or upper leg/hip area (Figure 6).

- The infusion sites should be at least 5 cm apart.
- Use different infusion sites than you used for the previous administration.
- Avoid inserting the needle into scars, tattoos, stretch marks or injured/inflamed/red skin areas.
- Clean your skin at your selected infusion site(s) with an antiseptic skin wipe and let the skin dry.
- Pinch the skin between your thumb and forefinger around the injection site (Figure 7), carefully remove the needle cover and insert the needle into the skin (Figure 8). The angle of the needle will depend on the type of infusion set being used.

7. Checking the infusion

- The solution should not be infused into a blood vessel.
- Secure the needle in place by applying sterile gauze and tape or a transparent dressing (Figure 9).
8. **Starting the infusion**
   - Start the infusion. If an infusion pump is used for administration, follow the manufacturer’s instructions.

9. **Recording the infusion**
   - On each vial of Cutaquig you will find a peel off label giving the batch number details. Stick this label in your patient’s treatment diary or infusion log book. Record details of the dose, date, time, infusion site location and any infections, side effects or other comments in connection with this infusion.

10. **After the infusion is complete**
    - Gently remove the needle(s) and immediately place into the sharps bin.
    - If necessary press a small piece of gauze on the needle site and apply a dressing.
    - Throw away all used disposable supplies as well as any unused product and the empty vial(s) as recommended by your healthcare professional and according to local requirements.

Tidy up and securely store all the reusable equipment (e.g. pump) until the next infusion.