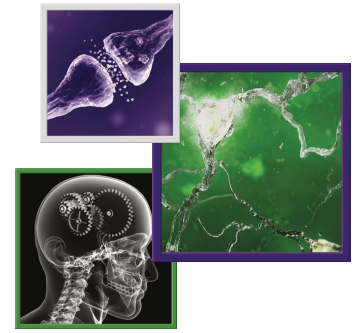
Plain Language Summary of Publication

Neurodegenerative Disease Management

A plain language summary of the impact of vaccines against flu and chickenpox in people with multiple sclerosis treated with cladribine tablets



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Summary

What is this summary about?

This is a summary of an article originally published in the *Multiple Sclerosis Journal*. Cladribine tablets (MAVENCLAD®) are an oral (taken by mouth) medication, approved for the treatment of people with relapsing forms of multiple sclerosis (MS, with episodes of new or worsening symptoms). They are administered for a maximum of 10 days per year, over a period of 2 years. Cladribine tablets work by temporarily reducing the number of lymphocytes, which are immune cells that help to fight off infections. Because of this, people with MS (also called PwMS) may have concerns about the effect of cladribine tablets on vaccines, as these work via immune cells to build protection against infection.

How to say

- **Cladribine:** CLAD-ree-BEEN
- **Influenza:** IN-floo-EN-zuh
- **Lymphocyte:** LIM-foh-site
- **Multiple sclerosis:** MUHL-tuh-pl sklr-OH-suhs
- **Varicella zoster:** VAYR-ih-SEL-uh ZO-stuh

What happened in the MAGNIFY-MS study?

A study called MAGNIFY-MS investigated how long it takes for cladribine tablets to begin to work in people with a type of MS called highly active relapsing MS. During the study, some participants received their usual vaccinations against flu (influenza) and against the chickenpox virus (also called varicella zoster virus) as part of their routine medical care. The MAGNIFY-MS study gave the researchers an opportunity to look at how cladribine tablets affect the way the flu and chickenpox virus vaccines work in the body.

What were the results?

Cladribine tablets do not affect how well the body responds to flu and chickenpox vaccines.

What do the results mean?

PwMS taking cladribine tablets who are vaccinated against chickenpox, flu or both can be protected against these diseases.

An animated video describing this study is also available online. Scan this QR code to watch the video.

Where can I find the original article on which this summary is based?

You can read the original article published in the *Multiple Sclerosis Journal* free of charge at: https://journals.sagepub.com/doi/10.1177/13524585221099413

Future Medicine part of fsg

Who is this article for?

This summary may be helpful for PwMS, their families and caretakers and patient advocates. Healthcare professionals who treat PwMS, such as doctors, nurses, nurse practitioners, physician assistants, etc., may also find the summary of interest.

What did this study look at?

Multiple sclerosis (also called MS) is a long-term condition, in which the immune system (the body's natural defence system) mistakenly attacks the nerves in the brain and spinal cord. This leads to the symptoms of MS, such as:

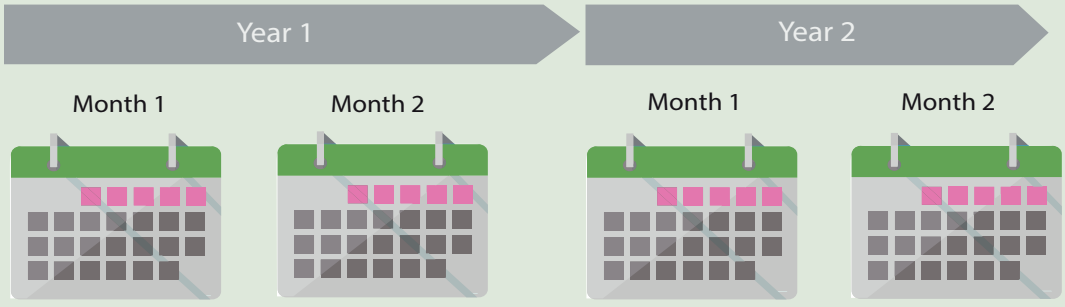
- weakness in the arms or legs
- problems with coordination
- problems with memory
- issues with bladder or bowel control

Cladribine tablets are an oral medication approved for the treatment of people with highly active relapsing forms of MS (MS with episodes of new or worsening symptoms).

Definition of highly active replasing MS

Relapsing	Highly active
MS with episodes of new or worsening symptoms	One relapse in the previous year, with brain lesions, while taking disease-modifying therapy (DMT) OR Two or more relapses in the previous year, whether taking DMT or not

Cladribine tablets are taken for a maximum of 10 days per year for 2 years. In each year, PwMS take tablets for 4–5 days at the start of Month 1 and again for 4–5 days at the start of Month 2.



A treatment week (4–5 days) at the start of Month 1, and again for 4–5 days at the start of Month 2

A treatment week (4–5 days) at the start of Month 1, and again for 4–5 days at the start of Month 2

The COVID-19 pandemic has highlighted how important it is to know how people taking treatments for their MS will be protected by vaccines.

A study called MAGNIFY-MS investigated how long it takes for cladribine tablets to begin to work in people with highly active relapsing MS. During the study, some participants received their usual vaccinations against flu (influenza) and against the chickenpox virus (also called varicella zoster virus).

This gave the researchers the opportunity to look at how cladribine tablets affected the way these vaccines work in the body.

Author's note

The results of the MAGNIFY-MS study have been published previously in the journal *Neurology: Neuroimmunology & Neuroinflammation* in June 2022.

You can access the full MAGNIFY-MS article free of charge at https://nn.neurology.org/content/9/4/e1187

Lymphocytes are important immune cells, used by the body to fight infection. They are needed for a vaccine to work.

Similar to some other drugs used to treat MS, cladribine tablets reduce the levels of certain cells in the immune system, called **lymphocytes**. With cladribine tablets this reduction is temporary.

Because cladribine tablets reduce lymphocytes, the study researchers decided to investigate whether this reduction would affect the vaccines against flu and chickenpox.

How do vaccines work?

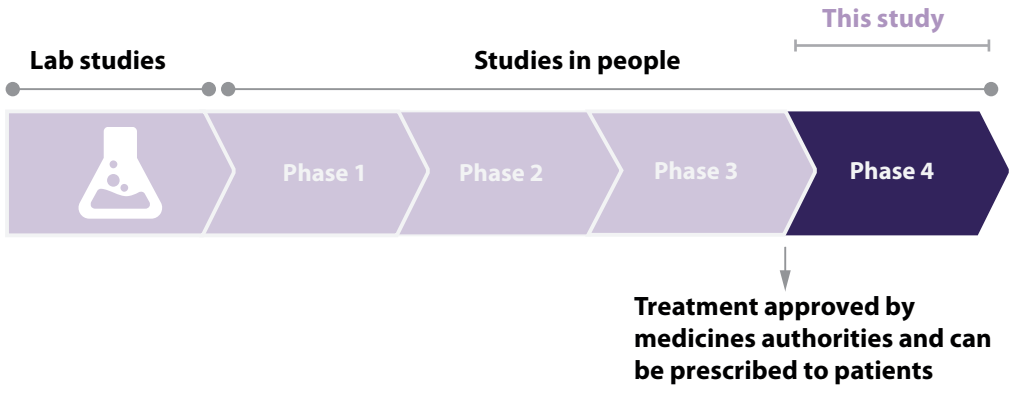
When the body is infected with bacteria or a virus, your immune system responds by:

- **Identifying** the unwanted foreign invader, such as the bacteria or virus;
- **Triggering** lymphocytes to start producing antibodies, which are proteins that fight disease;
- **Remembering** the bacteria or virus and how to fight it; if you are exposed to it again in the future, your immune system can quickly recognize and destroy it before you become ill.

Vaccines reduce the risk of getting an infection or a disease by working with the body's natural defences to build protection against it. Vaccines imitate an infection: they cause the immune system to produce antibodies, without causing illness.

Where is this study in the drug development timeline?

MAGNIFY-MS is a phase 4 study, which means that research continues after the drug has been approved and can be prescribed to PwMS.



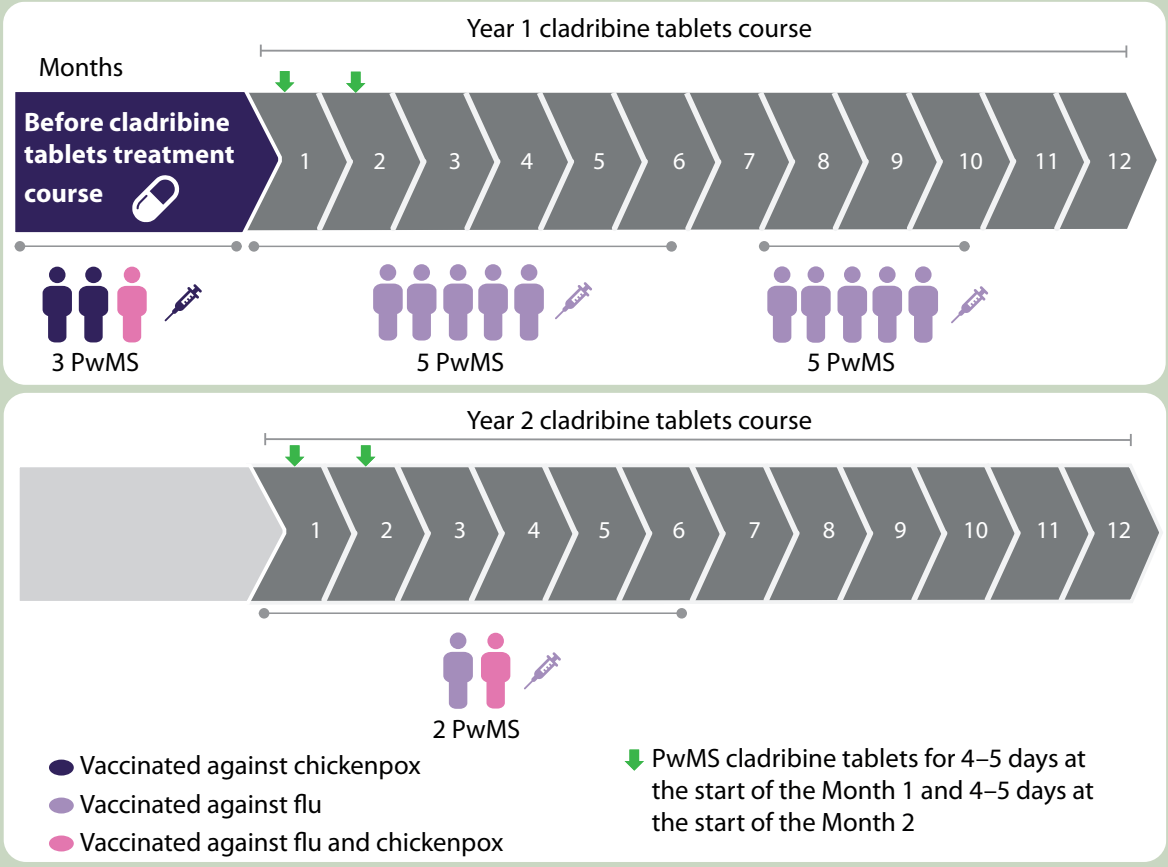
Who took part in this study?

During the study, a total of 14 people with highly active relapsing MS, aged 18 years or older, were vaccinated.

Some PwMS received the vaccine against chickenpox, and some received the vaccine against flu. One individual received both vaccines.

The PwMS in this study received their vaccines during the 2-year course of treatment with cladribine tablets. The timing of the vaccinations varied from person to person:

- Some PwMS were vaccinated within the first 6 months of taking cladribine tablets in Year 1.
- Others were vaccinated between 8.5 months and 10.5 months after taking cladribine tablets in Year 1.
- Some patients were vaccinated up to 6 months after taking cladribine tablets in Year 2.



Cladribine tablets temporarily reduce the levels of lymphocytes. Lymphocyte levels are expected to be lowest during Months 3 and 14 after cladribine tablets treatment starts. Some PwMS received their vaccinations during this time period.

How was the effect of cladribine tablets on vaccinations investigated?

Blood samples were taken from the PwMS in this study, before and after they had their vaccination.

- This was to see if taking cladribine tablets had any effect on the antibodies that are normally made by the body after vaccination.
- The blood samples also measured the level of lymphocytes.

What were the results of this study?

After being vaccinated against chickenpox, flu or both, and taking cladribine tablets, PwMS had the same or higher antibody levels than they had before they were vaccinated. Each participant had an antibody level that gave them protection against these diseases. This was true for all PwMS, even those with lymphocyte levels that were lower than normal because of the effect of cladribine tablets.

1 Effect of cladribine tablets on chickenpox vaccination

Antibodies were measured at 6 months after the PwMS started their treatment with cladribine tablets. All PwMS who received a chickenpox vaccination, as part of their routine care before the study, had high levels of antibodies after starting cladribine tablets.

2 Effect of cladribine tablets on flu vaccination

All PwMS who received the flu vaccine had the same level or an increase in antibodies after taking cladribine tablets. This was the case regardless of when the vaccination was given in relation to taking the cladribine tablets.

The study shows that PwMS who take cladribine tablets have the same or higher levels of antibodies after being vaccinated, compared with the levels before having the vaccine.

What were the main conclusions?

The PwMS taking cladribine tablets who were vaccinated against chickenpox, flu or both had antibody levels that were high enough to provide protection against these diseases.

These antibody levels were high enough to give protection even when the PwMS:

- Were vaccinated close to the time of taking cladribine tablets, or
- Had lymphocyte levels that were lower than normal because of the effect of cladribine tablets.

These increased antibody levels were present for at least 6 months after taking cladribine tablets.

This was a small study, so it will be important to get more information from larger numbers of PwMS. However, it is reassuring to see that cladribine tablets do not appear to affect vaccinations in people with highly active relapsing MS.

Questions from this research that can be used to talk to your doctor or nurse about your MS care
- What does this information mean for me?
- How can I use this information to make decisions about my MS care and having vaccinations?

Are there plans for further studies?

Further analyses in the future will give us greater understanding about the effect of cladribine tablets on vaccination, including the longer-term effects.

Where can readers find more information on this study?

This is a summary of an article called "*Varicella zoster virus and influenza vaccine antibody titres in patients from MAGNIFY-MS who were treated with cladribine tablets for highly active relapsing multiple sclerosis*" which was published in *Multiple Sclerosis Journal*. To read the original article being summarized, for free, please visit: https://doi.org/10.1177/13524585221099413

The full title of the article presenting results of the MAGNIFY-MS study is "*Early Reduction of MRI Activity During 6 Months of Treatment With Cladribine Tablets for Highly Active Relapsing Multiple Sclerosis*" which was published *Neurology: Neuroimmunology & Neuroinflammation*. To read the original article being summarized, for free, please visit: https://nn.neurology.org/content/9/4/e1187

More information on the study can be found on the website: https://clinicaltrials.gov/ by searching for the following trial number (ClinicalTrials.gov Identifier): NCT03364036

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Financial & competing interests disclosure

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Ethical conduct of research

Ethical approval for the MAGNIFY-MS study was obtained from independent ethics committees at each local trial site, and the study was performed in line with the principles of the Declaration of Helsinki. All participants provided written informed consent before participation in the study.