

## Global COVID-19 advice for people with MS

COVID-19 is an illness that can affect your lungs, airways and other organs. It is caused by a novel coronavirus (called SARS-CoV-2) that has spread around the world.

The advice below was developed by MS clinicians and research experts\*. It is based on the emerging evidence of how COVID-19 affects people with multiple sclerosis (MS) and expert opinion. This advice will be reviewed and updated as further evidence about COVID-19 and SARS-CoV-2 becomes available.

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### Advice for people with MS

Current evidence shows that simply having MS does not make you more likely to develop COVID-19 or to become severely ill or die from the infection than the general population. However, the following groups of people with MS are more susceptible to having a severe case of COVID-19:

- People with progressive MS
- People with MS over the age of 60
- Men with MS
- Black people with MS and possibly South Asian people with MS
- People with higher levels of disability (for example, [an EDSS score](#) of 6 or above, which relates to needing to use a walking stick)
- People with MS and obesity, diabetes or diseases of the heart or lungs
- People taking certain disease modifying therapies for their MS (see below)

All people with MS are advised to follow [World Health Organization](#) guidelines for reducing the risk of infection with COVID-19. People in the higher risk groups should pay particular attention to these measures. We recommend to:

- Practise social distancing by keeping at least 1.5 metres\*\*\* distance between yourself and others, to reduce your risk of infection when they cough, sneeze or speak. This is particularly important when indoors but applies to being outdoors as well.
- Make wearing a mask a normal part of being around other people and ensure that you are using it correctly by following [these instructions](#).
- Avoid going to crowded places, especially if indoors and the room is poorly ventilated. Where this is not possible, ensure to wear a mask and practise social distancing.
- Wash your hands frequently with soap and water or an alcohol-based hand rub (70% alcohol content is considered most effective).
- Avoid touching your eyes, nose and mouth unless your hands are clean.
- When coughing and sneezing, cover your mouth and nose with a flexed elbow or tissue.
- Clean and disinfect surfaces frequently especially those which are regularly touched.

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- Talk to your healthcare provider about optimal care plans, through video consultations or in-person visits where needed. Visits to health clinics/centres and hospitals should not be avoided if they are recommended based on your current health needs.
  - Stay active and try to take part in activities that will enhance your mental health and well-being. Physical exercise and social activities that can take place outside and with social distancing are encouraged.

Caregivers and family members who live with, or regularly visit, a person with MS in one of the higher risk groups should also follow these recommendations to reduce the chance of bringing COVID-19 infection into the home.

### **Advice for pregnant women with MS**

At this time there is no specific advice for women with MS who are pregnant. There is general information on COVID-19 and pregnancy from the [World Health Organization](#). It is important to note that COVID-19 can lead to premature birth and serious illness for the mother.

### **Advice regarding disease modifying therapies for MS**

Many disease modifying therapies (DMTs) for MS work by suppressing or modifying the immune system. Some MS medications might increase the likelihood of developing complications from COVID-19 but this risk needs to be balanced with the risks of stopping or delaying treatment.

We recommend that people with MS currently taking DMTs continue with their treatment, unless advised to stop by their treating clinician.

People who develop symptoms of COVID-19 or test positive for the infection should discuss their MS therapies with their MS care provider or another healthcare professional who is familiar with their care.

Before starting on any new DMT or changing an existing DMT, people with MS should discuss with their healthcare professional which therapy is the best choice for their individual circumstances. This decision should – among other factors - consider the following information:

- MS disease course and activity
- The risks and benefits normally associated with different treatment options
- Additional risks related to COVID-19, such as:
  - The presence of other factors for a more severe case of COVID-19, such as older age, obesity, pre-existing lung or cardiovascular disease, progressive MS, higher risk race/ethnicity etc, as listed above
  - The current and anticipated future COVID-19 risk in the local area
  - Risk of exposure to COVID-19 due to lifestyle, for example whether they are able to self-isolate or are working in a high-risk environment
  - Emerging evidence on the potential interaction between some treatments and COVID-19 severity
  - Previous infection with COVID-19
  - Availability of and access to a COVID-19 vaccine

### **Evidence on the impact of DMTs on COVID-19 severity**

Interferons and glatiramer acetate are unlikely to impact negatively on COVID-19 severity. There is some preliminary evidence that interferons may reduce the need for hospitalisation due to COVID-19.

The evidence available suggests that people with MS taking dimethyl fumarate, teriflunomide, fingolimod, siponimod and natalizumab do not have an increased risk of more severe COVID-19 symptoms. It is unlikely that people with MS taking ozanimod or ponesimod will have an increased risk either, as they are assumed to be similar to siponimod and fingolimod.

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There is some evidence that therapies that target CD20 – ocrelizumab, rituximab, ofatumumab – may be linked to an increased chance of having more severe COVID-19, including a greater risk of hospitalisation. However, these therapies should still be considered as an option for treating MS during the pandemic. People with MS who are taking them (or ublituximab that works in the same way) should be particularly vigilant regarding the advice above to reduce their risk of infection.

More data on the use of alemtuzumab and cladribine during the COVID-19 pandemic are required to make an assessment of their safety.

Recommendations on delaying second or further doses of alemtuzumab, cladribine, ocrelizumab and rituximab due to the COVID-19 outbreak differ between countries. People who take these medications and are due for the next dose should consult their healthcare professional about the risks and benefits of postponing treatment. People are strongly encouraged not to stop treatment without the advice of their clinician.

### **Advice regarding aHSCT**

Autologous Haematopoietic Stem Cell Transplantation (aHSCT) includes intensive chemotherapy treatment. This severely weakens the immune system for a period of time. People who have recently undergone aHSCT should consider extending the period they remain in isolation during the COVID-19 outbreak to at least six months. People who are due to undergo treatment should consider postponing the procedure in consultation with their healthcare professional. If aHSCT is given, chemotherapy should be administered in rooms isolated from other hospital patients.

### **Advice regarding relapses or other health concerns**

People with MS should still seek medical advice if they experience changes in their health that may suggest a relapse or another underlying issue such as an infection. This can be done using alternatives to in-person clinic visits (such as telephone or video consultations) if the option is available. In many cases, it is possible to manage relapses at home.

The use of steroids for treating relapses should be carefully considered and only used for relapses that need intervention. There is some evidence that receiving high-dose steroids in the month prior to contracting COVID-19 increases the risk of a more severe infection requiring a visit to hospital. Where possible, the decision should be made with a neurologist experienced in the treatment of MS. People who receive steroid treatment for a relapse should be extra vigilant and may want to consider self-isolation for at least a month to reduce their risk from COVID-19. Note that once someone has been infected with COVID-19, steroids may be used to treat COVID-19, to dampen the excessive immune response often referred to as a 'cytokine storm'. Note that the steroids and dosages used in this context are different from the situation of a MS relapse.

People with MS should continue to participate in rehabilitation activities and stay active as much as possible during the pandemic. This can be done through remote sessions where available or in clinics/centres as long as people with MS attending the clinics/centres follow safety precautions to protect themselves and limit the spread of COVID-19. People with concerns about their mental health should seek advice from their healthcare professional.

### **Flu vaccine**

The flu vaccine is safe and recommended for people with MS. For countries entering flu season, we recommend people with MS receive the seasonal flu vaccine where it is available.

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## COVID-19 vaccines and MS

In this section, we will review the current vaccine types and discuss vaccination timing and disease modifying therapy administration. Given the seriousness of COVID-19 - which carries a 1-3% mortality risk as well as risk for serious illness and prolonged ill-health for many - we wish to emphasise these key points:

- **All people with MS should be vaccinated against COVID-19<sup>1</sup>**
- **People with MS should be vaccinated as soon as the vaccine is available to them**
- **Even once you have received the vaccine, it is important to follow your country's guidelines regarding mask wearing (indoors and outdoors), social distancing, social group requirements, and hand washing.**

There are several COVID-19 vaccines in use in different countries around the world, with new ones being approved regularly. Instead of assessing each vaccine individually, we have provided information below about the main types of COVID-19 vaccines in use and in development. This guidance is based on available information and we will update it as new data become available. The spread of the SARS-CoV-2 virus spread is influenced by new COVID-19 variants and ongoing research is investigating how well the current COVID-19 vaccines protect against these new and emerging variants.

We do not know how many people in the COVID-19 vaccine clinical trials had MS, so our guidance is therefore based on data from the general population in the vaccine clinical trials, research on the effects of other types of vaccination of people with MS, and new data emerging on the safety and effectiveness of COVID-19 vaccines specifically for people with MS.

### *Astrazeneca and Johnson & Johnson (J&J) COVID-19 vaccines – important update*

We are aware that some countries are pausing the use of the Astrazeneca and Johnson & Johnson (J&J) COVID-19 vaccines, and other countries have issued specific health warnings. The Astrazeneca and to a lesser extent the J&J vaccines have both been linked to an infrequent side effect, known as vaccine-induced thrombosis and thrombocytopenia, which can lead to blood clots. These blood clots can occur in the brain (cerebral venous sinus thrombosis - CVST), in the legs or abdomen (deep vein thrombosis - DVT) or in the lungs (pulmonary embolism). People who have received the Astrazeneca or J&J vaccine and develop severe headache, abdominal pain, leg pain, or shortness of breath within three weeks after vaccination should seek immediate medical attention.

The investigation is at a very early stage but, currently, there does not appear to be any additional blood-clotting risk for people with MS. MSIF's expert group continues to monitor the situation, and we will swiftly communicate any potential safety concerns specific to those living with MS.

### *Types of COVID-19 vaccine and how they work*

Vaccines work by using a part of the virus that causes the disease (such as its genetic code or 'spike protein'), or an inactivated or weakened version of the virus, to prompt a response from the human immune system. In turn, this causes the body to produce antibodies and T-cells (a special population of white blood cells) to fight the virus, preventing it from entering and infecting other cells in the body. These vaccines do not lead to any genetic change in our bodies, will not get into the brain, and would not alter the genetic code of a foetus. There are currently five different types of COVID-19 vaccine in use or in development that work in different ways (with examples below). A useful COVID-19 vaccine tracker can be found at: <https://covid19.trackvaccines.org/>

1. **mRNA vaccines** have the genetic code for the coronavirus 'spike' protein made as an "mRNA" (a type of temporary genetic message), which is formulated into tiny fatty droplets for delivery. The mRNA directs production of the spike protein, which is seen and targeted by the immune system (that makes antibodies and T-cells).

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<sup>1</sup> Provided that they do not have any known allergies to any of the components of the vaccines.

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- Pfizer-BioNTech (Comirnaty)
  - Moderna (Moderna mRNA)
2. **Non-replicating viral vector vaccines** have the genetic code for the spike protein in a viral vector. These vectors are best understood as just the shell and delivery mechanism of a virus (commonly from an adenovirus), but they lack the parts a virus needs to replicate and so can never cause an infection. Similar to mRNA vaccines, viral vector vaccines direct the production of the spike protein so that it can be seen and targeted by the immune system.
    - AstraZeneca/Oxford (AZD1222)
    - Serum Institute of India (Covishield)
    - Gamaleya Research Institute (Gam-COVID-Vac or Sputnik V)
    - Janssen/Johnson & Johnson (Ad26.COV2.S)
  3. **Inactivated virus vaccines** use an inactivated form of the whole coronavirus. The coronavirus has been ‘killed’ so that it is unable to get into cells and replicate, and it cannot cause a COVID-19 infection. The immune system recognises the whole virus, even though it is inactivated.
    - Sinovac (CoronaVac)
    - Sinopharm (BBIBP-CorV)
  4. **Protein vaccines** have the coronavirus spike protein itself (not the genetic code), along with something that boosts the immune system (an ‘adjuvant’) to ensure the spike protein is targeted.
    - Novavax (NVX-CoV2373)
  5. **Live attenuated vaccines** use a weakened, but still replicating virus. Such vaccines work by causing a mild infection in people with regular immune function. **They can be dangerous in a person with a compromised immune system, so would not be suitable for many people with MS, due to the way some disease modifying treatments work.**
    - Currently (May 2021), there are no live attenuated COVID-19 vaccines in use – they are only being researched.

**The following guidance refers to the mRNA, non-replicating viral vector, inactivated virus or protein COVID-19 vaccines (types 1-4 listed above).**

### ***People with MS should get a COVID-19 vaccine***

The science has shown us that the COVID-19 vaccines are safe and effective. Like other medical decisions, the decision to get a vaccine is best made in partnership with your healthcare professional. You should get a COVID-19 vaccine as soon as it becomes available to you. The risks of COVID-19 disease outweigh any potential risks from the vaccine. In addition, members of the same household and close contacts should also get a vaccine as soon as they can to maximise protection against COVID-19.

Most of the COVID-19 vaccines require two doses<sup>2</sup>, and where this is the case, you need to follow your country’s guidelines on the timing of the second dose. The Johnson & Johnson (J&J) vaccine requires a single dose. Whichever vaccine you receive, it takes 2 weeks after receiving the only or second dose before you are considered immunised (protected).

If you have had COVID-19 and recovered, you should also get the vaccine, because people who have had COVID-19 infection in the past can get infected again. It is normal practice to wait until you have recovered from an illness before being vaccinated. But you should still get vaccinated as soon as you can after recovery, following the government guidelines in your country.

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<sup>2</sup> In some countries, you may get offered a third dose if you are categorised as having severe immunosuppression. See section on additional doses below.



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We do not know how long a person is protected from COVID-19 after being vaccinated, although clinical trial data indicate that protection is high for at least multiple months. Repeated doses of the COVID-19 vaccines may be required in future, similar to the flu vaccine.

***There is no evidence that people with MS are at higher risk of complications from the mRNA, non-replicating viral vector, inactivated virus or protein COVID-19 vaccines (1-4), compared to the general population.***

There is no vaccine preference for those living with MS. None of the currently available vaccines contain live virus and the vaccines will not cause COVID-19 disease. These types of vaccine are not likely to trigger an MS relapse or to worsen chronic MS symptoms.

However, **people with MS should avoid receiving live attenuated vaccines (5)**. Given that there may be COVID-19 vaccines developed in the future that use this technology, it is important to know which COVID-19 vaccine you are offered.

You do not need to self-isolate after the vaccination. The vaccines can cause side effects, including fever or fatigue, which should not last more than a few days after vaccination. A fever can make your MS symptoms worse temporarily, but they should return to previous levels after the fever is gone. Even if you have side effects from the first dose, it is important to get the second dose of the vaccine (for vaccines requiring two doses) for it to be fully effective. Having side effects, such as fever, muscle discomfort and fatigue are a sign that the vaccine is doing its job (it is getting your body to mount a response against the virus, and therefore is starting to protect you).

***It is safe to receive a COVID-19 vaccine when you are on disease modifying therapies (DMTs) for MS***

Continue taking your disease modifying therapy (DMT) unless you are advised by your MS healthcare professional to stop or delay it. Stopping some DMTs abruptly can cause severe worsening of MS.

***Some DMTs may reduce the effectiveness of the COVID-19 vaccinations***

There is some evidence that people taking some types of DMT (fingolimod, siponimod, ozanimod, ponesimod, ocrelizumab, rituximab, ofatumumab) may have a reduced antibody response to the COVID-19 vaccines. The data are limited so far, but are in line with what we expect, given our understanding of these treatments.

Note that there is a range of different antibody tests that are used to measure responses to the COVID-19 vaccines. There is currently no global agreement about which antibody is the best for monitoring vaccine responses and predicting protection from COVID-19.

If you use one of these DMTs and take an antibody test it may show a low or no response. This does not mean that the vaccine is ineffective. Antibodies are only one part of the immune response to vaccination. There are other components of the immune system that are triggered by the vaccine and could contribute to your protection. The COVID-19 vaccines may also activate T-cells, which could also protect against COVID-19. This T-cell response is not measured in antibody tests. However, it may be that people taking these DMTs have less protection from their vaccinations. We strongly advise people to still get vaccinated, but be aware that you could still be vulnerable to infection and take precautions against COVID-19 infection.

***Delaying the start of a DMT, or altering DMT timing, is a strategy to allow the vaccine to be fully effective***

If you are able to plan when you receive your vaccine, please discuss with your MS healthcare provider how and whether to coordinate the timing of your vaccine with the timing of your DMT dose - if you are on a DMT where this is relevant ([see section at end of document](#)). This should help ensure the vaccine is as effective as possible at generating an immune response to the coronavirus. **Given the potential serious**

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health consequences of COVID-19 disease, getting the vaccine when it becomes available to you may be more important than optimally timing the vaccine with your DMT.

**People with MS should receive an additional dose or a booster dose of a COVID-19 vaccine if it is offered to them**

People with MS who have received two doses of an mRNA vaccine (Pfizer-BioNTech or Moderna) or the AstraZeneca/Oxford vaccine may be eligible for an **additional (third) COVID-19 vaccine dose**, depending on which country you live in. An additional dose is intended to improve immunocompromised people's response to their first and second dose of vaccine. Studies of the COVID-19 vaccine responses in MS have shown a reduced or absent antibody response to the vaccine among those who use certain disease modifying therapies (DMTs). People with MS using certain DMTs (fingolimod, siponimod, ozanimod, ponesimod, alemtuzumab, ocrelizumab, ofatumumab, rituximab) may benefit from an additional COVID-19 vaccine dose. If this is available in your country, talk with your MS healthcare provider to determine the best time to get your additional dose.

People with MS may also be offered a **booster dose of the COVID-19 vaccine**, depending on which country you live in. A booster dose is given to people when the immune response to the first and second dose is likely to have waned over time. If booster doses of the COVID-19 vaccines are available in your country, talk with your MS healthcare provider to determine the best time to get your booster dose.

**Even once you have received the vaccine, it is important to continue to take precautions against COVID-19**

Even when vaccinated, you can still be infected with COVID-19 and give it to others. This is even more likely for those on DMTs that might reduce the effectiveness of the vaccines (fingolimod, siponimod, ozanimod, ponesimod, ocrelizumab, rituximab, ofatumumab). The safest approach is to ensure that those close to you are fully vaccinated, and that you continue wearing masks, practise social distancing, wash hands and follow your country's guidelines about getting tested for COVID-19 when necessary.

**Vaccination advice for young people**

The following guidance for young people applies to vaccines currently authorised for use for this age group, and should be read together with the [general advice above](#).

**Young people aged 12-17 should be vaccinated against COVID-19**

The science has shown us that the COVID-19 vaccines are safe and effective. Some countries recommend COVID-19 vaccination for all children and adolescents 12 years of age and older (who do not have 'contraindications' – a medical reason that prevents them from having the vaccine) using one of the COVID-19 vaccines that is authorised for this age group. Vaccination of this age group brings us one step closer to ending this pandemic and is an additional layer of protection for the most vulnerable among us.

**Young people are at risk of severe illness from COVID-19**

Cases of COVID-19 infection are rising in children and adolescents. While most COVID-19 infections in children and adolescents are mild, some infections are severe or even fatal. In addition to health risks due to COVID-19 infection, children and adolescents are at risk for [Multisystem inflammatory syndrome in children \(MIS-C\)](#) two to six weeks after infection with COVID-19. MIS-C is a condition where different body parts can become inflamed, including the heart, lungs, kidneys, brain, skin, eyes, or gastrointestinal organs. MIS-C is serious, even deadly, although with prompt and often intensive care most young people with MIS-C survive. The risks of COVID-19 and MIS-C outweigh any potential risks from the vaccine.

**Young people with MS should be vaccinated against COVID-19**

The importance of COVID-19 vaccination for young people with MS mirrors the advice for this age group in general, as well as the advice for adults with MS. While there is no evidence to date that young people with MS experience more severe COVID-19 infection, nor that they are at higher risk for MIS-C compared to young people who do not have MS, vaccination is strongly encouraged.

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### **Household and family members of people with MS should be vaccinated against COVID-19**

People who live in the same household as anyone with MS should also get vaccinated – **including young people over the age of 12**. Vaccination of an entire household reduces the risk of spreading COVID-19 between people in close contact with each other.

### **Recommendations for timing DMTs and the COVID-19 vaccines**

The decision of when to get the COVID-19 vaccine should include an evaluation of your risk of COVID-19, (see the list near the beginning of this advice on groups who are more at risk), and the current state of your MS. If the risk of your MS worsening outweighs your risk of COVID-19, do not alter your DMT schedule and get the vaccine when it is available to you. If your MS is stable, consider the following adjustments in the administration of your DMT to enhance the effectiveness of the vaccine. ***This suggested scheduling is not always possible and getting the vaccine when it becomes available to you may be more important than timing the vaccine with your DMT. Work with your MS healthcare provider to determine the best schedule for you.***

**Interferons, glatiramer acetate, teriflunomide, monomethyl fumarate, dimethyl fumarate, diroximel fumarate, natalizumab** — If you are about to start one of these DMTs for the first time, do not delay starting it for your COVID-19 vaccine injection. If you are already taking one of these DMTs, no adjustments to your DMT administration are needed.

**Fingolimod, siponimod, ozanimod, ponesimod** — If you are about to start one of these medicines, consider getting fully vaccinated\* two to four weeks before starting fingolimod, siponimod, ozanimod or ponesimod. If you are already taking one of these medicines, continue taking it as prescribed and get vaccinated as soon as the vaccine is available to you.

**Alemtuzumab** — If you are about to start alemtuzumab, consider getting fully vaccinated\* at least four weeks before starting alemtuzumab. If you are already taking alemtuzumab, consider getting vaccinated at least 24 weeks after the last alemtuzumab dose. When possible, resume alemtuzumab at least four weeks after getting fully vaccinated\*.

**Oral cladribine** — If you are about to start cladribine, consider getting fully vaccinated\* two to four weeks before starting cladribine. If you are already taking cladribine, the currently available limited data does not suggest that timing the vaccine in relation to your cladribine dosing is likely to make a significant difference in vaccine response. Getting the vaccine when it becomes available to you may be more important than coordinating timing of the vaccine with your cladribine treatment. If you are due for your next treatment course, when possible, resume cladribine two-four weeks after getting fully vaccinated\*.

**Ocrelizumab, rituximab** — If you are about to start ocrelizumab or rituximab, consider getting the fully vaccinated\* two to four weeks before starting ocrelizumab or rituximab. If you are already taking ocrelizumab or rituximab, consider getting vaccinated at least 12 weeks after the last DMT dose. When possible, resume ocrelizumab or rituximab at least 4 weeks after getting fully vaccinated\*.

**Ofatumumab** — If you are about to start ofatumumab, consider getting fully vaccinated\* two to four weeks before starting your DMT. If you are already taking ofatumumab, there is no data to currently guide timing of the vaccine in relation to your last DMT injection. When possible, resume ofatumumab injections two to four weeks after getting fully vaccinated\*.

**High-dose steroids** — Consider getting the vaccine injection three to five days after the last dose of steroids.

\*Fully vaccinated = once you have received the single dose of the J&J vaccine or the second dose of any other type of vaccine.

Note that vaccine protection occurs **2 weeks** after the single dose of the J&J vaccine or the second dose of any other type of vaccine.



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The individuals listed below were consulted in the development of this advice. The guidance relating to the COVID-19 vaccines was developed in conjunction with the [National MS Society working group](#). The guidance relating to young people was developed in conjunction with the [International Pediatric MS Study Group](#).

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\*\*\* National and international guidelines on physical distancing vary between at least one metre and two metres. People should consider their national guidance and be aware that these are minimum distances, longer being better.