The freedom of more personal time with HYQVIA, the only once-a-month subQ Ig*1

For adults with primary Immunodeficiency

What is HYQVIA?

- HYQVIA is a liquid medicine containing immune globulin and recombinant human hyaluronidase. HYQVIA contains IgG antibodies, collected from human plasma donated by healthy people. The antibodies help your body to fight off bacterial and viral infections. The hyaluronidase part of HYQVIA helps more of the immune globulin get absorbed into the body to fight infection.
- HYQVIA is indicated for the treatment of Primary Immunodeficiency (PI) involving the humoral immune system in adults.
- Safety and efficacy of chronic use of recombinant human hyaluronidase in HYQVIA have not been established in conditions other than PI.
- HYQVIA is infused under the skin (subcutaneous).
- If you and your healthcare professional decide that home self-infusion of HYQVIA is right for you, then be sure you get instructions and training from your healthcare professional before using HYQVIA at home.

Important Safety Information about HYQVIA

- HYQVIA can cause blood clots. Call your healthcare professional or go to your emergency department right away if you have pain, swelling, warmth, redness, or a lump in your legs or arms, other than at the infusion site(s), 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. These could be signs of a blood clot.
- Do not use HYQVIA if you are allergic to immune globulin (IgG), hyaluronidase, other blood products, human albumin (in the hyaluronidase solution), or have IgA deficiency.

These are not all the possible side effects with HYQVIA. Talk to your healthcare professional about any side effects that bother you or that don’t go away.

Please see the Indication and Important Safety Information on pages 17-18, and the FDA-approved patient labeling.
HYQVIA can cause serious side effects. Call your healthcare professional or go to your emergency department right away if you get:

- 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 swelling in 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, other than at the infusion site(s). 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 or blood problem.
- Chest pain or trouble breathing, blue lips or extremities. These could be signs of a lung problem.

These are not all the possible side effects with HYQVIA. Talk to your healthcare professional about any side effects that bother you or that don’t go away.
With HYQVIA, there’s freedom to personalize your Ig treatment administration with your doctor

With HYQVIA [Immune Globulin Infusion 10% (Human) with Recombinant Human Hyaluronidase], you have the option to infuse using 1 needle, 1 infusion site, 1 time a month, in the comfort of your own home, at your doctor’s office or infusion center. A second site can be used at the discretion of the physician and patient based on tolerability and total volume.

In the clinical trial, 2 infusion sites were used when the infusion volume was more than 600 mL.²

Please see the Indication and Important Safety Information on pages 17-18, and the FDA-approved patient labeling.
Just 1 HYQVIA infusion a month can help your body fight off bacterial and viral infections¹

As demonstrated in the clinical trial, once-a-month HYQVIA helped reduce the risk of serious infections:

0.025 acute serious bacterial infections

0 days in hospital due to infection

Infusion time with HYQVIA, the only once-a-month subQ Ig¹

Infusing once a month with HYQVIA doesn’t mean your infusions will take longer. Typically, infusions take less than 3 hours with HYQVIA [Immune Globulin Infusion 10% (Human) with Recombinant Human Hyaluronidase]. Instead, you’ll have more free time.

Please see the Indication and Important Safety Information on pages 17-18, and the FDA-approved patient labeling.
HYQVIA helps maintain even levels of Ig in your body*1

The peak to trough variation with HYQVIA is similar to conventional subQ administration, even with once-a-month administration (every 3 to 4 weeks). Also, HYQVIA [Immune Globulin Infusion 10% (Human) with Recombinant Human Hyaluronidase] does not have the high peak Ig level experienced with intravenous administration.

Dose adjustment

<table>
<thead>
<tr>
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<th>IVIG 10%</th>
<th>HYQVIA</th>
<th>Conventional SubQ 10%</th>
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<tbody>
<tr>
<td>100%</td>
<td>108%</td>
<td>137%</td>
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*Comparison of mean Ig values for HYQVIA vs IVIG 10% and Conventional SubQ 10%. IVIG 10% and HYQVIA data at 28 day dosing interval; Conventional SubQ 10% data at 7 day dosing interval; Conventional SubQ 10% dotted line shows weekly dose extrapolated over 21 additional days.

Important Safety Information

What are the possible or reasonably likely side effects of HYQVIA?

• After HYQVIA infusion a temporary, soft swelling may occur around the infusion site, which may last 1 to 3 days, due to the volume of fluid infused. Mild or moderate pain, redness, swelling, or itching may occur at the site of infusion and generally go away in a few hours. Local reactions are less likely after the first few infusions.

• The most common side effects of HYQVIA are headache, fatigue, nausea, fever, and vomiting.

• Antibodies to the hyaluronidase component of HYQVIA were formed in some patients taking HYQVIA. It is not known if there is any long term effect. In theory, these antibodies could react with your body’s own PH20. PH20 is present in the male reproductive tract. So far, these antibodies have not been associated with increased or new side effects.

These are not all the possible side effects with HYQVIA. Talk to your healthcare professional about any side effects that bother you or that don’t go away.
Recombinant Human Hyaluronidase: it’s the reason you can infuse HYQVIA up to once a month using 1 or 2 needles

Conventional subQ Ig treatments require multiple infusions with multiple needlesticks to receive your monthly dose. HYQVIA [Immune Globulin Infusion 10% (Human) with Recombinant Human Hyaluronidase] is the only once-a-month subQ Ig with Recombinant Human Hyaluronidase (hy•lah•RON•ah•dase). The hyaluronidase temporarily opens the subQ space, allowing a larger amount of Ig to reach the subQ tissue and be absorbed into the bloodstream to help fight infection.

It’s the reason you can infuse your monthly dose of HYQVIA using 1 needle, 1 infusion site, 1 time a month. A second site can be used at the discretion of the physician and patient based on tolerability and total volume. In the clinical trial, 2 infusion sites were used when the infusion volume was more than 600 mL.

HYQVIA is supplied as a dual-vial unit and is infused sequentially through 1 needle: 1. Recombinant Human Hyaluronidase (HY) and 2. Human Immune Globulin Infusion 10% (IG).
Talk to your doctor to determine the best option for you.

Important Safety Information

- Your healthcare professional may perform blood tests regularly to check your IgG level.
- With your consent, your healthcare professional may provide blood samples to Shire plc, to test for antibodies that may form against the hyaluronidase part of HYQVIA.
- Do not infuse HYQVIA into or around an infected or red swollen area because it can cause infection to spread.
- Women who become pregnant during HYQVIA treatment are encouraged to enroll in the HYQVIA Pregnancy Registry by calling 1-866-424-6724.

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Without Recombinant Human Hyaluronidase, hyaluronan limits the flow of Ig.¹

The subQ tissue (directly beneath the skin) is filled with a substance called hyaluronan. Hyaluronan turns over naturally in your body every day because of an enzyme called hyaluronidase. Because hyaluronan limits the flow of fluids through subQ tissue at local infusion sites, conventional subQ Ig treatments may require that you infuse more frequently and at multiple infusion sites.²

HYQVIA helps fight infections.¹

Please see the Indication and Important Safety Information on pages 17-18, and the FDA-approved patient labeling.
Recombinant Human Hyaluronidase locally increases the natural turnover of hyaluronan.\textsuperscript{1}

As part of your infusion of HYQVIA, Recombinant Human Hyaluronidase locally increases the amount of hyaluronan that is turned over, temporarily opening up the subQ tissue.

Recombinant Human Hyaluronidase enhances the flow of Ig into the subQ tissue and into the bloodstream.\textsuperscript{1}

Recombinant Human Hyaluronidase enhances the flow of Ig into the subQ tissue and into the bloodstream. The effect of Recombinant Human Hyaluronidase on hyaluronan is reversible and the hyaluronan is restored within 24 to 48 hours after your infusion. During the clinical trial and extension study, no changes to the skin or subcutaneous tissue were observed.
Here’s what it looks like when you infuse with HYQVIA¹

Following your infusion with HYQVIA [Immune Globulin Infusion 10% (Human) with Recombinant Human Hyaluronidase], it’s not uncommon to experience a temporary, soft swelling at the infusion site. This is due to the volume of fluid infused and may last 1 to 3 days after your infusion.

Pre-Infusion | Post-Infusion | 24 Hours After Infusion
---|---|---

HYQVIA infused: 400 mL split into 2 infusion sites (200 mL each)*

Local infusion-site reactions such as mild or moderate pain, swelling, redness, and itching may also occur and generally go away within a few hours. Local reactions are less likely to occur after the first few infusions.

In the clinical trials there were no observable changes in the skin or subcutaneous tissue in almost 3000 infusions and maximum exposure of over 3 years.¹

Here is an example of a mild local site reaction:

Pre-Infusion | Post-Infusion
---|---

HYQVIA infused: 494 mL*

*Volume infused as per the doctor’s guidance based on this patient’s specific clinical condition; it may be different for you.

¹2959 infusions and 188 subject-years.
Once a month or more frequently, if needed.‡

In clinical trials, no serious side effects were found related to HYQVIA [Immune Globulin Infusion 10% (Human) with Recombinant Human Hyaluronidase].¹

More than 98% of infusion-site reactions seen with HYQVIA were mild to moderate.¹

Important Safety Information

• HYQVIA can cause blood clots. Call your healthcare professional or go to your emergency department right away if you have pain, swelling, warmth, redness, or a lump in your legs or arms, other than at the infusion site(s), 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. These could be signs of a blood clot.

What are the possible or reasonably possible side effects of HYQVIA?

• After HYQVIA infusion a temporary, soft swelling may occur around the infusion site, which may last 1 to 3 days, due to the volume of fluid infused. Mild or moderate pain, redness, swelling, or itching may occur at the site of infusion and generally go away in a few hours. Local reactions are less likely after the first few infusions.

• The most common side effects of HYQVIA are headache, fatigue, nausea, fever, and vomiting.

• Antibodies to the hyaluronidase component of HYQVIA were formed in some patients taking HYQVIA. It is not known if there is any long term effect. In theory, these antibodies could react with your body’s own PH20. PH20 is present in the male reproductive tract. So far, these antibodies have not been associated with increased or new side effects.

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‡ As determined by your healthcare provider.
Here’s what you can expect when starting on HYQVIA

Infusing HYQVIA [Immune Globulin Infusion 10% (Human) with Recombinant Human Hyaluronidase] may be different than what you’re used to. If you and your doctor decide that self-administration at home is right for you, you will receive instruction from your doctor during the ramp-up period but will not begin self-administration until you feel comfortable enough to infuse on your own.

You’ll also be provided with a training kit that will include the tools you’ll need to infuse at home. If you haven’t received your HYQVIA Training Kit, please call 1-855-250-5111.

7 week HYQVIA ramp-up period begins approximately 1 week after your last subQ Ig or IV Ig dose

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After Week 7, your HYQVIA personalized maintenance treatment begins

Please see the Indication and Important Safety Information on pages 17-18, and the FDA-approved patient labeling.
The ramp-up period

To help you become comfortable with your treatment, you will receive the first dose of HYQVIA and will ramp up gradually. Your dose will eventually shift from 1 time a week to 1 time a month (every 3 to 4 weeks). An example of a ramp-up period for a 4-week interval maintenance dose of HYQVIA is shown below.

Dose adjustment of HYQVIA [Immune Globulin Infusion 10% (Human) with Recombinant Human Hyaluronidase] may be necessary based on your clinical response.

<table>
<thead>
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<th>Week after your last subQ Ig or IV Ig dose</th>
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Before the infusion

- Make sure you have received appropriate training from your healthcare provider on how to self-infuse HYQVIA [Immune Globulin Infusion 10% (Human) with Recombinant Human Hyaluronidase] and always follow his/her instructions, especially regarding the dose and schedule.
- Ensure you’re hydrated by drinking plenty of fluids before you infuse.
- Choose a less busy day and plan ahead to avoid disruptions while infusing.
- Set up your supplies in a clean area and carefully read the instructions provided to you.
- Allow HYQVIA to reach room temperature (this may take up to 60 minutes).
- HYQVIA can be held at room temperature (up to 77°F [25°C]) for up to 3 months.* Be sure to keep it in the box to protect it from light.

*During the first 24 months from the date of manufacturing.

Please see the Indication and Important Safety Information on pages 17-18, and the FDA-approved patient labeling.
During the infusion

- Get comfortable and try to relax during your infusion
- Local infusion-site reactions such as mild to moderate pain, temporary soft pancake-like swelling, itching, and skin redness are common with HYQVIA [Immune Globulin Infusion 10% (Human) with Recombinant Human Hyaluronidase]
  - Flat, pancake-like swelling may last 1 to 3 days
  - Other infusion-site reactions generally go away within a few hours
- In addition to local reactions, most common side effects may include headache, fatigue, nausea, fever, and vomiting
- If side effects increase in severity or persist for more than a few days, call your doctor or hospital emergency services immediately
- Never infuse HYQVIA into or around an infected or red swollen area

After the infusion

- Continue drinking fluids to remain hydrated
- Record your infusion time, date, dose, infusion-site location, and any reactions you may experience in your infusion log
- Make sure to follow up with your doctor routinely

Important Safety Information

Before starting HYQVIA, tell your healthcare professional if you:

- Have or had any kidney, liver, or heart problems or history of blood clots because HYQVIA can make these problems worse.
- Have IgA deficiency or a history of severe allergic reactions to IgG or other blood products.
- Are pregnant, trying to become pregnant or are breast feeding.

You are encouraged to report suspected side effects by contacting FDA at 1-800-FDA-1088 or www.fda.gov/medwatch or Shire Drug Safety at 1-800-999-1785.
Enjoy life’s moments.

Life is full of beginnings, and a primary immunodeficiency (PI) diagnosis is one of them. MyIgSource is here to support you throughout your PI journey, helping you to enjoy life’s moments.

Reach out for support today!
Call 1-855-250-5111 or visit MyIgSource.com to enroll in the program.
We’ve got eligible patients with PI covered

Now, eligible patients with PI can save up to $5,000* on their out-of-pocket deductible/co-payment/co-insurance costs within a 12-month period for all Shire immune globulin (Ig) products.

Only Shire offers a copay program for eligible patients with PI that covers all of its Ig products. We believe in supporting patients with the financial resources they need along their journey with PI. Eligible patients can now lower their out-of-pocket monthly costs for prescribed Shire Ig treatments because we believe costs associated with Ig treatments for PI shouldn’t be a barrier to patient care.

For more information, visit MyIgSource.com or call 855-250-5111.

*Not valid for prescriptions reimbursed, in whole or in part, by Medicaid, Medicare, Medigap, VA, DoD, TRICARE or any other federal or state healthcare programs, including state pharmaceutical assistance programs, and where prohibited by the health insurance provider or by law. Commercial insurance must cover medication costs for prescribed Shire Immune Globulin (Ig) treatment for primary immunodeficiency (PI) and allow for copay or co-insurance assistance. Shire reserves the right to change or discontinue this program at any time without notice. Please see full treatment-specific Terms and Conditions on product web sites for additional program restrictions and eligibility requirements or call MyIgSource for more information (855-250-5111).

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Indication and Important Safety Information

What is HYQVIA?

• HYQVIA is a liquid medicine containing immune globulin and Recombinant Human Hyaluronidase. HYQVIA contains IgG antibodies, collected from human plasma donated by healthy people. The antibodies help your body to fight off bacterial and viral infections. The hyaluronidase part of HYQVIA helps more of the immune globulin get absorbed into the body to fight infection.

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• If you and your healthcare professional decide that home self-infusion of HYQVIA is right for you, then be sure you get instructions and training from your healthcare professional before using HYQVIA at home.

Important Safety Information

What is the most important information that I should know about HYQVIA?

• HYQVIA can cause blood clots.

• Call your healthcare professional if you have pain, swelling, warmth, redness, or a lump in your legs or arms, other than at the infusion site(s), 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.

• Your healthcare professional may perform blood tests regularly to check your IgG level.

• With your consent, your healthcare professional may provide blood samples to Shire plc, to test for antibodies that may form against the hyaluronidase part of HYQVIA.

• Do not infuse HYQVIA into or around an infected or red swollen area because it can cause infection to spread.

• Talk to your healthcare professional if you become pregnant. Women who become pregnant during HYQVIA treatment are encouraged to enroll in the HYQVIA Pregnancy Registry by calling Medical Information at 1-866-424-6724.

Who should not take HYQVIA?

Do not take HYQVIA if you:

• Are allergic to IgG, hyaluronidase, other blood products, or human albumin (in the hyaluronidase solution).

• Have IgA deficiency with antibodies to IgA.
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- Bad headache with nausea, vomiting, stiff neck, fever, and sensitivity to light. These could be signs of swelling in your brain.
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Before starting HYQVIA, tell your healthcare professional if you:

- Have or had any kidney, liver, or heart problems or history of blood clots because HYQVIA can make these problems worse.
- Have IgA deficiency or a history of severe allergic reactions to IgG or other blood products.
- Are pregnant, trying to become pregnant or are breast feeding.

You are encouraged to report suspected side effects by contacting FDA at 1-800-FDA-1088 or www.fda.gov/medwatch or Shire Drug Safety at 1-800-999-1785.

The risk information provided here is not comprehensive. To learn more, talk about HYQVIA with your healthcare provider or pharmacist. Click here for the FDA-approved patient labeling or visit www.HYQVIA.com.

References
Schedule an appointment with your doctor to see if HYQVIA is right for you.

To learn more about HYQVIA, visit www.HYQVIA.com

Create a treatment plan with your doctor that fits your lifestyle.

Please see the Indication and Important Safety Information on pages 17-18, and the FDA-approved patient labeling.