

Recommendations for GPA/MPA*



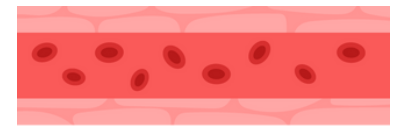
These are recommendations written by a group of doctors and patients based on research studies for people with GPA/MPA.

These recommendations suggest the best treatment for most people, but your individual situation and treatment may be different. Talk to your doctor about what treatment is best for you.

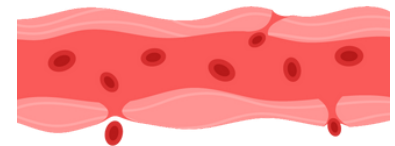
What is vasculitis?

Vasculitis: A group of conditions that involve inflammation (swelling) of your blood vessels. ANCA-associated vasculitis (AAV) is a group of disorders that include:

- **EGPA:** One of the rarest types of vasculitis that mostly affects the small blood vessels. It can affect the lungs, sinuses, skin, heart, digestive tract, kidneys, nerves, and other organs.
- **GPA:** A type of vasculitis that can affect blood vessels in your nose, sinuses, throat, lungs, and kidneys.
- **MPA:** A type of vasculitis that mostly affects small to medium-sized blood vessels. It can affect your kidneys, lungs, nerves, skin, and joints.



Healthy blood vessel



Inflamed blood vessel

Words to know about vasculitis

- **Active disease:** New, ongoing, or worsening signs or symptoms.
- **Severe disease:** Symptoms that may cause death or organ failure (when a major organ stops working, such as the heart).
- **Nonsevere disease:** Symptoms not likely to cause death or organ failure.
- **Refractory:** When a disease does not get better with treatment.
- **Relapse:** When symptoms return after a period of improvement (or remission).
- **Remission:** When the signs and symptoms of a disease decrease or go away.
 - **Remission induction treatment:** Treatments for active disease to get to a place where there are no active symptoms and no new damage to your body from the disease.
 - **Remission maintenance:** Treatments given after a disease goes into remission. These treatments help keep the disease in remission.

See a glossary of health terms at the end of this document.



Treatment recommendations for active GPA/MPA

If you have **active, severe GPA/MPA**, we recommend:

➔ **Use rituximab over cyclophosphamide.**

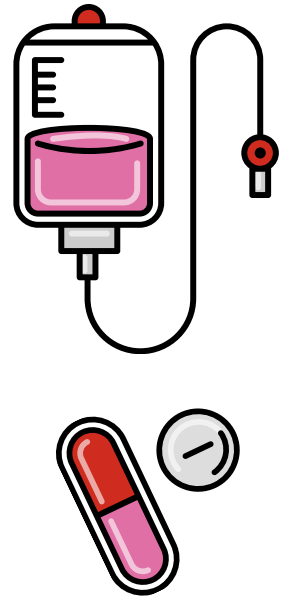
- Studies have shown that rituximab works as well as cyclophosphamide and has fewer and less serious side effects.

➔ **Use a lower-dose prednisone regimen over a standard-dose prednisone regimen.**

- Studies show that a lower-dose prednisone regimen has the same benefit as a standard-dose prednisone.
- Lowering the amount of prednisone can help avoid side effects and lessen the damage when you use them for a long time.

➔ **Use either IV pulse prednisone or high-dose oral prednisone as a part of initial therapy.**

- We recommend either because there are no studies that compare how well they work.



If you have **active, severe GPA/MPA, with glomerulonephritis**:

➔ **You may not need plasma exchange.**

- Plasma exchange is most helpful to those with the highest chance of kidney failure.
- Plasma exchange can raise your chance of serious infection.
- The risk of infection may outweigh the benefit of plasma exchange if you have a low chance of kidney failure.
- When **should** I get plasma exchange?
 - If you have anti-glomerular basement membrane disease.
- When **might** I get plasma exchange?
 - If you have a high chance of kidney failure, then the benefit of plasma exchange may outweigh the risk of infection.
 - If you are critically ill and other treatments have not worked.

If you have **active, severe GPA/MPA, with alveolar hemorrhage**:

➔ **Do not add plasma exchange to your treatment.**

- Studies have **not** shown that plasma exchange helps people with alveolar hemorrhage, and it can raise your chance of serious infection.



If you have **active, nonsevere GPA/MPA**, we recommend:

→ Use methotrexate over cyclophosphamide or rituximab.

- Methotrexate is less likely to cause serious side effects than cyclophosphamide.
- We know more about how methotrexate works in people with active, nonsevere GPA/MPA than we do about rituximab.
- When **might** I take rituximab over methotrexate?
 - If you have liver damage.
 - If you have kidney damage.
 - If your GPA/MPA gets worse when taking methotrexate.
 - If you have trouble taking your medicine a certain way, such as by mouth.

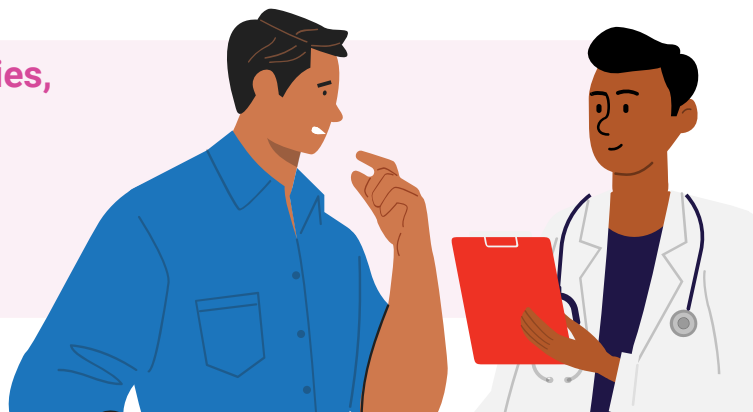
→ Use methotrexate and prednisone over:

- Only prednisone with no methotrexate
- Azathioprine and prednisone
- Mycophenolate mofetil and prednisone
- Trimethoprim/sulfamethoxazole and prednisone
 - If you use prednisone alone, you may need a higher dose, which can cause negative side effects. Methotrexate with prednisone can lower these side effects by lowering the amount of prednisone you need.
 - Methotrexate is better studied than azathioprine, mycophenolate mofetil, or trimethoprim/sulfamethoxazole.
 - Some conditions make it hard for people to take azathioprine, such as total thiopurine S-methyltransferase (TPMT) deficiency or high-risk TPMT and/or NUDT15 genotypes.
- When would I **not** use methotrexate and prednisone?
 - If you have moderate to severe kidney damage, liver damage, or are pregnant.
 - We recommend azathioprine if you:
 - Are pregnant.
 - Can't take methotrexate or mycophenolate mofetil.

If you have **GPA with nose or sinus symptoms, such as swelling in your nose or sinuses, runny nose, nosebleeds, or nasal crusting**, we recommend:

→ Try nasal rinses and topical nasal therapies, such as antibiotics, lubricants, and prednisone.

- We suggest seeing an ENT doctor who has experience treating GPA to see if these may help you.



If you have **actively inflamed windpipe and/or narrowed airways**, we recommend:

➔ **Use immunosuppressive treatments over surgical dilation with intralesional prednisone injection alone.**

- When **might** I get surgical dilation with intralesional prednisone injection?
 - If you have had the stenosis (narrowing) for a long time, the stenosis is fibrotic (damaged or scarred), or it doesn't get better after immunosuppressive treatment.
 - If the stenosis needs treatment right away, such as because it is stopping your body from getting enough air (called critical narrowing) – in this case, it may be used with other treatments.

If you have **mass lesions**, we recommend:

➔ **Use immunosuppressive treatments over debulking surgery with immunosuppressive treatment.**

- When **might** I get debulking surgery?
 - If there is an urgent need to lower the pressure from the lesion (called decompression). This can include pressure on the optic nerve that could cause vision loss, or pressure that could threaten an organ or cause death.

Treatment recommendations for remission maintenance

If you have **severe GPA/MPA, and it has entered remission after taking cyclophosphamide or rituximab**, we recommend:

➔ **Use rituximab over methotrexate or azathioprine.**

- Because people are less likely to relapse with rituximab than with methotrexate or azathioprine.
- When **might** I use methotrexate or azathioprine?
 - If the cost is too high or you can't tolerate rituximab

➔ **Use methotrexate or azathioprine over mycophenolate mofetil or leflunomide.**

- People are less likely to relapse with methotrexate or azathioprine than with mycophenolate mofetil.
- We know less about leflunomide as a remission maintenance treatment compared to methotrexate or azathioprine.

If you have **GPA**, and it has entered remission, we recommend:

- ➔ **Use methotrexate or azathioprine over trimethoprim/sulfamethoxazole.**
 - Do not add trimethoprim/sulfamethoxazole to other treatments (such as rituximab, azathioprine, or methotrexate) because it could potentially cause bad reactions.
- When **might** I take trimethoprim/sulfamethoxazole with other treatments?
 - If you have nose or sinus symptoms, such as swelling in your nose or sinuses, runny nose, nosebleeds, or nasal crusting.
 - To prevent pneumonia caused by a fungus called *Pneumocystis jirovecii*.

If you have **GPA/MPA** and are taking rituximab for remission maintenance, we recommend:

- ➔ **Get rituximab as scheduled doses, instead of doses based on ANCA test results or B cell counts.**
 - People may have flares even when their ANCA test results are negative or they have low B cell counts.
- ➔ **If you have hypogammaglobulinemia and repeating infections, get IVIG.**
 - IVIG can help your immune system fight infections.

If you have **GPA/MPA**, the length of time you take either prednisone or other treatments for remission maintenance should depend on your clinical condition, preferences, and values.

- ➔ **With treatments other than prednisone, we recommend remission maintenance treatment for 18 months or longer.**
 - This can vary from person-to-person.
- ➔ **With prednisone, remission maintenance treatment should be balanced with potential side effects.**
 - You should get screening for prednisone side effects if you are taking prednisone long term.



Treatment recommendations for disease relapse

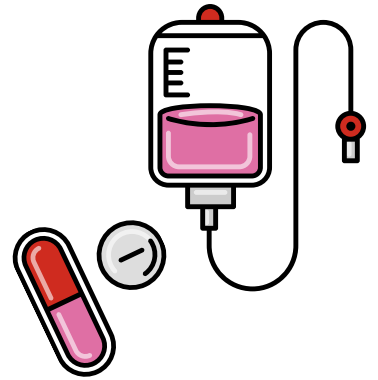
If you have **GPA/MPA** and it relapsed with severe symptoms while on remission maintenance treatments, we recommend:

➔ **If you are not using rituximab:**

- Use rituximab over cyclophosphamide because rituximab works better to put the disease back into remission.

➔ **If you are using rituximab:**

- Switch from rituximab to cyclophosphamide over getting more rituximab.



Treatment recommendations for refractory disease

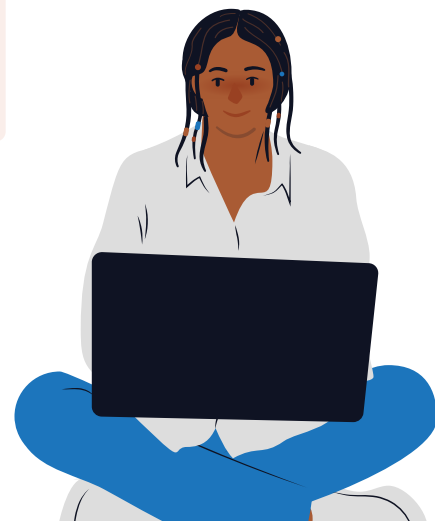
If you have **severe GPA/MPA** that is refractory to treatment with rituximab, we recommend:

- ➔ **Switch to cyclophosphamide, over taking both rituximab and cyclophosphamide.**

If you have **GPA/MPA** that is refractory to remission induction treatment, we recommend:

➔ **Add IVIG to your current treatments.**

- IVIG should not be used long term, but can be used short term while you wait for the remission induction treatment to work.



General recommendations

If you have **GPA/MPA**, we recommend:

➔ **Not changing your dose of immunosuppressants based on ANCA test results alone. Instead, base all treatment decisions on symptoms along with diagnostic tests, such as labs, imaging, and biopsy findings.**

- A high ANCA level does not always predict if you will have a disease flare (worsening symptoms).
- If immunosuppressants are increased based on ANCA levels alone, it can lead to suppressing the immune system too much, which can cause harmful side effects like infections.

If you have **GPA or MPA and take immunosuppressants (such as cyclophosphamide or rituximab)**, we recommend:

➔ **Use certain antimicrobial medicines (such as trimethoprim/sulfamethoxazole) to prevent pneumonia caused by a fungus called *Pneumocystis jirovecii*.**

- Medicines for vasculitis can lower your body's ability to fight infection. This can make you more likely to get pneumonia, which is a serious lung infection.
- Antimicrobial medicines fight microbes such as the fungus that causes pneumonia.
- When **should** I take trimethoprim/sulfamethoxazole?
 - If you take cyclophosphamide or rituximab.
- When **might** I take trimethoprim/sulfamethoxazole?
 - If you are taking prednisone with methotrexate, azathioprine, or mycophenolate mofetil.

If you have **active GPA/MPA and can't be treated with immunosuppressants (such as cyclophosphamide or rituximab)**, for example due to an infection, we recommend:

➔ **Get IVIG (intravenous immunoglobulin)**

- IVIG is an immunomodulatory therapy (which changes your immune system), not an immunosuppressant. It does not raise your chance of infection.

Health terms

- A**
 - **ANCA (antineutrophil cytoplasmic antibodies):** An antibody that attacks a type of white blood cell called neutrophils. ANCA tests help doctors diagnose certain types of vasculitis.
 - **Alveolar hemorrhage:** Bleeding in the lungs that fills your alveoli. Alveoli are tiny air sacs in your lungs that fill with oxygen as you breathe.
 - **Antibodies:** Proteins in your immune system that fight infections.
 - **Anti-glomerular basement membrane disease:** An autoimmune disorder in which your immune system attacks your kidneys and lungs.
 - **Antimicrobial medicines:** Medicines that fight microbes such as the bacteria and fungus that cause infections like pneumonia.
 - **Azathioprine:** An immunosuppressant. Lowers inflammation (swelling) in your body.
- B**
 - **Blood thinners:** Medicines that prevent blood clots. Blood clots can lead to heart attacks or strokes.
- C**
 - **Cyclophosphamide:** An immunosuppressant. Lowers inflammation (swelling) in your body.
- D**
 - **Debulking surgery:** A surgery to remove a lesion (abnormal tissue due to disease).
- E**
 - **ENT doctor:** A doctor who treats diseases of your ear, nose, and throat.
- G**
 - **Glomerulonephritis:** Inflammation (swelling) of the tiny blood vessels (glomeruli) in your kidneys that filter wastes and extra fluid from the blood.
- H**
 - **Hypogammaglobulinemia:** Low levels of immunoglobulin. Immunoglobulins are antibodies that help you fight germs and disease.
- I**
 - **Immune system:** A system of cells, tissues, and organs that helps your body fight infection or illness.
 - **Immunosuppressant:** A medicine that lowers your body's immune response to stop your immune system from causing inflammation (swelling) and damaging your body.
 - **Inflamed subglottic or endobronchial tissue with stenosis:** When a part of the windpipe or lungs narrows, usually caused by swelling or scar tissue.
 - **IVIG (intravenous immunoglobulin):** Immunoglobulin given as an IV through a vein in the arm. Immunoglobulins are antibodies that help you fight germs and disease.



K

- **Kidney failure, or end-stage renal disease (ESRD):** The last stage of chronic kidney disease in which your kidneys do not work well enough for you to live without dialysis or a transplant.

M

- **Mass lesion:** Non-cancerous, tumor-like masses or swollen tissue.
- **Methotrexate:** An immunosuppressant. Lowers inflammation (swelling) in your body.
- **Mycophenolate mofetil:** An immunosuppressant. Lowers inflammation (swelling) in the body.

P

- **Plasma exchange:** A procedure that removes the plasma (the liquid part of blood) from your blood and replaces it with donor plasma or plasma substitute.
- **Pneumocystis jirovecii pneumonia (PCP):** A serious lung infection caused by the fungus *Pneumocystis jirovecii*.
- **Prednisone:** A medicine that lowers inflammation (swelling) in your body, and can be given as:
 - **IV pulse** – A tube into a vein as an IV.
 - **Oral** – A pill by mouth.

R

- **Rituximab:** A medicine that lowers the number of B cells (white blood cells) to lower inflammation (swelling).

S

- **Sepsis:** A dangerous reaction to an infection that can cause inflammation (swelling) and low blood pressure, which can lead to tissue damage, organ failure, and even death.
- **Stenosis:** When something becomes narrower.
- **Surgical dilation with intralesional prednisone injection:** First a surgery to widen a narrowed area of your airways, then prednisone injected directly into the lesions that caused the narrowing.

T

- **Thiopurine S-methyltransferase (TPMT) deficiency:** A condition in which your body can't break down medicines called thiopurines, which treat some autoimmune conditions. People with TPMT deficiency have a higher chance of serious side effects from thiopurines, such as azathioprine.
- **TPMT and NUDT15 genotypes:** Changes in the TPMT and NUDT15 genes that can affect how your body breaks down thiopurines, such as azathioprine. These changes can be passed down from parents to children.
- **Trimethoprim/sulfamethoxazole:** 2 medicines taken together that kill bacteria or fungi that cause infections.

V

- **Venous thrombotic events:** Blood clots that block the flow of blood through your veins.



*Chung, S.A., Langford, C.A., Maz, M., et al. 2021 American College of Rheumatology/Vasculitis Foundation Guideline for the Management of Antineutrophil Cytoplasmic Antibody–Associated Vasculitis. *Arthritis Rheumatol*, 73: 1366-1383. <https://doi.org/10.1002/art.41773> You can find the full ACR/VF recommendations at www.vasculitisfoundation.org.