Cuvitru
[Immunoglobulin Subcutaneous (Human) 20%]

Getting Started with Your Subcutaneous Immunoglobulin(Ig) Treatment

Please read through this booklet to learn about:

- Immunodeficiency disorders
- What CUVITRU® does, how to use it and how to store it
- Important information on safety, warnings and side effects.

Takeda

PART I

Disease Information for Patients Receiving CUVITRU

Your Doctor has prescribed CUVITRU to treat one of the following conditions:

- **Primary Immunodeficiency (PI)**
  CUVITRU is used as replacement therapy for patients with primary immunodeficiency diseases.
- **Secondary Immunodeficiency (SI)**
  CUVITRU is used as replacement therapy for patients with secondary humoral immunodeficiency diseases.

Following is a brief description of these conditions, what causes them and primary symptoms.

Part II of this booklet provides you with information on CUVITRU and addresses key questions such as how to use the drug appropriately, what it contains, common side effects and potential warnings or contraindications.

What are Primary Immunodeficiency Diseases (PI)?

The immune system is composed of a variety of cells, especially white blood cells, and proteins, for which one of the principal functions is microbial defense. A deficit in the immune system can therefore lead to unusually severe or uncommon recurrent infections. Immune deficits (immunodeficiencies) may be primary or secondary. Primary immunodeficiencies, often genetic, are caused by problems in the formation of the immune system itself and not by external factors.[1]

How does a primary immunodeficiency present?

One must suspect an immune deficit in the context of infections that are recurrent, atypical, severe, or that do not respond well to standard treatments. A family history or growth delay and failure to thrive in the infant may also lead to this diagnosis.[1]

Although relatively rare, primary immune deficiencies are numerous:

- Prevalence is more common than originally thought. It is estimated that as many as 1 in every 1,200–2,000 people may have some form of primary immunodeficiency.[2]
- Primary immunodeficiency diseases can occur in individuals of any age. The original descriptions of these diseases were in children. However, as medical experience has grown, many adolescents and adults have been diagnosed with primary immunodeficiency diseases.[2]
- In addition to an increased susceptibility to infection, people with primary immunodeficiencies may also have autoimmune diseases in which the immune system attacks their own cells or tissues as if these cells were foreign, or non-self.[2]

- All PI disorders result from a defect in one or more of the elements or functions of the normal immune system such as T-cells, B-cells, NK cells, neutrophils, monocytes, antibodies, cytokines or the complement system.[2]

Because the most important function of the immune system is to protect against infection, people with primary immunodeficiency diseases have an increased susceptibility to infection. This may include too many infections, infections that are difficult to cure, unusually severe infections, or infections with unusual organisms. The infections may be located anywhere in the body. Common sites are the sinuses (sinusitis), the bronchi (bronchitis), the lung (pneumonia) or the intestinal tract (infectious diarrhea).[2]

PI is different from secondary immunodeficiency conditions, which are not hereditary but acquired, and autoimmune conditions, in which a person's immune system attacks his or her own body. Rather, PI is usually inherited or caused by errors in the genes of the cells that make up the immune system.[2]

How does one diagnose an immunodeficiency?

The diagnosis is suspected by history. Following this, very specific testing might be ordered by the allergist-immunologist. Sometimes the tests are sent to specialized centres. It is important to test for the number and function of certain cells (e.g. white blood cells) and proteins (e.g. antibodies and complement proteins) in the blood. It is possible that the doctor will also order radiological tests or genetic tests.[1]

What are Secondary Immunodeficiency Diseases (SI)?

As discussed in the previous section, a deficit in the immune system can lead to unusually severe or uncommon recurrent infections. Secondary immune deficiencies (or acquired deficiencies) are more frequent than primary immune deficiencies, and are problems of the immune system that are not genetic and which are caused by external factors.[3]

Secondary immune deficiencies are common and can occur as part of another disease or as a consequence of certain medications.[2] The most well-known example of a secondary immune deficiency is the immunodeficiency caused by the **H**uman **I**mmunodeficiency **V**irus, or HIV. HIV attacks certain cells in the immune system and prevents them from carrying out their proper functions against microbes. When the immune system is sufficiently weakened, infected people catch atypical and severe infections. This is then called the **A**cquired **I**mmunodeficiency **S**yndrome, or AIDS. AIDS at this time is often treated by a specialized multidisciplinary team.[4]

Regardless of the root cause, recognition of the secondary immune deficiency and provision of immunologic support can be helpful. The types of support offered are comparable to what is used for primary immune deficiencies.[2]

Summary

Immunoglobulin (Ig) therapy replaces the missing antibodies in your immune system, so it is easier for your body to fight off an infection, should one develop.[5]

However, since the existing immunodeficiency disease remains, you will require subsequent Ig injections on a regular basis. [4]

Your Immunologist will recommend an appropriate medication, dosage and treatment schedule that best meets your requirements. [4]

Subcutaneous (SC) injections are administered just under the skin. Subcutaneous Ig is usually infused at home by the patient or caregiver at a frequency ranging from once per day, up to every two weeks.[5]

PART II

Medication Information for Patients Receiving CUVITRU Immunoglobulin Subcutaneous (Human) 20% Solution

About this Medication – Read this for safe and effective use of your medicine.

This section is based on part III of a three-part "Product Monograph" published when CUVITRU was approved for sale in Canada and is designed specifically for Patients. Read this carefully before you start taking CUVITRU and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about CUVITRU.[5]

What is CUVITRU used for?

CUVITRU is a ready-to-use liquid medicine that contains immunoglobulin G (IgG) antibodies, which protect the body against infection. CUVITRU is used as replacement therapy for patients with primary immunodeficiency diseases (PI) and with secondary humoral immunodeficiency diseases (SI).[5]

How does CUVITRU work?

There are many forms of PI. The most common types of PI and SI result in an inability to make a very important type of protein called antibodies, which help the body fight off infections from bacteria or viruses. CUVITRU is made from human plasma that is donated by healthy people. CUVITRU contains antibodies collected from these healthy people that replace the missing antibodies in PI and SI patients.[5]

Serious Warnings and Precautions about CUVITRU

CUVITRU can cause the following serious reactions: [5]

- **Severe allergic reactions causing difficulty in breathing or skin rashes**
- **Decreased kidney function or kidney failure**
- **Blood clots in the heart, brain, lungs, or elsewhere in the body**
- **Severe headache, drowsiness, fever, painful eye movements, or nausea and vomiting**
- **Dark-coloured urine, swelling, fatigue, or difficulty breathing**

What are the ingredients in CUVITRU?[5]

- Medicinal ingredients: Human Immunoglobulin
- Non-medicinal ingredients: Glycine, Water for injections

CUVITRU comes in the following dosage forms:

Sterile Solution, subcutaneous administration.[5]

Do not use CUVITRU if:

Do not use CUVITRU if you have a known history of a severe allergic reaction to immunoglobulin or other blood products. If you have such a history, discuss this with your healthcare provider to determine if CUVITRU can be given to you. Tell your healthcare provider if you have a condition called selective (or severe) immunoglobulin A (IgA) deficiency.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you administer CUVITRU. Talk about any health conditions or problems you may have, including if you:

- Are with an increased risk of kidney damage including those with any degree of existing kidney disease
- Have diabetes
- Are at an age greater than 65
- Are dehydrated
- Have an overwhelming infection
- Have abnormal proteins in the blood, or
- Are receiving drugs known to damage the kidneys

Especially in these people, immunoglobulin products should be administered at the lowest possible concentration and as slowly as is practical. While these reports of kidney disease and failure of the kidneys have been associated with the use of many of the licensed IGIV products, those containing sucrose produced more kidney problems than expected.

CUVITRU does NOT contain sucrose.

People with increased risk to blood clots in their veins or arteries include those that have high blood pressure, diabetes mellitus, history of blood vessel disease or previous clots, acquired or inherited increased numbers or activity of platelets which help the blood clot, prolonged periods of not moving, such as lying in bed, increased activity of the proteins that make blood clot, conditions, obesity, advanced age, use of estrogens, long-term catheters that go into a central vein, and other cardiovascular risk factors. Thrombosis may occur even in the absence of known risk factors.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with CUVITRU:

CUVITRU can make vaccines (like measles/mumps/rubella or chickenpox vaccines) not work as well for you. Before you get any vaccines, tell your healthcare provider that you take CUVITRU. Tell your healthcare provider if you are pregnant, or plan to become pregnant, or if you are nursing.[5]

How to use CUVITRU:

Do not use CUVITRU at home until you get instructions and training from your healthcare professional. Whenever giving yourself treatments at home, you should have another responsible person present to help treat side effects or get help if you have a serious adverse reaction. Ask your healthcare provider whether you should have rescue medications, such as antihistamines or epinephrine.

Prepare CUVITRU vial(s):[5]

- Remove CUVITRU from the box. Allow vials to reach room temperature. This may take up to 90 minutes.
- Do not apply heat or place in microwave.
- Do not shake the vial(s).

Detailed CUVITRU usage instructions and diagrams

1. Check the vial(s):

- Do not use beyond expiration date.
- Do not use if the protective cap is missing or broken.
- Look at the colour: it should be clear and colourless to pale yellow or light brown.
- Do not use if the solution is cloudy or has particles.

2. Gather all supplies:

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  Items include: vial(s) of CUVITRU, infusion supplies: subcutaneous needle set, transfer device(s), syringe(s), sterile tip caps, sterile clear bandage, tape, gauze, sharps container, infusion pump, infusion log.

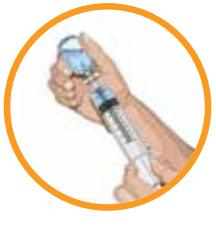
- Clean work area.
- Program the infusion pump according to prescribed infusion rates and manufacturer's instructions.
- Wash hands thoroughly and allow to dry.
- Open supplies as shown by your healthcare professional.

3. Prepare the syringe:

- Remove the cap from the vial.
- Wipe each stopper with a sterile alcohol wipe and allow to dry.

- Attach a sterile syringe to a vented spike.
- Insert the vented spike into the center of the IG vial.
- Turn the vial upside down and pull back on the plunger to pull the IG into the syringe(s).

- Repeat these steps, if using multiple vials to achieve the desired dose.
- Start the infusion promptly after drawing CUVITRU into the syringe(s). It is suggested to complete the administration within 2 hours.



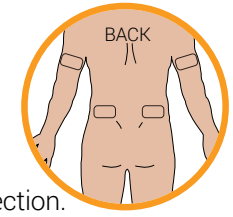
If using a sterile needle: Attach a sterile syringe to the sterile needle and pull back the plunger of syringe to fill with air, which should equal the amount of the solution you will be taking from the vial. Insert the needle into the center of the stopper **and** inject air in. Pull back on the plunger to withdraw the desired volume.

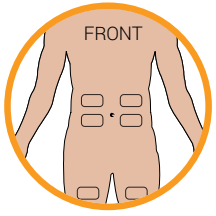
4. Prepare the infusion pump and tubing:

- Use manufacturer directions for filling the tubing and using the pump.
- Attach the syringe filled with CUVITRU to the needle set.
- Point the syringe tip up and gently push the plunger of the syringe to remove the air and fill the needle set up to the needle hub.

5. Prepare the infusion site(s):

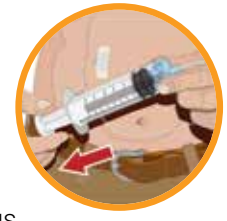
- Select the number of infusion sites based on the volume of the total dose.
- Choose infusion site(s): upper arms, abdomen, thighs, or lower back.
- Avoid: bony areas, visible blood vessels, scars and any areas of inflammation (irritation) or infection.
- Infuse CUVITRU from 1 to 4 infusion sites at the same time.
- Select sites at least 4 inches apart.
- Rotate sites between future infusions.
- Wipe the infusion site(s) with a sterile alcohol wipe beginning at the center of each infusion site and moving outward in circular motion.
- Allow the infusion site(s) to dry (at least 30 seconds).





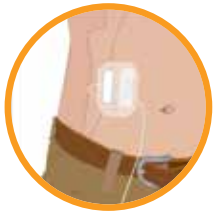
6. Insert and secure the subcutaneous needle set:

- Remove the needle cover. Firmly grasp and pinch at least 1 inch of skin between two fingers.
- Insert needle with a rapid motion straight into the skin at a 90-degree angle. Tape needle in place with sterile tape (included on transparent dressing).
- If more than one site is used, repeat the steps.
- Check for proper needle placement by pulling back on the syringe plunger to check for blood return in the tubing of the needle set.
- If blood is seen in the tubing, remove and discard the subcutaneous needle and repeat steps 4, 5 and 6 with a new subcutaneous needle and infusion site.
- Secure the needle set in place by applying a sterile protective dressing over the site(s).

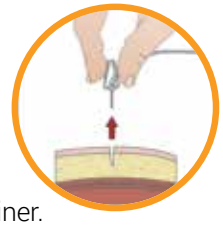


7. Start the infusion:

- Follow the manufacturer's instructions to turn pump on and start the infusion.
- Check infusion site(s) occasionally throughout the infusion.



8. Remove subcutaneous needle(s) from the infusion site(s):



- Remove the needle set by loosening the tape on all edges.
- Pull the needle wings straight up and out.
- Gently press a small piece of gauze over the needle site and cover with a dressing.
- Throw away the needle(s) into the sharps container.

9. Record the infusion

- Remove the peel-off label from the vial(s), which has the product lot number and expiration date and place the label in your treatment record/infusion log.
- Write down the date, time, dose, site(s) of infusion (to assist in rotating sites) and any reactions after each infusion.
- Throw away the disposable supplies, vials, and unused product as recommended by your healthcare professional.

What is the usual dose for CUVITRU?

CUVITRU is given under the skin (subcutaneously). It is given to you by your doctor or nurse, or by yourself. Dosage will vary depending on your condition and your bodyweight. Your healthcare professional should individualize your dose based on your clinical response to CUVITRU therapy and serum immunoglobulin G trough levels.
Doses may be adjusted over time to achieve the desired clinical response and serum IgG levels.[5]

What to do if you have missed a dose?

Inform your doctor if you missed a dose.[5]

What is the risk of overdose and what to do if you suspect an overdose?

The consequences of an overdose are not known.

If you believe that you have taken too much CUVITRU, contact your healthcare professional, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.[5]

What are possible side effects from using CUVITRU?

These are not all the possible side effects that you may feel when taking CUVITRU. If you experience any side effects not listed here, contact your healthcare professional. Please also see Warnings and Precautions.
The following one or more possible reactions may occur at the site of infusion. These generally go away within a few hours, and are less likely after the first few infusions.

- Mild or moderate pain
- Redness
- Itching

The most common side effects with CUVITRU are:

- Headache
- Nausea
- Fatigue
- Diarrhea
- Vomiting

If any of the following problems occur after starting treatment with CUVITRU, stop the infusion immediately and contact your healthcare professional or call emergency services. These could be signs of a serious problem.

- Hives, swelling in the mouth or throat, itching, trouble breathing, wheezing, fainting or dizziness. These could be signs of a serious allergic reaction.
- Bad headache with nausea, vomiting, stiff neck, fever, and sensitivity to light. These could be signs of irritation of the lining around your brain.
- Reduced urination, sudden weight gain, or swelling in your legs. These could be signs of a kidney problem.

- Pain, swelling, warmth, redness, or a lump in your legs or arms. These could be signs of a blood clot.
- Brown or red urine, fast heart rate, yellow skin or eyes. These could be signs of a liver problem or a blood problem.
- Chest pain or trouble breathing, or blue lips or extremities. These could be signs of a serious heart or lung problem.
- Fever over 100°F. This could be a sign of an infection.

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, or any side effect that bothers you or that does not go away, talk to your healthcare professional.[5]

How to report side effects

You can help improve the safe use of health products for Canadians by reporting serious and unexpected side effects to Health Canada. Your report may help to identify new side effects and change the product safety information.

3 ways to report:

- Online at MedEffect;
- By calling 1-866-234-2345 (toll-free);
- By completing a Patient Side Effect Reporting Form and sending it by:
  - Fax to 1-866-678-6789 (toll-free), or
  - Mail to: Canada Vigilance Program
    Health Canada, Postal Locator 1908C
    Ottawa, ON K1A 0K9

Postage-paid labels and the Patient Side Effect Reporting Form are available at MedEffect.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.[5]

How do I store CUVITRU?

Store CUVITRU refrigerated or at room temperature.[5]

- You can store CUVITRU in the refrigerator (2°C to 8°C) for up to 36 months or
- You can store CUVITRU at room temperature (not more than 25°C) for up to 24 months from the date of manufacture.
- Do not return CUVITRU to the refrigerator if you take it out to room temperature.
- Do not freeze.
- Do not shake.
- Check the expiration date on the carton and vial label. Do not use CUVITRU after the expiration date.
- Protect from light. You can use the original CUVITRU containers to protect it from light.
- Keep out of reach and sight of children.

If you want more information about CUVITRU

- The full product monograph prepared for health professionals can be found at www.takeda.com/siteassets/en-ca/home/what-we-do/our-medicines/product-monographs/shire-products/cuvitru-pm-en.pdf
- Or by calling the sponsor, Takeda Canada at: 1-800-268-2772.

References:

1. The Association of Allergists and Immunologists of Québec website www.allerg.qc.ca AAIQ 2016, authors - Nha Uyen Nguyen-Luu, MD FRCPC, Hugo Chapdelaine, MD FRCPC.
2. Immune Deficiency Foundation website www.primaryimmune.org - Navigation: Learn About Primary Immunodeficiencies/Relevant Information/The Immune System/The Immune System and Primary Immunodeficiency.
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