

Treatment recommendations for active severe, or active nonsevere GPA/MPA



These are recommendations written by a group of doctors and patients based on research studies* for people with a new active diagnosis of GPA or MPA vasculitis. They are for “remission induction,” which means getting to a place where there are no active symptoms and no new damage to the body from vasculitis.

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

What is vasculitis?

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

- **GPA:** A type of vasculitis that affects small to medium-sized blood vessels. It can affect the nose, sinuses, throat, lungs, and kidneys.
- **MPA:** A type of vasculitis that mostly affects small to medium-sized blood vessels. It can affect the kidneys, lungs, nerves, skin, and joints.

Active disease: New, ongoing, or worsening signs or symptoms.

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Healthy blood vessel



Inflamed blood vessel

Treatment recommendations for active GPA/MPA

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

→ Use rituximab over cyclophosphamide

- Why? 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

- Why?
 - A recent study showed that a lower-dose prednisone regimen has the same benefit as a standard-dose.
 - Lowering the amount of prednisone can help avoid side effects and lessen the damage from using prednisone for a long time.

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

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

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

→ Use methotrexate over cyclophosphamide or rituximab

- Why?
 - 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 or 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
- Why?
 - Prednisone alone can mean you need a higher dose, which can cause negative side effects. Methotrexate with prednisone can lower these side effects by lowering the amount of prednisone.
 - 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 deficiency (TPMT) 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



*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.



Health terms

- **Azathioprine:** An immunosuppressant. Lowers inflammation (swelling) in the body.
- **Cyclophosphamide:** An immunosuppressant. Lowers inflammation (swelling) in the body.
- **Immunosuppressant:** Lowers the body's immune response to stop the immune system from causing inflammation (swelling) and damaging the body.
- **Methotrexate:** An immunosuppressant. Lowers inflammation (swelling) in the body.
- **Mycophenolate mofetil:** An immunosuppressant. Lowers inflammation (swelling) in the body.
- **Prednisone:** Lowers inflammation (swelling) in the body, and can be given as:
 - **IV pulse** – A tube into a vein as an IV
 - **Oral** – A pill by mouth
- **Rituximab:** Lowers the number of B cells (white blood cells) to lower inflammation (swelling).
- **Thiopurine S-methyltransferase (TPMT) deficiency:** A condition in which the 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.
- **TPMT and NUDT15 genotypes:** Changes in the TPMT and NUDT15 genes that can affect how the body breaks down thiopurines.
- **Trimethoprim/sulfamethoxazole:** 2 medicines taken together that kill bacteria or fungi that cause infections.

Recommendations for specific symptoms in active GPA



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Healthy blood vessel



Inflamed blood vessel

Recommendations for sinonasal symptoms in people with GPA

If you have 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

- To see if these may help you, we suggest seeing an ENT doctor who has experience treating GPA.

Recommendations for airway symptoms in people with GPA

If you have actively inflamed subglottic and/or endobronchial tissue with stenosis, we recommend:

➔ Use immunosuppressive treatments over surgical dilation with steroid injection alone

- When **might** I get surgical dilation with intralesional steroid injection?
 - If you have had the stenosis for a long time, it 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.

Recommendations for mass lesions in people with GPA

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.

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Health terms

- **Debulking surgery:** A surgery to remove a lesion.
- **ENT doctor:** A doctor who treats the ear, nose, and throat.
- **Immune system:** A system of cells, tissues, and organs that helps the body fight infection or illness.
- **Immunosuppressive treatments:** Lowers the body's immune response to stop the immune system from causing inflammation (swelling) and damaging the body.
- **Inflamed subglottic or endobronchial tissue with stenosis:** When a part of the windpipe or lungs narrows, usually caused by swelling or scar tissue.
- **Mass lesion:** Non-cancerous, tumor-like masses or swollen tissue.
- **Prednisone:** A type of steroid. It can be given as:
 - **IV pulse** – A tube into a vein as an IV
 - **Oral** – A pill by mouth
- **Stenosis:** When something becomes narrower.
- **Steroid:** Lowers inflammation (swelling) in the body.
- **Surgical dilation with intralesional steroid injection:** Surgery to inject a steroid directly into a lesion.

Medication recommendations for active GPA/MPA



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Inflamed blood vessel

Medication recommendations for GPA/MPA

If you have active GPA/MPA, in general, we recommend:

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

- Why?
 - A high ANCA level does not always predict if you will have a disease flare (worsening symptoms).
 - If immunosuppressive therapy is 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 active GPA and you take immunosuppressive therapy (such as cyclophosphamide or rituximab), we recommend:

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

- Why?
 - 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 have other immunosuppressive therapy (such as cyclophosphamide or rituximab), for example for an infection, we recommend:

➔ Get IVIG (intravenous immunoglobulin)

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



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Health terms

- **ANCA** (antineutrophil cytoplasmic antibodies): An antibody that recognizes a type of white blood cell called neutrophils. ANCA tests help doctors diagnose certain types of vasculitis.
- **Antibodies**: Proteins in your immune system that fight infections.
- **Antimicrobial medicines**: Fight microbes such as the bacteria and fungus that cause infections like pneumonia.
- **Azathioprine**: An immunosuppressant. Lowers inflammation (swelling) in the body.
- **Cyclophosphamide**: An immunosuppressant. Lowers inflammation (swelling) in the body.
- **Immune system**: A system of cells, tissues, and organs that helps the body fight infection or illness.
- **Immunosuppressive therapy**: Lowers the body's immune response to stop the immune system from causing inflammation (swelling) and damaging the body.
- **IVIG** (intravenous immunoglobulin): Immunoglobulin given as an IV through a vein in the arm. Immunoglobulin is a part of your blood that has antibodies to help you fight germs and disease.
- **Methotrexate**: An immunosuppressant. Lowers inflammation (swelling) in the body.
- **Mycophenolate mofetil**: An immunosuppressant. Lowers inflammation (swelling) in the body.
- ***Pneumocystis jirovecii* pneumonia** (PCP): A serious infection caused by the fungus *Pneumocystis jirovecii*.
- **Prednisone**: Lowers inflammation (swelling) in the body, and can be given as:
 - **IV pulse**: A tube into a vein as an IV
 - **Oral**: A pill by mouth
- **Rituximab**: An immunosuppressant that lowers the number of B cells (a type of white blood cell) to lower inflammation (swelling).
- **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.
- **Trimethoprim/sulfamethoxazole**: 2 medicines taken together that kill bacteria or fungi that cause some infections.

Recommendations for conditions related to active GPA/MPA



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Recommendations for conditions related to GPA/MPA

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

➔ Not everyone needs plasma exchange

- Why?
 - 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, we recommend:

➔ **Not adding plasma exchange to your treatment**

- Why? Studies have **not** shown that plasma exchange helps people with alveolar hemorrhage, and it can raise your chance of serious infection.
- When **should** I get plasma exchange?
 - If you have anti-glomerular basement membrane disease.
- When **might** I get plasma exchange?
 - If you have glomerulonephritis with a high chance of kidney failure.
 - If you are critically ill and other treatments have not worked.

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Health terms

- **Alveolar hemorrhage:** Bleeding in the lungs that fills the alveoli. Alveoli are tiny air sacs in your lungs that fill with oxygen as you breathe.
- **Anti-glomerular basement membrane disease:** An autoimmune disease that affects your kidneys and lungs.
- **Blood thinners:** Medicines that prevent blood clots. Blood clots can lead to heart attacks or strokes.
- **Glomerulonephritis:** Inflammation (swelling) of the tiny blood vessels (glomeruli) in the kidneys that filter wastes and extra fluid from the blood.
- **Kidney failure or end-stage renal disease (ESRD):** The last stage of chronic kidney disease in which the kidneys do not work well enough for someone to live without dialysis or a transplant.
- **Plasma exchange:** Removes the harmful materials in the blood by removing a person's plasma (the liquid part of blood) and replacing it with donor plasma or plasma substitute.
- **Venous thrombotic events:** Blood clots that block the flow of blood through your veins.