

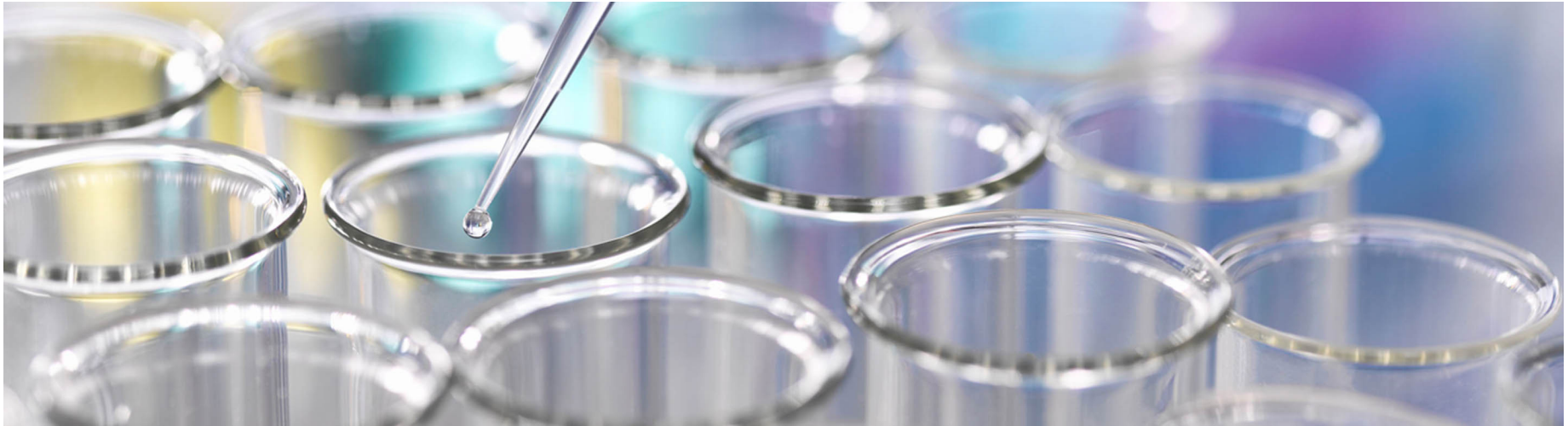


ROUTES OF ADMINISTRATION (ROA) OF IMMUNOGLOBULIN (IG) TREATMENTS

Prescribing information and adverse event reporting information can be found on page 54.



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TABLE OF CONTENTS

ACCESSING YOUR INTERACTIVE TABLE OF CONTENTS	02	PROGRESS CHECK: SECTION 03	26
WELCOME & LEARNING OBJECTIVES	04	SECTION 04: FACILITATED SUBCUTANEOUS IMMUNOGLOBULIN (ESIG)	32
SECTION 01: HISTORY OF IIG TREATMENT OPTIONS	06	PROGRESS CHECK: SECTION 04	39
SECTION 02: INTRAVENOUS IMMUNOGLOBULIN (IVIg)	10	MODULE SUMMARY	46
PROGRESS CHECK: SECTION 02	15	GLOSSARY	51
SECTION 03: CONVENTIONAL SUBCUTANEOUS IMMUNOGLOBULIN (SCIG)	21	REFERENCES	52

To quickly navigate across different parts of the module, click on the section titles in the Table of Contents on page 3.

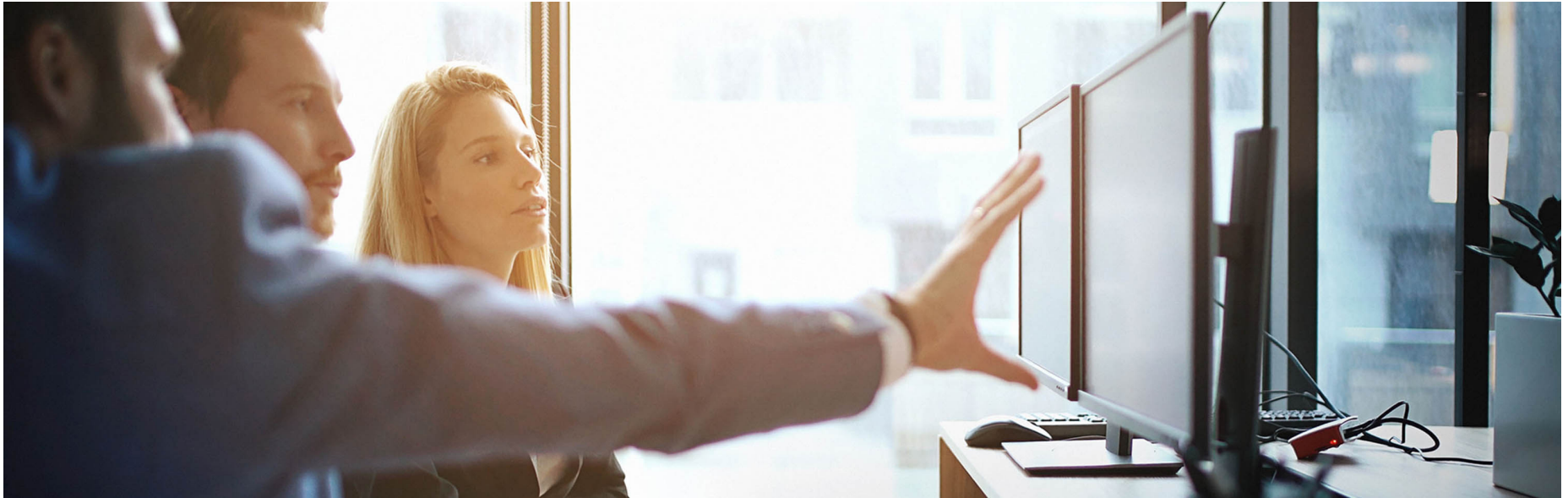


To quickly return to the Table of Contents from any location in the module, click on the icon found at the top right corner of every page.



TABLE OF CONTENTS

ACCESSING YOUR INTERACTIVE TABLE OF CONTENTS	02	PROGRESS CHECK: SECTION 03	26
WELCOME & LEARNING OBJECTIVES	04	SECTION 04: FACILITATED SUBCUTANEOUS IMMUNOGLOBULIN (fSCIG)	32
SECTION 01: HISTORY OF IG TREATMENT OPTIONS	06	PROGRESS CHECK: SECTION 04	39
SECTION 02: INTRAVENOUS IMMUNOGLOBULIN (IVIG)	10	MODULE SUMMARY	46
PROGRESS CHECK: SECTION 02	15	GLOSSARY	51
SECTION 03: CONVENTIONAL SUBCUTANEOUS IMMUNOGLOBULIN (SCIG)	21	REFERENCES	52



WELCOME & LEARNING OBJECTIVES

Upon completion of this module, you will be expected to demonstrate that you can...

- Describe the key features and history of intravenous infusion of IG treatment
- Describe the key features and history of conventional subcutaneous infusion of IG treatment
- Describe the key features and history of facilitated subcutaneous infusion of IG treatment



Welcome to the Routes of Administration (ROA) of Immunoglobulin (IG) Treatments module!

Fred has recently been diagnosed with primary immunodeficiency (PI). He was told that he will need to get regular infusions of IG replacement treatment. Fred is a working professional with an unpredictable travelling schedule. As such, Fred would like to learn about the different IG treatment options available to him and how often he would have to receive infusions to help fight infections.

In this course, you will learn about the different ROA of IG treatments. While we do mention Takeda's IG products as examples, this course is not intended to provide product specific training. Please refer to product specific training for full safety and efficacy information.



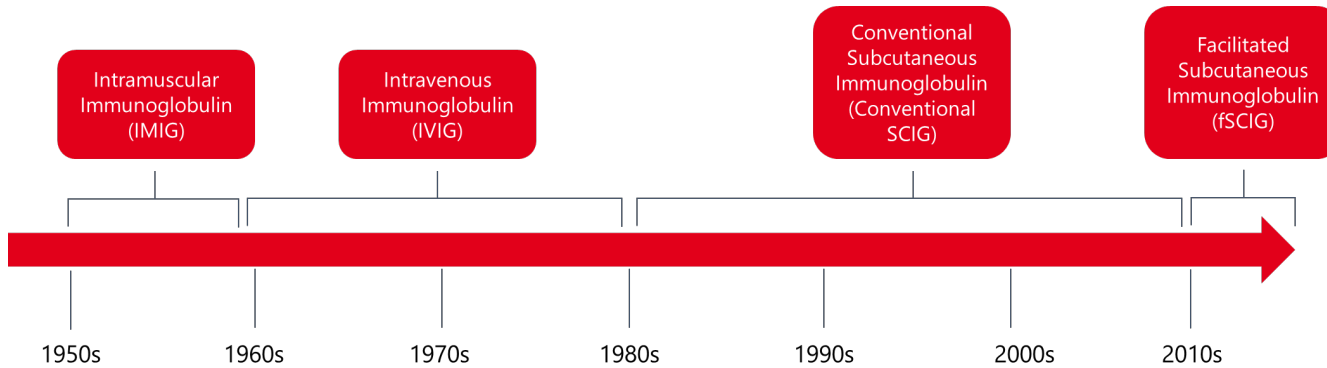
SECTION 01: HISTORY OF IG TREATMENT OPTIONS



History of IG Treatment Options

Historically, the limitations of one type of **immunoglobulin (IG)** treatment administration have prompted the development of another option. A historical perspective of IG treatment provides insight into the technology that allowed for each to emerge as a standard or common route of administration.

You will learn about the different routes of administration in more detail in the coming sections of the course.



Immunoglobulin (IG)

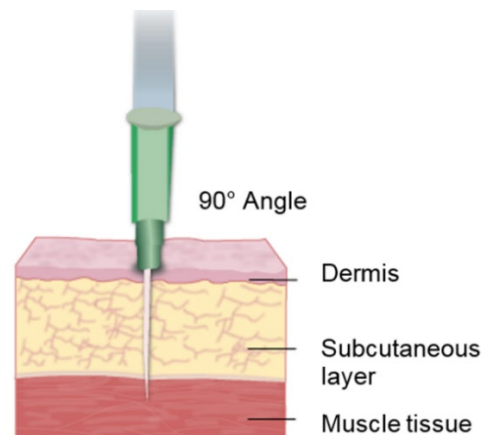
Any of a diverse group of plasma polypeptides that binds antigenic proteins and serves as one of the body's primary defences against disease. There are five types of immunoglobulins (IgA, IgD, IgE, IgG, and IgM). Also known as antibodies. IG (or Ig) is frequently used as a general term when referring to treatment with IgG.



History of IG Treatment Options (Cont.)

Intramuscular Immunoglobulin

- Historically, **intramuscular** Immunoglobulin (IMIG) was the first standard of care ROA
- Issues with limited volume of administration, and poor tolerability and compliance
- No longer a preferred ROA for IG treatment



Intravenous Immunoglobulin

- 1960s: Early **intravenous** immunoglobulin (IVIg) treatment attempts were problematic
 - Resulted in aggregation of IgG molecules and associated with severe systemic side effects
- 1980s: New manufacturing processes were introduced to prevent aggregation and reduce related systemic adverse events
 - IV treatment became favoured ROA of IG treatment



Intramuscular (IM)
Within a muscle.

Intravenous (IV)
Within or into a vein.



History of IG Treatment Options (Cont.)

Conventional Subcutaneous Immunoglobulin

- 1980s: Limited infusion rates were a challenge for conventional **subcutaneous** immunoglobulin (conventional SCIG) treatment
 - Conventional SCIG was considered an option for patients unable to tolerate IM or IV administration
- 1991: Discovery of the **rapid push technique** was a milestone
- Early 2000s: Medical literature substantiated the effectiveness and tolerability of rapidly administered conventional SCIG



Facilitated Subcutaneous Immunoglobulin

- Addresses the limitations that SC tissue poses to infusion rate and volume
- Since 1948: Animal-derived **hyaluronidase** has been used to facilitated subcutaneous immunoglobulin (facilitated SC) infusion of fluids for rehydration and local anaesthesia
- 2005: FDA approved Halozyme Therapeutics' **Recombinant Human Hyaluronidase (rHuPH20)**, used to facilitate delivery of medications and fluids
- 2013: EMA approved HyQvia▼ (Human Normal Immunoglobulin [10%] Recombinant Human Hyaluronidase), the first IG product developed for SC infusion facilitated by Recombinant Human Hyaluronidase



Subcutaneous (SC)

Beneath the skin.

Rapid push technique

Subcutaneous infusion of immunoglobulin with a syringe under the skin as fast as the patient is comfortable.

Hyaluronidase

A naturally occurring enzyme that facilitates the turnover of hyaluronan.

Recombinant Human Hyaluronidase (rHuPH20)

A genetically engineered form of human hyaluronidase. In HYQVIA (Human Normal Immunoglobulin [10%] Recombinant Human Hyaluronidase), it is used to temporarily increase the permeability of the subcutaneous tissue and increase dispersion and absorption of the IG component.



SECTION 02: INTRAVENOUS IMMUNOGLOBULIN (IVIG)

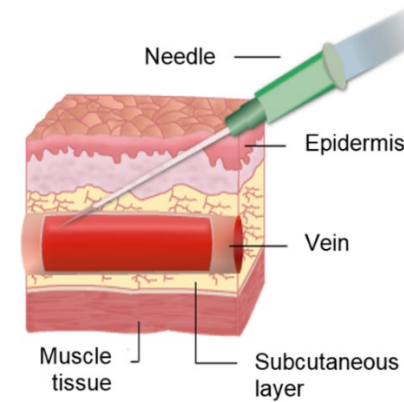


IVIG

IVIG treatments can be used to treat PI. Let's take a closer look at IVIG.

Anatomy and Physiology

- IVIG refers to when the IG is delivered through a needle into the patient's vein, straight into the patient's bloodstream



Administration Equipment

- Typically delivered with an infusion pump, IV tubing, and IV needle
- IG is infused from a container through tubing into an IV needle inserted into vein
- An infusion pump allows for controlled delivery of IG



Note: IVIG treatment is also used to manage patients with multifocal motor neuropathy (MMN), chronic inflammatory demyelinating neuropathy (CIDP) and Guillain-Barré syndrome (GBS). IV is the only ROA option for MMN. The information contained in this section of the course is specific to the IG treatment of PI. See disorder-specific training for more details on treatment of MMN, CIDP and GBS.



IVIG (Cont.)

Dose

- Based on local product-specific labelling and patient clinical response
- Patient weight is also a factor



Infusion Duration

- Typically, 2–4 hours per single infusion
- Based on total dose, rate of infusion, and patient tolerance
- Some patients may not tolerate the maximum infusion rate

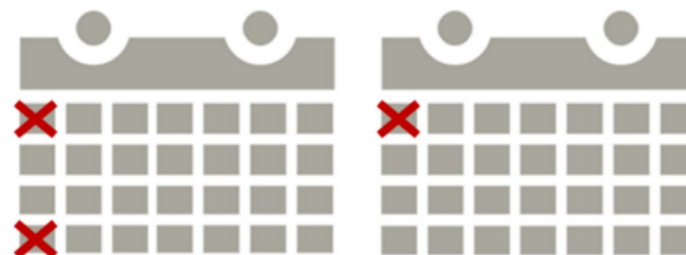




IVIg (Cont.)

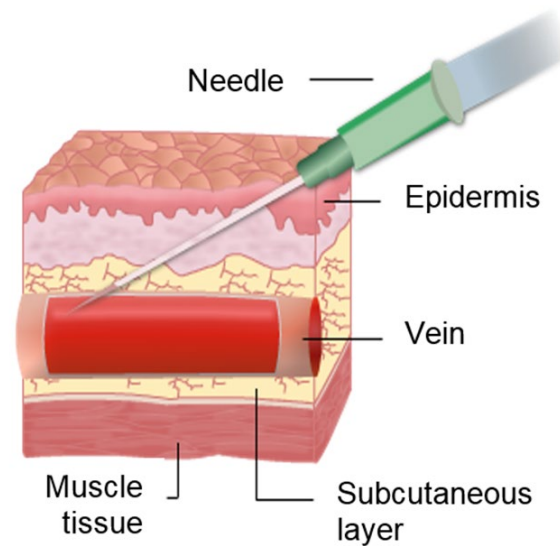
Infusion Frequency

- Typically, every 3–4 weeks



Infusion Sites

- Single needlestick per infusion





IVIG (Cont.)

Site of Care

- IVIG is usually administered at a clinic/infusion centre
- IVIG can be administered at home by an infusion nurse or rarely by a caregiver or patient themselves

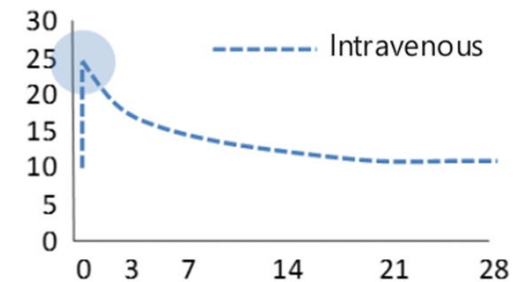


Treatment Considerations

- Rapid rise in serum IgG levels during IV infusion may pose a risk of systemic adverse reactions, in elderly patients with cerebrovascular risk factors or a history of renal disease or diabetes mellitus, during or just after infusion
- Such systemic adverse reactions include, but are not limited to, headache, fatigue, fever, nausea, chills, and rigors
- Low serum IgG levels towards end of 3–4 weeks IVIG treatment cycle may be associated with feelings of fatigue and malaise
- Venous access issues can present a challenge



Serum IgG concentrations over time following 10% IGIV infusion



Adapted from Misbah et al. Clin Exp Pharmacol. 2009; 158(1): 51-59.



PROGRESS CHECK

QUESTION ONE

Think about how you would complete the following question, then select the Check Your Answer button.
Fill in the blanks by selecting the correct option below.

IVIg treatment is typically administered every _____. A single infusion typically lasts _____ and is given with _____.

A 1–2 weeks; 2–4 hours; multiple needlesticks

B 3–4 weeks; 2–4 hours; a single needlestick

C 3–4 weeks; 3–5 hours; multiple needlesticks

D 1–2 weeks; 3–5 hours; a single needlestick

CHECK YOUR ANSWER



PROGRESS CHECK (CONT.)

ANSWER: QUESTION ONE

Fill in the blanks by selecting the correct option below.

IVIg treatment is typically administered every 3–4 weeks. A single infusion typically lasts 2–4 hours and is given with a single needlestick.

A 1–2 weeks; 2–4 hours; multiple needlesticks

B 3–4 weeks; 2–4 hours; a single needlestick

C 3–4 weeks; 3–5 hours; multiple needlesticks

D 1–2 weeks; 3–5 hours; a single needlestick



PROGRESS CHECK (CONT.)

QUESTION TWO

Think about how you would complete the following question, then select the Check Your Answer button.
Fill in the blanks by selecting the correct term from the corresponding lettered options.

IVIg is administered through a ____ inserted into the patient's ____ B ____, thereby delivering IG directly into the patient's ____ C ____.

Options A: needle / tube

Options B: artery / vein

Options C: bloodstream / lymphatic system

CHECK YOUR ANSWER



PROGRESS CHECK (CONT.)

ANSWER: QUESTION TWO

Fill in the blanks by selecting the correct term from the corresponding lettered options.

IVIg is administered through a needle inserted into the patient's vein, thereby delivering IG directly into the patient's bloodstream.



PROGRESS CHECK (CONT.)

QUESTION THREE

Think about how you would complete the following question, then select the Check Your Answer button.

Which of the following treatment consideration(s) need to be factored in when using IVIG treatment?

- A** A rapid rise in serum IgG levels occurs during the infusion
- B** Venous access issues can make administration challenging
- C** Serum IgG levels remain constant for a period of 3–4 weeks
- D** Multiple infusion sites are typically required to administer a full monthly dose

CHECK YOUR ANSWER



PROGRESS CHECK (CONT.)

ANSWER: QUESTION THREE

Which of the following treatment consideration(s) need to be factored in when using IVIG treatment?

- A** A rapid rise in serum IgG levels occurs during the infusion
- B** Venous access issues can make administration challenging
- C** Serum IgG levels remain constant for a period of 3–4 weeks
- D** Multiple infusion sites are typically required to administer a full monthly dose



SECTION 03: CONVENTIONAL SUBCUTANEOUS IMMUNOGLOBULIN (SCIG)

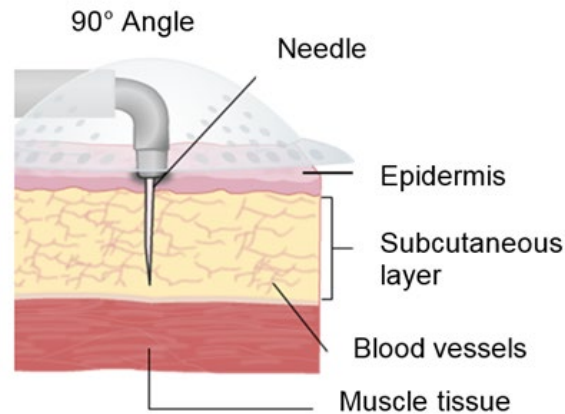


Conventional SCIG

Conventional SCIG treatments are used to treat PI. Let's take a closer look at conventional SCIG treatment.

Anatomy & Physiology

- Conventional SCIG is administered through a needle into **subcutaneous (SC) tissue**, where the IG disperses and is then absorbed into the bloodstream through local blood and **lymphatic** vessels
- The rate of infusion and volume of fluid that can be administered at one time are limited by the SC tissue itself
- Naturally occurring components of the SC tissue, including **hyaluronan**, create resistance to the flow of IG across the tissue and limit dispersion and absorption into the bloodstream



Administration Equipment

- Requires an infusion pump, syringe(s), pump tubing (as needed), and SC needle set
- The infusion pump pushes the IG from its administration container through tubing connected to a SC needle set
- The SC needle or needles are placed into the SC tissue



Subcutaneous (SC) tissue

Innermost layer of skin. Contains blood vessels that extend to the dermal layer, forming capillary networks that supply nutrients and remove waste.

Lymphatic

Pertaining to lymph and to the system of endothelial vessels that carry it.

Hyaluronan

An acid mucopolysaccharide found in the extracellular matrix of connective tissue that acts as a binding and protective agent.



Conventional SCIG (Cont.)

Dose

- Maintenance dose is based on patient clinical response and target serum IgG **trough** level
- Patient weight is also a factor



Infusion Duration

- Typically, 1–2 hours per single weekly infusion
- Depends on dose, number of infusion sites, infusion frequency, infusion rate, and patient tolerance



Trough

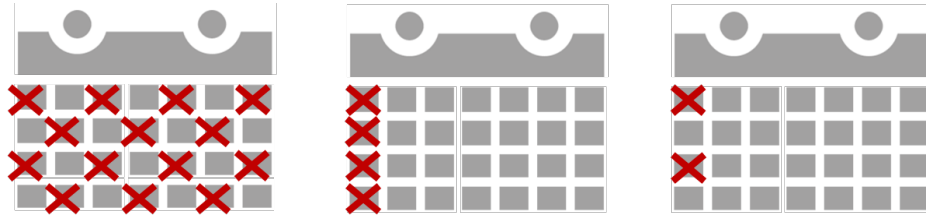
The lowest serum level of IgG prior to the next infusion.



Conventional SCIG (Cont.)

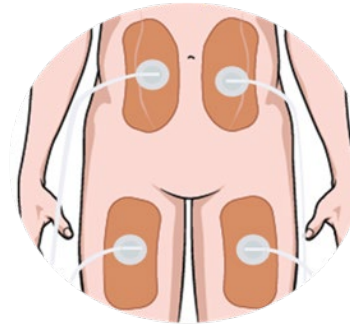
Infusion Frequency

- Ranges from 2–7 times per week, to weekly, to every 2 weeks
- Depends on IG treatment formulation and dose



Infusion Sites

- Multiple needlesticks may be needed per single infusion



Site of Care

- Typically, at home via self-administration or administration via caregiver after appropriate training

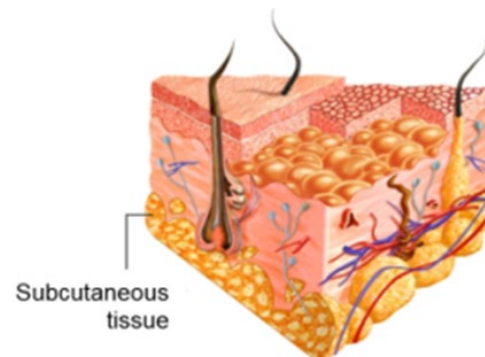




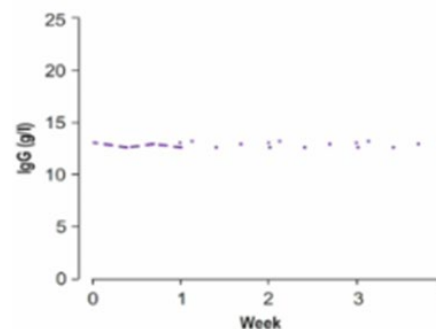
Conventional SCIG (Cont.)

Treatment Considerations

- Limitations on infusion volume mean the possibility of multiple needlesticks per infusion and the need for more frequent infusions (compared to IVIG)
- Compared to IVIG:
 - Gradual absorption of conventional SCIG into bloodstream means no rapid increases in serum IgG levels, which may reduce risk of systemic side effects in certain patients
 - More consistent serum IgG levels with conventional SCIG eliminates high peaks and low troughs between infusions
- SC infusion is associated with local adverse reactions (e.g., pain, swelling, redness, itching)



Serum IgG concentrations over time following 10% conventional IGSC infusion



Adapted from Wasserman et al. *J Allergy Clin Immunol.* 2012; 130: 951-957. Dotted lines are extrapolations.



PROGRESS CHECK

QUESTION FOUR

Think about how you would complete the following question, then select the Check Your Answer button.
Fill in the blanks by selecting the correct option below.

Conventional SCIG treatment is typically administered _____. A single weekly infusion typically lasts _____ and is given with _____.

- A** every 3–4 weeks; 1–2 hours; multiple needlesticks
- B** every 3–4 weeks; 1–3 hours; a single needlestick
- C** 2–7 times/week, weekly, or every 2 weeks; 1–3 hours; a single needlestick
- D** 2–7 times/week, weekly, or every 2 weeks; 1–2 hours; multiple needlesticks

CHECK YOUR ANSWER



PROGRESS CHECK (CONT.)

ANSWER: QUESTION FOUR

Fill in the blanks by selecting the correct option below.

Conventional SCIG treatment is typically administered 2–7 times/week, weekly, or every 2 weeks. A single weekly infusion typically lasts 1–2 hours and is given with multiple needlesticks.

- A every 3–4 weeks; 1–2 hours; multiple needlesticks
- B every 3–4 weeks; 1–3 hours; a single needlestick
- C 2–7 times/week, weekly, or every 2 weeks; 1–3 hours; a single needlestick
- D 2–7 times/week, weekly, or every 2 weeks; 1–2 hours; multiple needlesticks**



PROGRESS CHECK (CONT.)

QUESTION FIVE

Think about how you would complete the following question, then select the Check Your Answer button.
Fill in the blanks by selecting the correct options below.

Conventional SCIG is administered into the _____ tissue; it is then dispersed and absorbed into the bloodstream through local blood or _____ vessels.

Options: dermal, subcutaneous, epidermal, lymphatic, hepatic, biliary

CHECK YOUR ANSWER



PROGRESS CHECK (CONT.)

ANSWER: QUESTION FIVE

Fill in the blanks by selecting the correct options below.

Conventional SCIG is administered into the subcutaneous tissue; it is then dispersed and absorbed into the bloodstream through local blood or lymphatic vessels.



PROGRESS CHECK (CONT.)

QUESTION SIX

Think about how you would complete the following question, then select the Check Your Answer button.
Fill in the blanks by selecting the correct term from the corresponding lettered options.

Compared to IVIG treatments, conventional SCIG treatments require A frequent infusions and typically B needlesticks per single infusion.

Options A: less / more

Options B: fewer / more

CHECK YOUR ANSWER



PROGRESS CHECK (CONT.)

ANSWER: QUESTION SIX

Fill in the blanks by selecting the correct term from the corresponding lettered options.

Compared to IVIG treatments, conventional SCIG treatments require more frequent infusions and typically more needlesticks per single infusion.



SECTION 04: FACILITATED SUBCUTANEOUS IMMUNOGLOBULIN (fSCIG)



Facilitated SCIG (fSCIG)

fSCIG is used to treat PI and other diseases such as lymphocytic leukaemia and multiple myeloma. Let's take a closer look at fSCIG treatment.

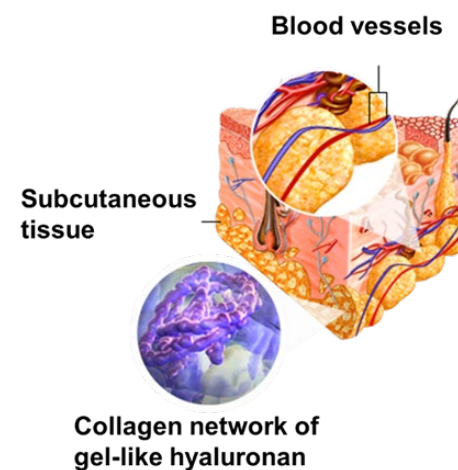
- Takeda's HyQvia (Human Normal Immunoglobulin [10%] Recombinant Human Hyaluronidase) is currently the only fSCIG product available on the market.

Note: Product availability varies by region.

Anatomy & Physiology

fSCIG addresses the limitations that the SC tissue poses to infusion rate and infusion volume.

- SC tissue:
 - Innermost layer of skin
 - Contains capillaries and blood and lymphatic vessels which absorb medications and fluids that are infused into SC tissue
 - Contains a collagen network filled with hyaluronan



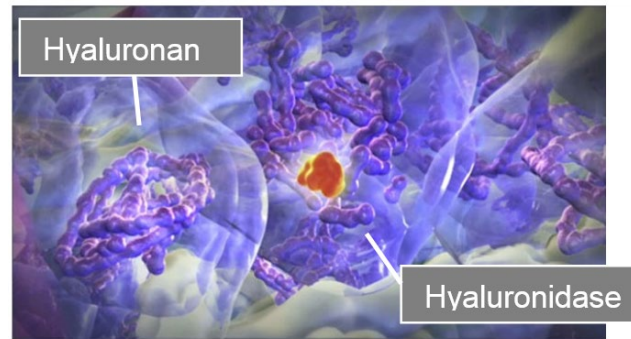
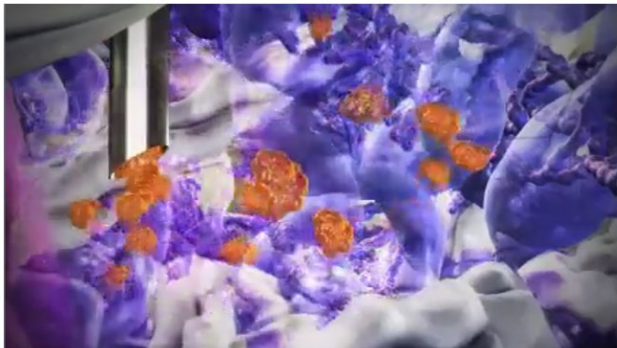


Facilitated SCIG (fSCIG) (Cont.)

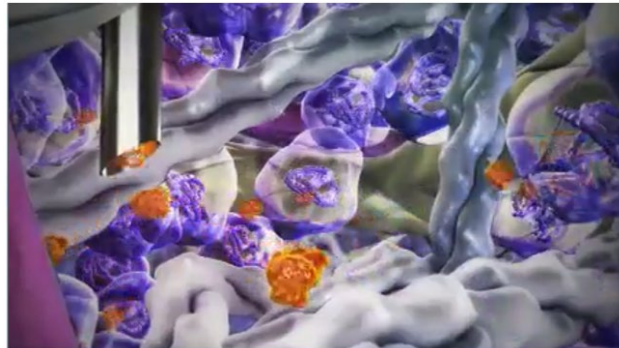
Anatomy & Physiology (Cont.)

- Hyaluronan
 - Hyaluronan creates resistance to flow of IG and limits dispersion and absorption, and thereby limits the volume and infusion rate of IG
 - Recombinant Human Hyaluronidase accelerates the natural local turnover of hyaluronan in the SC tissue and temporarily increases permeability of the SC tissue for a period of 24 to 48 hours
 - This enhances the dispersion, absorption, and **bioavailability** of IG

Recombinant Human Hyaluronidase infused into SC tissue



Accelerated turnover of hyaluronan



Bioavailability

The rate and extent to which a drug enters the body, permitting access to the site of action.



Facilitated SCIG (fSCIG) (Cont.)

Administration Equipment

- Requires an infusion pump or syringe driver, syringe(s), high flow SC needle set, solution container (bag or syringe), sterile clear bandage and tape, pump tubing, gauze, a sharps container, and possibly a pooling bag
- Recombinant Human Hyaluronidase component is subcutaneously infused first, followed within 10 minutes by the IG component into the same SC site via the same needle.

Recombinant Human Hyaluronidase component of HyQvia is infused first

...within 10 minutes...

The IG component is administered via the same site/needle





Facilitated SCIG (fSCIG) (Cont.)

Dose

- Patients switching from IVIG:
 - Same monthly dose and frequency as the previous IV treatment
- Patients switching from conventional SCIG:
 - Same monthly dose as previous conventional SCIG treatment
- Patients naïve to IG treatment:
 - 0.4 to 0.8 g/kg per month
- Based on the patient’s clinical response, the dose and frequency of the fSCIG infusion may be adjusted



Infusion Duration

- In a clinical trial for HyQvia, the median duration of individual infusions was approximately 2 hours
- Depends on dose, number of infusion sites (1 or 2), infusion rate, patient tolerance, and patient weight



Infusion Frequency

- Because of the higher volumes per site achievable with HyQvia, administration is typically every 3–4 weeks, which matches the number of infusions per month with IVIG treatment
- Can be increased to every 2 weeks

Every 3 weeks

Every 4 weeks





Facilitated SCIG (fSCIG) (Cont.)

Infusion Sites

- Typically administered via one needlestick per single infusion
- A second infusion site may be used based on maximum volume/site per patient weight, tolerability, and treatment goals as discussed by the physician and patient



Site of Care

- Typically, at home via self-administration or administration via a caregiver after appropriate training by a healthcare professional
- Option for administration at home by a nurse, or at a healthcare facility by a healthcare professional





Facilitated SCIG (fSCIG) (Cont.)

Treatment Considerations

- Unique to HyQvia is the infusion of Recombinant Human Hyaluronidase before administration of the IG component. When the Recombinant Human Hyaluronidase component of HyQvia is subcutaneously infused, it temporarily increases the permeability of the SC tissue. Then, when the IG component is subsequently infused into the same SC site, its dispersion and absorption into the SC tissue is enhanced.

The table below outlines the key differences and similarities between administration of HyQvia compared to conventional SCIG and IVIG.

	HyQvia vs conventional SCIG	HyQvia vs IVIG
Differences	<ul style="list-style-type: none"> • Higher infusion volume per site • Fewer needlesticks per month • Less frequent infusions • A patient can receive a full month’s dose of IG in one infusion using just one or two sites • The Recombinant Human Hyaluronidase component is infused before the IG • The relatively higher infusion volume per site can result in soft swelling lasting 1 to 3 days post-infusion 	<ul style="list-style-type: none"> • No venous access required • Local infusion site reactions are the most common adverse event • Systemic adverse events are less common* • With training, treatment can be self-administered • Recombinant Human Hyaluronidase component infused before IG
Similarities	<ul style="list-style-type: none"> • No venous access required • With training, treatment can be self-administered 	<ul style="list-style-type: none"> • Can be administered once a month • Single infusion site option (although a second site may be needed with HyQvia) • Treatment can be given at home or in an office setting by an HCP

**Based on HyQvia clinical trial data with KIOVIG (Human normal immunoglobulin G [IgG]).*



PROGRESS CHECK

QUESTION SEVEN

Think about how you would complete the following question, then select the Check Your Answer button.
Fill in the blanks by selecting the correct option from the corresponding lettered options.

Facilitated SCIG treatment is typically administered _____ **A** _____. In the clinical trial for HyQvia, the median duration of individual infusions was approximately _____ **B** _____. A single infusion is typically given with _____ **C** _____.

Options A: 2–7 times/week, weekly, or every 2 weeks / every 3–4 weeks

Options B: 4 hours / 2 hours

Options C: a single needlestick / multiple needlesticks

CHECK YOUR ANSWER



PROGRESS CHECK (CONT.)

ANSWER: QUESTION SEVEN

Fill in the blanks by selecting the correct option from the corresponding lettered options.

Facilitated SCIG treatment is typically administered every 3–4 weeks. In the clinical trial for HyQvia, the median duration of individual infusions was approximately 2 hours. A single infusion is typically given with a single needlestick.



PROGRESS CHECK (CONT.)

QUESTION EIGHT

Think about how you would complete the following question, then select the Check Your Answer button.
Fill in the blanks by selecting the correct option below.

The dispersion and absorption of IgG into the bloodstream during conventional SCIG infusion is limited by _____ in the subcutaneous tissue.

Options: lymphatic vessels, epidermis, hyaluronan, capillaries, hyaluronidase

CHECK YOUR ANSWER



PROGRESS CHECK (CONT.)

ANSWER: QUESTION EIGHT

Fill in the blanks by selecting the correct option below.

The dispersion and absorption of IgG into the bloodstream during conventional SCIG infusion is limited by hyaluronan in the subcutaneous tissue.



PROGRESS CHECK (CONT.)

QUESTION NINE

Think about how you would complete the following question, then select the Check Your Answer button.
Fill in the blanks by selecting the correct option from the corresponding lettered options.

Compared to conventional SCIG treatments, facilitated SCIG treatment typically requires __A__ needlesticks per single infusion and allows for __B__ volume per site.

Options A: fewer / more

Options B: higher / lower

CHECK YOUR ANSWER



PROGRESS CHECK (CONT.)

ANSWER: QUESTION NINE

Fill in the blanks by selecting the correct option from the corresponding lettered options.

Compared to conventional SCIG treatments, facilitated SCIG treatment typically requires fewer needlesticks per single infusion and allows for higher volume per site.












BACK TO FRED

Recall that Fred is a 34-year-old, 80 kg man newly diagnosed with PI*. Fred and his physician are discussing all the IG route of administration options to determine which would work best for him.

The following table is an example comparison chart that shows different treatment experiences Fred would have – such as number of needlesticks, infusion frequency, and infusion duration – depending on which ROA is chosen. The features of each ROA for IG treatment are among the considerations that help inform a specific IG treatment choice for a specific patient.



ROA	IVIg 10%	Conventional SCIG 20%	fSCIG 10%
Dose	500 mg/kg or 40 g every 4 weeks	500 mg/kg or 40 g every 4 weeks, or 10 g per week	500 mg/kg or 40 g every 4 weeks
Infusion volume	400 mL	50 mL [†]	20 mL Recombinant Human Hyaluronidase + 400 mL IG
Needlesticks per single infusion			
Duration per single infusion [‡]	1.5 hours	50 minutes	1.5 hours
Infusion frequency			
Site of care			
Adverse effects (occurs in 1 in 10 patients)	Headache, hypertension, nausea, rash, local reactions	Headache, diarrhoea, nausea, local reactions, fatigue	Local reactions

*Note: This is just one example of a PI patient's possible infusion experience with IG administration.

[†]Note: Vials come in sizes of 5 mL (1 g), 10 mL (2 g), 20 mL (4 g), and 40 mL (8 g).

[‡]Based on maximum maintenance infusion rate.



MODULE SUMMARY

History of IG Treatment Options

IMIG

- 1950s: First standard of care ROA, but due to issues with limited volume of administration and poor tolerability and compliance, no longer a preferred ROA for IG treatment

IVIG

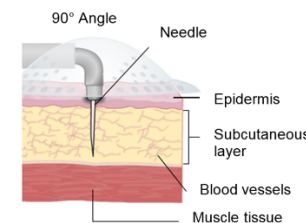
- 1960s: Early IVIG treatment attempts had problems with IgG aggregates and severe systemic side effects
- 1980s: New manufacturing processes were introduced to address these problems and IVIG treatment became favoured ROA of IG treatment

Conventional SCIG

- 1980s: At first, limited infusion rates were a challenge
- 1991: The discovery of the rapid push technique was a milestone
- Early 2000s: Medical literature substantiated the effectiveness and tolerability of rapidly administered conventional SCIG

Facilitated SCIG

- Since 1948: Animal-derived hyaluronidase has been used to facilitate SC infusion
- 2005: Halozyme Therapeutics' Recombinant Human Hyaluronidase was approved by the FDA to facilitate the delivery of medications and fluids
- 2013: EMA approved HyQvia (Human Normal Immunoglobulin with Recombinant Human Hyaluronidase), the first IG product developed for SC infusion facilitated by Recombinant Human Hyaluronidase

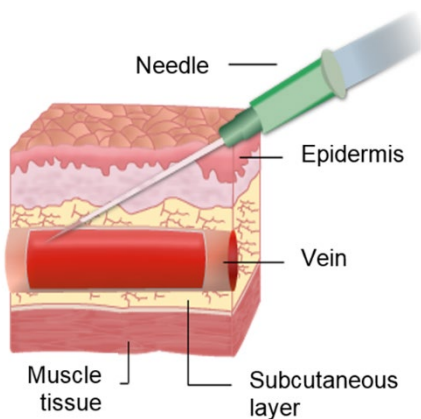




MODULE SUMMARY (CONT.)

IVIG

- IG delivered through needle into vein, straight into patient's bloodstream
- Typically delivered with an infusion pump, IV tubing, IV needle
- Dose based on specific product labelling, patient weight, and patient clinical response
- Infusion duration typically 2 to 4 hours per single infusion
- Infusion frequency typically every 3 to 4 weeks
- Single needlestick per infusion
- Site of care usually at clinic/infusion centre
- High peak serum IgG levels may pose a risk of systemic side effects in certain patients; low trough serum IgG levels may be associated with feelings of fatigue and malaise
- Venous access can present a challenge

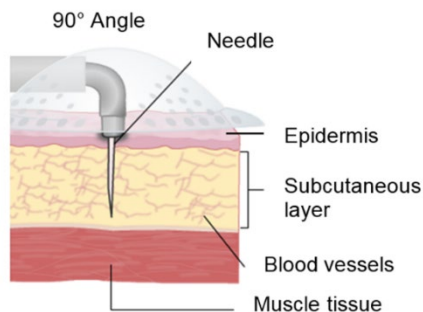




MODULE SUMMARY (CONT.)

Conventional SCIG

- Administered into SC tissue, then absorbed into bloodstream through local blood and lymph vessels
- Requires an infusion pump, syringe(s), pump tubing (as needed), and SC needle set
- Maintenance dose based on patient clinical response and target serum IgG trough level
- Patient weight is also a factor
- Infusion duration typically 1–2 hours per single weekly infusion
- Infusion frequency ranges from 2–7 times per week, to weekly, to every 2 weeks
- Multiple needlesticks may be needed per single infusion
- Site of care typically at home via self-administration or administration via a caregiver after appropriate training
- Compared to IVIG:
 - Limitations on infusion volume mean the possibility of multiple needlesticks per infusion and the need for more frequent infusions
 - Gradual absorption into bloodstream means no rapid increases in serum IgG levels, which may reduce risk of systemic side effects in certain patients
 - More consistent serum IgG levels eliminates high peaks and low troughs between infusions
- SC infusion is associated with local adverse reactions (e.g., pain, swelling, redness, itching)





MODULE SUMMARY (CONT.)

Facilitated SCIG

- Recombinant Human Hyaluronidase is infused into SC tissue just before the IG component to facilitate the dispersion and absorption, and therefore bioavailability, of IG
- Requires an infusion pump or syringe driver, syringe(s), high flow SC needle set, solution container (bag or syringe), sterile clear bandage and tape, pump tubing, gauze, a sharps container, and possibly a pooling bag
- Dose:
 - Patients switching from IVIG: same monthly dose and frequency as the previous IV treatment
 - Patients switching from conventional SCIG: same monthly dose as previous conventional SCIG treatment
 - Patients naïve to IG treatment: 0.4 to 0.8 g/kg per month
 - Adjustments made based on patient clinical response
- In the clinical trial for HyQvia, the median duration of individual infusions was approximately 2 hours
- Infusion frequency typically every 3–4 weeks
- Typically administered via one needlestick per single infusion, although two sites may be used based on maximum volume/site per patient weight, tolerability, and treatment goals
- Site of care typically at home via self-administration or administration via a caregiver after appropriate training by a healthcare professional
- Compared to conventional SCIG:
 - Differences:
 - Higher infusion volume per site
 - Fewer needlesticks per month
 - Less frequent infusions
 - Recombinant Human Hyaluronidase component infused before IG
 - Similarities:
 - No venous access required
 - With training, treatment can be self-administered

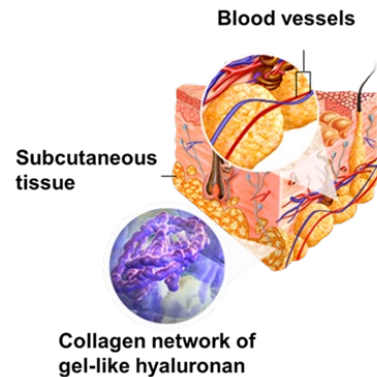


MODULE SUMMARY (CONT.)

Facilitated SCIG (Cont.)

- Compared to IVIG:
 - Differences:
 - No venous access required
 - Local infusion site reactions are more common
 - Systemic adverse events are less common*
 - With training, treatment can be self-administered
 - Recombinant Human Hyaluronidase component infused before IG
 - Similarities:
 - Can be administered once-a-month
 - Single infusion site option (although a second site may be needed with HyQvia)
 - Treatment can be given at home or in an office setting by an HCP

*Based on HyQvia clinical trial data.



Note: Product names and availability vary by region.



GLOSSARY

Bioavailability

The rate and extent to which a drug enters the body, permitting access to the site of action.

Hyaluronan

An acid mucopolysaccharide found in the extracellular matrix of connective tissue that acts as a binding and protective agent.

Hyaluronidase

A naturally occurring enzyme that facilitates the turnover of hyaluronan.

Immunoglobulin (IG)

Any of a diverse group of plasma polypeptides that binds antigenic proteins and serves as one of the body's primary defences against disease. There are five types of immunoglobulins (IgA, IgD, IgE, IgG, and IgM). Also known as antibodies. IG (or Ig) is frequently used as a general term when referring to treatment with IgG.

Intramuscular (IM)

Within a muscle.

Intravenous (IV)

Within or into a vein.

Lymphatic

Pertaining to lymph and to the system of endothelial vessels that carry it.

Rapid push technique

Subcutaneous infusion of immunoglobulin with a syringe under the skin as fast as the patient is comfortable.

Recombinant Human Hyaluronidase (rHuPH20)

A genetically engineered form of human hyaluronidase. In HYQVIA (Human Normal Immunoglobulin [10%] Recombinant Human Hyaluronidase), it is used to temporarily increase the permeability of the subcutaneous tissue and increase dispersion and absorption of the IG component.

Subcutaneous (SC)

Beneath the skin.

Subcutaneous (SC) tissue

Innermost layer of skin. Contains blood vessels that extend to the dermal layer, forming capillary networks that supply nutrients and remove waste.

Trough

The lowest serum level of IgG prior to the next infusion.



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PRESCRIBING INFORMATION

Full prescribing information:

Cuvitru available [here](#)

HyQvia available [here](#)

Kiovig available [here](#)