

Choices

Disease modifying therapies



Multiple sclerosis information

Welcome to this Choices booklet about disease modifying therapies...

MS-UK believes we must listen to the voices of people affected by multiple sclerosis (MS) to shape the information and support we provide. It is these people that bring us perspectives that no one else can give.

For every Choices booklet we produce, MS-UK consults the wider MS community to gather feedback and uses this to inform our content. All of our Choices booklets are then reviewed by the MS-UK Virtual Insight Panel before they are published.

This Choices booklet has been designed with you in mind. We hope it will answer some of your questions and also provide some first-hand experience from those who have been in your position - people who can truly understand and empathise with your current thoughts and feelings.

Every time you find bold text with quotation marks like this, it is a quote directly from someone affected by multiple sclerosis

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Disease modifying therapies (DMTs)

Disease modifying therapies (DMTs) are medications that change the course of MS. They are designed to reduce the number of relapses and slow condition progression. In this booklet we will delve deeper into what they are, how they work and their impact on the management of MS.

There are many forms of DMT available, each of which affect the number and severity of relapses to varying degrees. According to the National Institute for Care Excellence's (NICE) clinical guidelines for MS, a relapse can be diagnosed by a GP or neurologist if, 'The person with MS has developed new symptoms or has a worsening of existing symptoms, and these symptoms have lasted for more than 24 hours in the absence of infection or any other cause, after a stable period of at least one month.' (1).


Additionally, some of these drugs have been found to delay the long-term progression of MS and reduce the number of new lesions forming.

Not everyone with MS will benefit from DMTs in the same way and people will respond differently to treatment. Equally, it is important to note that not all side effects will be experienced and sometimes it can take a while to find the right drug for you.


A treatment algorithm was first published in 2018 by NHS England which sets out the eligibility criteria for the prescribing of these drugs. It can be used by MS specialists and their patients as an aid to decision making and underpin equality in terms of accessing different DMTs (2).

The supporting reference document for the algorithm sets out some important criteria which should be accounted for when making DMT decisions. For example, it states that treatment should be recommended as soon as a patient becomes eligible. This eligibility should consider important factors such as disability, given that patients only qualify for a DMT if they are showing sustained disability to a level of less than 7.0 on the Expanded Disability Status Scale (EDSS). For females, pregnancy planning should also be considered so that a suitable DMT can be prescribed (2). While this treatment algorithm was produced for use within NHS England, MS health professionals in other UK nations will follow similar frames of reference.

People with MS should be supported by a specialist neurologist, one who has experience of managing patients with this condition. They should assess your eligibility and suitability for DMTs and should explain the options available to you, if any. You may also be offered a choice of DMTs to take. Once treatment has started, patients should remain under the supervision of MS specialist neurologists and nurses.



The choice can be overwhelming at first, but you have control. You can change a drug if it doesn't agree with you



For relapsing remitting MS (RRMS) the current list of licensed DMTs is divided broadly into three classes

Moderately effective

- Aubagio (teriflunomide)
- Avonex (beta interferon 1a)
- Brabio (glatiramer acetate)
- Copaxone (glatiramer acetate)
- Plegridy (beta interferon 1a)
- Rebif (beta interferon 1a)

More effective

- Gilenya (fingolimod)
- Mavenclad (cladribine)
- Ponvory (ponesimod)
- Tecfidera (dimethyl fumarate)
- Vumerity (diroximel fumarate)
- Zeposia (ozanimod)

Highly effective


- Briumvi (ublituximab)
- Kesimpta (ofatumumab)
- Lemtrada (alemtuzumab)
- Ocrevus (ocrelizumab)
- Tysabri/Tyruko (natalizumab)

It is important to note that if treatment is found to be ineffective, or intolerable side effects are experienced, it should be stopped under the support and guidance of your neurologist and an alternative offered if possible.


Other reasons for stopping treatment are if secondary progressive MS (SPMS) is confirmed along with the absence of relapse activity.

It is also important to be aware that autologous hematopoietic stem cell transplantation (AHSCT/HSCT) is considered to be a DMT and is available as a second or third-line treatment option (2). AHSCT/HSCT is usually reserved for those with highly active RRMS who have tried the highly effective medication-based DMTs without success. We have produced a **booklet** dedicated to this treatment which provides more detail on this complex medical process.

Pregnancy can also lead to a drug being stopped as many are not suitable to continue use. However, some DMTs may be considered safe or can be used instead of other drugs for an interim period until the original drug can be resumed safely.



You have to find what works for you based on your needs and preferences. Different drugs achieve different outcomes, so have outcomes at the front of your mind. All drugs come with an upside and a downside



For people affected by SPMS and primary progressive MS (PPMS) where there is still inflammatory activity evidenced via MRI scans, the following DMTs may also be available.

Secondary Progressive MS

- Mayzent (siponimod)

Primary Progressive MS

- Ocrevus (ocrelizumab)

Again, additional qualifying criteria apply to underpin individual eligibility for each of these treatments (2).

More information

Our 'HSCT and MS' Choices information booklet provides more details about this treatment. www.ms-uk.org/hsct-choices-booklet

Treating MS with DMTs

Relapsing remitting multiple sclerosis (RRMS)

Patients with RRMS who have had two or more clinical relapses in the previous two years are considered to have 'active' disease which means they are eligible for treatment with a DMT. People who have not had any clinical relapses yet show new MRI lesions are also considered for treatment.

All people with active RRMS should be considered for treatment as early as possible. Those with higher levels of disease activity may prefer to start with the more effective drugs (2).

More active relapsing remitting MS

If a patient is experiencing frequent clinical relapses and/or further

MRI activity when either untreated or on a moderately effective drug, they are considered to have more active MS (2).

To meet the criteria for high disease activity, a person must show unchanged, increased or more severe ongoing relapses, compared to the previous 12 months, despite taking beta interferon or glatiramer acetate.

Also called highly active or severe RRMS, rapidly evolving severe RRMS (RES-RRMS) is defined as having two or more disabling relapses in one year, as well as new MS activity in the brain showing up as lesions on an MRI (2).

For patients with more active MS, a highly effective DMT is recommended.

Secondary and primary progressive multiple sclerosis (SPMS and PPMS)

Currently, there are no DMTs recommended to treat non-relapsing, or non-active SPMS. However, some people who experience relapsing SPMS, or 'active' SPMS, whereby relapses are present or there is disease activity shown on MRI scans, may be eligible for one.

Mayzent is approved to treat 'active' SPMS, evidenced by at least one relapse in the previous two years and/or inflammatory activity is shown via MRI, and/or progression is identified independent of relapses (3)(4).

Ocrevus is available to treat early-stage, inflammatory PPMS (5) (6). It is the first drug to show evidence in clinical trials of slowing down and reducing disability progression in PPMS.

Clinically Isolated Syndrome (CIS)

Although not technically a classification of MS, CIS is used to

describe a first neurological episode that lasts at least 24 hours and is caused by inflammation/demyelination in one or more areas of the central nervous system. CIS is sometimes diagnosed by neurologists before a formal diagnosis of MS can be made. If a neurologist believes that a patient with CIS has a high risk of developing MS, they may suggest taking a DMT, as it may prevent or at least delay the occurrence of a further neurological episode.

People aged under 18 years

The NHS England treatment algorithm states that children should be treated using the same guidelines as adults. Children may receive DMTs if they are licensed for children, or if there is a recommended dose for children.

Ideally, children with MS who are aged under 16 should be treated in a specialist clinic with a combined team preferably including adult and paediatric neurologists with a particular interest in MS (2).

Starting, stopping or changing a DMT

For further information on starting DMT treatment, changing to a DMT that you feel could be more suitable or indeed stopping treatment altogether, please speak to your MS nurse or neurologist. It is important to be aware that DMTs should be accessible to people of all ages, with eligibility based on clinical need alone.

More information

Our 'Types of MS' Choices information booklet provides further reading on the different variants of MS.

www.ms-uk.org/types-of-multiple-sclerosis-choices-booklet

DMTs – a closer look

Earlier in this booklet we listed the different DMTs that are currently available for some people with MS in the UK. Below we take a closer look at these, but first we will attempt to clarify two issues which have become more prominent over the past few years. These being the availability of generic and biosimilar versions of DMTs.

To explain this, we need to understand that when a pharmaceutical company develops a drug, they can request that it is patented, which is a legal protection that prevents any other company from making and selling it. This patent is not finite and therefore will eventually expire and cannot be renewed. This then leaves the door ajar for other companies to create and sell copies or similar versions of the drug, known as ‘generic’ and ‘biosimilar’ medicines respectively.

Generic medicines

These are an identical copy of the drug which was originally developed, this includes its active ingredients, how efficacious it is and its safety.

An example of generic DMTs can be found with fingolimod in the UK. This was originally developed and marketed with the brand name Gilenya by Novartis Pharmaceuticals UK Ltd. Now the UK patent has expired, there a number of generic versions of fingolimod available provided by a range of pharmaceutical companies (7).

Biosimilar medicines

Medicines that are biosimilar are those whose make-up is very close to the original, including the same active ingredients, biological

activity, efficacy and safety, but with some slight differences – hence they cannot be classed as a generic medicine. There must be strong evidence that shows biosimilar medicines hold no clinically meaningful difference to the original version.

A recent example can be found with natalizumab in the UK. Originally developed and marketed by Biogen under the brand name Tysabri, a biosimilar version is now available with the brand name Tyruko, developed and distributed by Sandoz Ltd. A recent randomised clinical trial which compared this biosimilar form of natalizumab to Tysabri found no difference between both in terms of efficacy, safety, and immunogenicity for patients with RRMS (8).

In the UK, as with all medicines, the safety of generic and biosimilar DMTs must be approved by the Medicines and Healthcare products Regulatory Agency (MHRA) prior to being made available.

The following DMTs are currently available to treat MS in the UK

Aubagio (teriflunomide)

How does it work?

Aubagio inhibits the function of specific immune cells that have been implicated in MS. It targets the production of a key mitochondrial enzyme required by white blood cells, which in turn reduces the activated T and B immune cells associated with MS. Additionally, it has been shown to have other anti-inflammatory and immune-modulating properties (9) (10).

How can it help?

Studies showed that Aubagio reduced relapses by one-third. They also evidenced that a higher dose reduced the risk of disability progression by just over 30 per cent (9) (10).

Interestingly, studies have also shown that teriflunomide can reduce the levels of the antibody IgG in the system. Elevated levels of this antibody are connected to the Epstein-Barr virus (EBV) which is linked to MS onset and progression (11).

How is it administered?

Aubagio is taken as a tablet, once a day.

Who manufactures it?

Sanofi

Generic forms available?

Yes. Teriflunomide forms available from AAH Pharmaceuticals, Accord, Alliance Healthcare, Dr Reddy's, Perennial Pharma, Teva and Viatrix (12).

What type of MS is it prescribed for?

Aubagio is licensed for relapsing remitting MS (2).

What are the side effects?

Common side effects are gastrointestinal upset, hair thinning and changes in liver function. Aubagio should not be taken by women considering pregnancy because of potential risks to the unborn baby. A woman of child-bearing age considering Aubagio must take a pregnancy test and ensure adequate contraception is in place before starting the drug.

The drug stays in the body for a long time and if a woman taking Aubagio suspects pregnancy, she must immediately contact her GP and, if a pregnancy is confirmed, it can be flushed out of the body by taking activated charcoal or cholestyramine over several days (9) (10).

Avonex (beta interferon 1a)

How does it work?

Interferons are proteins produced naturally by the body that help us fight infection. Avonex blocks the action of one type of protein called gamma interferon. It reduces the autoimmune reaction that causes inflammation and destruction of myelin (13) (14).

How can it help?

It has been shown to reduce the rate of relapse by about one-third in people with RRMS. It also reduces the severity of relapses that occur (13) (14).

How is it administered?

Avonex must be injected into the muscle once a week and should be stored in the fridge.

Who manufactures it?

Biogen

Generic forms available?

No

What type of MS is it prescribed for?

Avonex is used to treat RRMS (2).

What are the side effects?

The most common side effect experienced when taking Avonex is flu-like symptoms after injecting.

Injection-site irritations may also occur, such as redness, swelling, and itching.

Other less common side effects from Avonex can be mood swings, fever and blood abnormalities. Most people find these effects reduce

over a three-month period of taking the drug. If they persist, a conversation with an MS nurse or neurologist would be recommended (13) (14).

Brabio (glatiramer acetate)

How does it work?

Brabio works differently from interferons in that it is a synthetic combination of four amino acids that resemble the myelin protein. It is thought to work by preventing the production of immune cells that attack myelin (13) (15) (16).

How can it help?

The rate of relapse in people taking Brabio is generally reduced by one-third (13) (1) (16).

How is it administered?

It needs to be injected subcutaneously, which is under the skin. There are two doses, 20mg and 40mg. One is taken as a daily injection, and the other is taken three times a week. It needs to be stored in the fridge.

Who manufactures it?

Viatrix

Generic forms available?

Brabio is a generic version of Copaxone.

What type of MS is it prescribed for?

Brabio is licensed for RRMS and some people with CIS (2).

What are the side effects?

Common side effects are injection-site reactions, indentations under the skin known as lipoatrophy, chest tightness, headache,

anxiety and nausea. Less common side effects include thyroid changes, blood cell changes, and palpitations (13) (15) (16).

Briumvi (ublituximab)

How does it work?

In MS, the immune system mistakenly attacks the protective covering of nerve cells, and B cells are a key player in this attack. Briumvi is a monoclonal antibody that works by targeting and eliminating these B cells, which helps to lower the risk of relapses, eases symptoms, and slows condition progression (17).

How can it help?

Studies have found that relapse rates in people with RRMS were reduced by over 50 per cent in those taking ublituximab when compared with participants taking teriflunomide (17).

How is it administered?

Briumvi is administered by infusion every six months. The initial infusion usually takes around four hours to complete, with a second dose administered two weeks later. This will take approximately one hour. Subsequent doses are applied by infusion every six months thereafter, each taking approximately one hour to complete (17).

Who manufactures it?

Neuraxpharm

Generic forms available?

No

What type of MS is it prescribed for?

Briumvi is recommended for people with active forms of RRMS (18).

What are the side effects?

Infusion reactions are the most frequently reported side effects, such as itching, rash and difficulty breathing. These are generally short-lived. At the start of each infusion, a corticosteroid and an antihistamine are given to the patient to help prevent any reactions (17).

The most common potential side effects include the risk of contracting respiratory tract infections, coughs and colds and herpes virus infections, for example cold sores or shingles (17).

Copaxone (glatiramer acetate)

How does it work?

Copaxone works differently from interferons in that it is a synthetic combination of four amino acids that resemble the myelin protein. It is thought to work by preventing the production of immune cells that attack myelin (13) (19) (20).

How can it help?

The rate of relapse in people taking Copaxone is generally reduced by one-third (13) (19) (20).

How is it administered?

It is injected subcutaneously. There are two doses, 20mg and 40mg. One is taken as a daily injection, and the other is administered three times per week. It needs to be stored in the fridge.

Who manufactures it?

Teva

Generic forms available?

Yes. Brabio is a generic version of Copaxone (21)

What type of MS is it prescribed for?

Copaxone is licensed for RRMS and some people with CIS (2).

What are the side effects?

Common side effects are injection-site reactions and lipoatrophy (indentations under the skin), chest tightness, headache, anxiety, nausea. Less common side effects include thyroid changes, blood cell changes and palpitations. (13) (19) (20).



Don't be put off by those who didn't get on with the medication



Gilenya (fingolimod)

How does it work?

Gilenya is an immune-modulating drug, which attaches to the surface of certain white blood cells, known as lymphocytes, causing a number of them to be retained within the body's immune system.

As a result, fewer lymphocytes get into the bloodstream and fewer reach the central nervous system meaning the potential for an immune attack on the cells of the brain and spinal cord is reduced (22) (23).

How can it help?

Gilenya was shown to reduce the risk of relapses by 67 per cent compared to a placebo in trials (24).

How is it administered?

It is taken in the form of a capsule, orally, once a day.

Who manufactures it?

Novartis

Generic forms available?

Yes. Fingolimod forms available from AAH Pharmaceuticals, Accord, AmaroX, Dr Reddy's, Glenmark Pharmaceuticals, Sandoz, Sun Pharma, Teva, Tillomed, Viatrix and Zentiva Pharma (25).

What type of MS is it prescribed for?

Gilenya is a 'more effective' drug treatment which is licensed for adults with highly active relapsing remitting MS. This is characterised as experiencing one relapse in the previous year despite being on another disease modifying therapy, such as an interferon, for at least 12 months (2).

What are the side effects?

Possible side effects include changes to liver function, macular oedema which is an accumulation of fluid in the macular area of the eye that sometimes causes blurred vision, headache, respiratory tract infection, shortness of breath, diarrhoea and nausea. Gilenya can also cause a decrease in heart rate, so your first dose will be monitored in hospital for six hours (22) (23) (24).

Kesimpta (ofatumumab)

How does it work?

Kesimpta is a monoclonal antibody, similar to that of Ocrevus (ocrelizumab). It targets and attaches to specific markers in the

immune system called CD20. These form on the surface of a type of white blood cell called B cells. It is thought that these B cells attack the myelin that surrounds nerve cells and causes inflammation. Kesimpta targets these B cells and removes them, reducing their overall activity (26) (27).

How can it help?

Compared to Aubagio (teriflunomide), Kesimpta reduces the risk of relapse by 50 to 59 per cent. Trials showed that people taking this drug had fewer, smaller, or no new areas of active lesions on an MRI scan. It also helps to relieve symptoms and slow down the progression of the condition (26) (27).

It is suggested Kesimpta is as effective as Lemtrada, Tysabri and Ocrevus (28).

How is it administered?

Kesimpta is self-injected, subcutaneously. It is injected weekly for the first three weeks, then you skip a week, before continuing with monthly injections.

It needs to be stored in the fridge and taken out 15 to 30 minutes before injecting to allow it to reach room temperature (27).

Who manufactures it?

Novartis

Generic forms available?

No

What type of MS is it prescribed for?

Kesimpta is approved for use in adults with active RRMS. It is classed as a highly effective treatment. It can be offered as a first-line drug therapy (2).

What are the side effects?

The most common side effects reported for Kesimpta include upper respiratory tract infections, urinary tract infections, injection-related reactions such as fever, headache, muscle pains, and tiredness. Injection-site reactions are also common, such as redness, itching and swelling. These reactions mostly clear up the same day. Other common side effects include oral herpes, and a reduction in the blood level of immunoglobulins which help to protect against infection (27).

Lemtrada (alemtuzumab)

How does it work?

Lemtrada was originally licensed for the treatment of leukaemia. It is a monoclonal antibody which kills T-cells, a type of lymphocyte involved in the MS immune response. Once the T-cells are killed, the immune system repopulates, leading to a modified immune response that no longer regards myelin and nerves as foreign, and therefore stops attacking them (29) (30).

How can it help?

In two studies, Lemtrada was shown to be effective in reducing the number of relapses in people with RRMS. One clinical trial compared Lemtrada to Rebif in people who had not previously been treated with a DMT. Relapses were reduced by 55 per cent compared to Rebif (31).

In the second trial the drug was again compared to Rebif. In people who had experienced at least one relapse whilst on therapy, Lemtrada reduced the number of relapses by 49 per cent compared to Rebif (32).

How is it administered?

Lemtrada is delivered by two infusions, 12 months apart. The first infusion is delivered over five days, and the second over three days. Infusions take place in a hospital or infusion clinic.

Who manufactures it?

Sanofi

Generic forms available?

No


What type of MS is it prescribed for?

Lemtrada is highly effective when treating more active forms of RRMS (2).


What are the side effects?

Side effects reported for Lemtrada include one-third of people reporting changes to their thyroid function, which while treatable, can mean lifelong medication is necessary. One per cent of people reported a blood clotting disorder called immune thrombocytopenic purpura (ITP). While serious, ITP can be treated effectively. Other adverse effects reported relate to kidney function, reactions at the infusion site and respiratory infections.

More common reported side effects were flu-like symptoms after the infusion was given, and some may experience an itchy rash which can be managed by antihistamines (29) (30).



Everyone's experience is different and which DMT works for who and for how long, you can't tell. But, in my case, I have not had a relapse since I went on a DMT. They work for a lot of people. Go for it!



Mavenclad (cladribine)

How does it work?

Mavenclad is an immune-modulating drug that targets specific lymphocytes, T-cells and B-cells.

The drug interferes with DNA synthesis and repair, therefore reducing the number of these lymphocytes. It is these cells that are thought to be involved in the immune response which attacks myelin, causing demyelination (33) (34).

How can it help?

Studies have shown that Mavenclad reduces relapse rate significantly and delays disability progression by reducing the loss of brain cells, sustained for six months compared with a placebo (35).

How is it administered?

Mavenclad is taken as a tablet via two courses, one year apart. The first course is taken over five consecutive days in the first month and over five consecutive days in the second month. The

second course is given 12 months later in the same way as the first course. The number of tablets taken in each course is dependent on the individual's weight.

Who manufactures it?

Merck-Serono

Generic forms available?

No

What type of MS is it prescribed for?

Mavenclad was initially approved to treat highly active RRMS. Its use has since been extended to treat less active RRMS.

What are the side effects?

One of the most common side effects of taking Mavenclad is lymphopenia, which means a reduction in white blood cells. This can increase the risk of getting infections. Other common side effects include shingles, cold sore, rash, and hair loss. If a patient has shingles, then Mavenclad may need to be stopped until the infection is treated and cleared (34).

Mayzent (siponimod)

How does it work?

Mayzent is an immune-modulating drug which works by reducing the amount of circulating white blood cells, known as lymphocytes, preventing them from being able to move freely within the body. Fewer cells are then able to reach the brain and spinal cord, therefore reducing nerve damage caused by SPMS (36).

How can it help?

Studies have shown that Mayzent helped to slow disability

progression by 37 per cent, in those with active SPMS, compared to placebo. In slowing the progression, it also delayed the time to wheelchair dependency in a subgroup of patients, with an EDSS score of 6.5, who were high risk of reaching wheelchair dependency, compared to placebo (37).

How is it administered?

It is to be taken by tablet, once a day. Tests will be required before starting treatment to determine the correct dosage. This will depend on how well the tablet is broken down in the body (36). Dosage is increased gradually over the first five days of treatment. This is to reduce the impact on the heart in case of irregular or slowed heartbeat.

Who manufactures it?

Novartis

Generic forms available?

No

What type of MS is it prescribed for?

Mayzent is approved for treating SPMS when there is evidence of disease activity. This could be in the form of relapses or inflammatory activity on MRI (3).

What are the side effects?

Most commonly associated side effects include slow heart rate, headache, high blood pressure, infections due to lowered white cell count and visual disturbances (36).

Ocrevus (ocrelizumab)

How does it work?

Ocrevus is a monoclonal antibody that has been designed to target

and attach to a specific marker in the immune system called CD20 on the surface of certain types of white blood cells known as B cells. These B cells are what attack the immune system and cause inflammation and damage. Ocrevus targets these cells to help reduce their activity (38).

How can it help?

Studies have shown that Ocrevus can reduce annual relapse by 50 per cent compared to Rebif. There is also evidence that the drug reduced disability progression and the number of lesions shown on an MRI when compared with beta interferon. Loss of brain cells was also reduced, and no evidence of disease activity (NEDA) was seen in patients taking Ocrevus, again when compared to Rebif (39).

How is it administered?

Ocrevus is administered by infusion or injection.

The initial infusion is given in two separate doses, two weeks apart. After that it is one single dose administered every six months. Each infusion takes around three to four hours to complete (38).

The injectable form is subcutaneous and is only administered by a doctor or nurse every six months. It takes around 10 minutes for the injection process to complete and you will be monitored for around 60 minutes after the initial injection has taken place. This is to ensure that any reactions to the injection are managed appropriately (40).

Who manufactures it?

Roche

Generic forms available?

No

What type of MS is it prescribed for?

Ocrevus is highly effective when treating more active forms of RRMS. It is usually only available if Lemtrada (alemtuzumab) is contraindicated or unsuitable (40). It is also available for those with early stage inflammatory PPMS (5).

What are the side effects?

Infusion and injection reactions are the most frequently reported side effects, such as itching, rash and difficulty breathing. These are generally short-lived. Before each treatment, a corticosteroid and an antihistamine are given to the patient to help prevent any reactions (41) (42).

Infections are also common, such as chest infections, coughs and colds and herpes virus infections, for example cold sores or shingles (41) (42).

Plegridy (beta interferon 1a)

How does it work?

Interferons are proteins, produced naturally by the body that help us fight infection. Plegridy blocks the action of one type of protein called gamma interferon. It reduces the autoimmune reaction that causes inflammation and destruction of myelin (43).

How can it help?

It has been shown to reduce the rate of relapse by about one-third in people with RRMS. It has also shown to reduce the severity of relapses that occur (43).

How is it administered?

Plegridy is self-injected under the skin every two weeks and should be stored in the fridge. You may be advised to start

treatment on a low dose and gradually increase it, to avoid any potential side effects (44).

Who manufactures it?

Biogen

Generic forms available?

No

What type of MS is it prescribed for?

Plegridy is used to treat RRMS (2).

What are the side effects?

The most common side effect experienced when taking Plegridy is flu-like symptoms after injecting. Injection-site irritations may also occur, such as redness, swelling, and itching. Other less common side effects can be mood swings, fever and blood abnormalities.

Most people find these effects reduce over a three-month period of taking the drug. If they persist, a conversation with an MS nurse or neurologist is recommended (43) (44).

Ponvory (ponesimod)

How does it work?

Ponvory is an immune-modulating drug. It reduces the amount of circulating white blood cells, known as lymphocytes and keeps them in the lymph nodes. Fewer cells are then available to attack the myelin sheath. This leads to a reduction in nerve damage and relapses (45).

How can it help?

A randomised clinical trial showed that people taking ponesimod

have fewer relapses than those taking teriflunomide.

A significant improvement in fatigue was also seen in comparison (46). It has also been evidenced that higher dose ponesimod led to a 52 per cent reduction in annualised relapse rate, compared to placebo (47).

How is it administered?

It is taken as a tablet, once per day. Dosages are started low and gradually increased over the first 14 days (45).

Who manufactures it?

Janssen-Cilag

Generic forms available?

No


What type of MS is it prescribed for?

Ponvory is used as a first-line treatment for people with active RRMS as defined by MRI. It can also be used as a second line treatment (48).


What are the side effects?

The most common side effects include the common cold, raised liver enzymes and upper respiratory tract infection. Other less common side effects include dizziness, headache, vertigo, macular oedema, and anxiety.

Ponvory can also cause an initial decrease in heart rate. An electrocardiogram (ECG) will be given to check the electrical activity of the heart before the first dose. If there is an increased risk of a slowed heart rate you will be monitored for up to four hours after your first dose. An ECG will also be repeated at the end of this initial monitoring (45).



Take the neurologists advice but also choose what suits you and your lifestyle in terms of pill/injection/infusion and regularity of dosage



Rebif (beta interferon 1a)

How does it work?

Interferons are proteins, produced naturally by the body that help us fight infection. Rebif blocks the action of one type of protein called gamma interferon. It reduces the autoimmune reaction that causes inflammation and destruction of myelin (13) (49).

How can it help?

Rebif has been shown to reduce the rate of relapse by about one-third in people with RRMS. It also reduces the severity of relapses that occur (13) (49).

How is it administered?

Rebif must be injected under the skin three times per week and should be stored in the fridge. It comes in two dosages – 22mcg and 44mcg (49).

Who manufactures it?

Merck-Serono

Generic forms available?

No

What type of MS is it prescribed for?

Rebif is used to treat RRMS (2).

What are the side effects?

The most common side effect experienced when taking Rebif are flu-like symptoms after injecting. Injection-site irritations may also occur, such as redness, swelling, and itching.

Other less common side effects can be weakness and tiredness, fever and blood abnormalities. Most people find these effects reduce over a three-month period of taking the drug. If they persist, a conversation with an MS nurse or neurologist would be recommended (13) (49).

Tecfidera (dimethyl fumarate)

How does it work?

It is thought that Tecfidera promotes an anti-inflammatory effect when the immune system attacks myelin, therefore reducing any damage that may be caused to the central nervous system (50) (51).

How can it help?

Studies have shown that Tecfidera reduces the annual MS relapse rate by around one-half. During trials, MRI scans showed fewer, smaller or no new active lesions. Some studies also showed a significant reduction in the progression of the condition (50) (51).

How is it administered?

Tecfidera is taken as a tablet, twice a day. Initial dosage is low and gradually increased over a two-week period.

Who manufactures it?

Biogen

Generic forms available?

Yes. Dimethyl fumarate forms available from Almirall, Celix Pharma, Genus Pharmaceuticals, Teva, Viatrix, Wockhardt and Zentiva (52).

What type of MS is it prescribed for?

Tecfidera is used as a first-line treatment for people with active RRMS, defined as two clinically significant relapses experienced over the previous two years (2) (52).

What are the side effects?

Common side effects reported are flushing and feeling hot, headaches, gastrointestinal upset and decreased white blood cell count (50) (51).



I believe my path through MS has been so good because I got my DMT right at the start of my diagnosis and therefore it has slowed down the progression and severity of the illness



Tysabri/Tyruko (natalizumab)

How does it work?

A monoclonal antibody that works in a different way to injectable therapies, Tysabri binds to specific adhesion molecules within the immune cells. This stops the cells from crossing the blood brain barrier and entering the central nervous system, thereby reducing inflammation and nerve damage (53) (54).

Tyruko is a biosimilar version of Tysabri which is now available. See the section titled 'Biosimilar medicines' for more information.

How can it help?

In studies, people with rapidly evolving severe RRMS showed a decrease of 81 per cent in relapses when taking natalizumab. People with RRMS showed a reduction of around two-thirds in the number of relapses, fewer MS lesions detected during MRI scans and a significantly reduced rate of condition progression (53) (54) (55).

How is it administered?

Tysabri is administered by intravenous infusion every four weeks at either an infusion centre or a hospital. It has been evidenced that Tysabri is as effective when administered every six weeks, lowering the risk of potential side effects (56).

In 2021, Tysabri was authorised for use in injection form. This is to be given as a monthly subcutaneous injection by a healthcare professional. Studies show that subcutaneous Tysabri is as effective and safe as the intravenous infusion version (57).

Who manufactures it?

Biogen

Generic forms available?

No

What type of MS is it prescribed for?

Tysabri is highly effective when treating more active forms of RRMS (2).

What are the side effects?

Side effects can include dizziness, nausea, joint pain, shivering and sometimes inflammation of the nose and throat.

People taking natalizumab are at an increased risk of developing a serious condition called progressive multifocal leukoencephalopathy (PML), which is a rare but sometimes fatal brain infection that affects the central nervous system. PML is caused by a virus called the John Cunningham virus (JCV). Each potential natalizumab patient is tested to check whether they are positive for JCV as this can help to establish their risk of developing PML.

Risk factors associated with PML are the presence of anti-JCV antibodies and the length of time on treatment. There is a slightly increased risk for patients who remain on the therapy for more than two years. As the JCV is airborne, patients can develop it at any time. This means that those who test negative for JCV should be retested at regular intervals.

Patients who have been on immune suppressants prior to treatment also have an increased PML risk factor. Despite the

risks, the benefits of natalizumab continue to outweigh the risks for many people with highly active RRMS (53) (54).

Vumerity (diroximel fumarate)

How does it work?

Vumerity is thought to have an anti-inflammatory effect when the immune system attacks myelin, therefore reducing any damage that may be caused to the central nervous system (58).

How can it help?

Studies show that Vumerity significantly reduces the amount of active MS lesions on MRI scans. It has also been found to reduce relapse rates on a similar level to Tecfidera (59).

How is it administered?

It is taken as a tablet, twice a day. A low dose is taken for an initial seven days at which point a higher maintenance dose is required (58).

Who manufactures it?

Biogen

Generic forms available?

No

What type of MS is it prescribed for?

Vumerity is prescribed for people with RRMS who have moderately active disease in the form of a recent relapse, or new lesions (60).

What are the side effects?

Studies show Vumerity is well tolerated when compared to

Tecfidera, with gastrointestinal upset being mild to moderate. It is still one of the more common side effects, but with a lesser impact on daily life (60). Other common side effects include flushing, nausea and an increased risk of acquiring infections (58).

Zeposia (ozanimod) – approved for MS patients in Scotland only.

How does it work?

Zeposia belongs to a group of drugs which work by reducing the amount of circulating white blood cells, known as lymphocytes, and preventing them from being able to move freely within the body. This reduces inflammation and nerve damage (62).

How can it help?

Studies have shown that Zeposia is more effective than Avonex in reducing the amount of new active lesions on MRI and at reducing brain volume loss. Higher dose Zeposia was shown to reduce relapse rate significantly compared to Avonex (63).

How is it administered?

It is taken as a tablet, once a day. The dosage is gradually increased over a period of eight days to help lessen the occurrence of side effects (62).

Who manufactures it?

Bristol Myers Squibb

Generic forms available?

No

What type of MS is it prescribed for?

Zeposia can be prescribed for people with active RRMS, for MS patients in Scotland only (64).

It is currently not recommended by NICE to treat people with MS in the rest of the UK nations.

What are the side effects?

The most common side effects are an increased risk of infection including coughs, colds, respiratory infection, lowered blood pressure, slowed heart rate and increased liver enzyme levels. Those taking Zeposia should have their blood pressure checked regularly (62).

Choosing a DMT



Do your research very thoroughly first, so that your choice is fully informed



Once diagnosed with MS, your neurologist will talk to you about any medication you may require and be eligible for. They should discuss with you all of your possible options. One thing to consider when looking at these medications is your lifestyle and how the administration of these drugs will fit into your day-to-day living.

There are several factors you may want to consider and discuss with your family and neurologist. Examples may include,

- What are the benefits of a DMT in the short, mid and long term?
- What are some of the common side effects?
- How is the therapy administered? Tablet, injection, or infusion?
- Is this right for my lifestyle?

Openly discuss all of the options with your MS nurse and/or neurologist to come to a decision on what the best course of treatment is for you.



Don't be afraid to ask questions and don't always rely on how a DMT has affected others. Each person will have a different experience



More information

The MS Trust website has a useful tool called 'MS Decisions aid' which allows you to compare different DMTs to help you find the one that is most suitable for you. www.mstrust.org.uk/information-support/ms-drugs-treatments/ms-decisions-aid

Side effects

The side effects of DMTs will differ with each therapy and vary from person to person. It is important to talk to your MS nurse or neurologist about any concerns you may have.

Side effects are generally not severe and there are various ways to manage them. For example, if you experience flu-like symptoms after injecting, try changing the time of day that you take your injection, possibly to just before bedtime so you can sleep through the side-effects.

Read any information available. You can seek advice but ultimately the choice is yours. Any problems speak to your MS nurse

Alternatively, providing they do not interfere with any other medication you are taking, it is recommended that you take paracetamol or ibuprofen two hours before the injection to ease the symptoms.

If you have injection-site reactions, you could try using Emla cream which numbs the area prior to the injection. Always

rotate the injection site to avoid using the same area each time. It may also help to ensure that the drug is at room temperature and also to warm your skin before injecting.

If you are taking any of the oral therapies, ask your MS nurse how to manage any side effects you are experiencing.

If the side effects become severe or you feel unable to cope with them, contact your MS nurse or neurologist who will be able to provide further support. Contact the **MS-UK Helpline** if you need help to find your nearest MS nurse.



You are always in control and if you wish to stop or change a DMT you can absolutely do that



What if I choose not to take a DMT?

While you may be eligible for DMTs it is entirely your choice whether you wish to take them or not. Should you wish not to, this may be referred to as being 'drug naïve' by health professionals. If you choose not to take a DMT it would be useful to keep a symptom diary in case you change your mind in the future.

More information

Our Choices range of booklets offer more information about the different ways which can help you to manage the impact of MS, incorporating diet, exercise and complementary therapies.

www.ms-uk.org/multiple-sclerosis-choices-booklets



You have to weigh up the pros and cons personally, but I think taking a DMT has helped slightly on balance. I believe this needs to go alongside living a healthy life – good diet, regular exercise and try and live in the moment



About MS-UK

MS-UK is a national charity supporting anyone affected by multiple sclerosis. Our hope for the future is a world where people affected by MS live healthier and happier lives.

MS-UK has always been at the forefront of promoting choice, of providing people with all the information and support they need to live life as they wish to with multiple sclerosis, whether that be through drugs, complementary therapies, lifestyle changes, a mixture of these or none at all.

We will always respect people's rights to make informed decisions for themselves.

The MS-UK Helpline

We believe that nobody should face multiple sclerosis alone and our helpline staff are here to support you every step of the way.

Our service is informed by the lived experience of real people living with MS, so we can discuss any treatments and lifestyle choices that are of benefit, whether they are clinically evidenced or not.



New Pathways

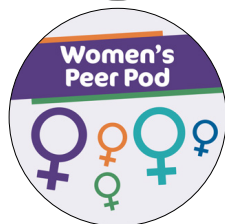
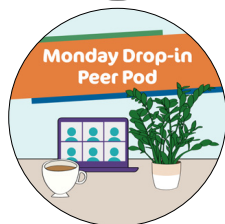
Our bi-monthly magazine, New Pathways, is full of the latest MS news regarding trials, drug development and research as well as competitions, special offers and product reviews. The magazine connects you to thousands of other people living with MS across the country.

Available in print, audio version, large print and digitally.
 Visit [ms-uk.org/new-pathways-magazine](https://www.ms-uk.org/new-pathways-magazine)

About MS-UK

Peer support service

Our peer support service enables people to connect with others in a safe space and share experiences on topics of interest. Our Peer Pods take place regularly and are all volunteer led. Please visit the website to find out more [ms-uk.org/peer-support-service](https://www.ms-uk.org/peer-support-service) or email peersupport@ms-uk.org.





MS-UK's online activities

MS-UK offers a variety of online activities for those affected by MS to stay active, connected with others and to manage their symptoms to live happier and healthier lives. Activities include exercise sessions, mindfulness courses, chair yoga classes, information sessions and workshops. To get involved, please go to www.ms-uk.org or email register@ms-uk.org.

MS-UK E-learning

Do you work with or support someone living with MS and want to increase your understanding and knowledge of this long-term health condition? Professionals at MS-UK have created an accredited eLearning course that can help you do this. Visit www.ms-uk.org/ms-awareness-e-learning to find out more.

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www.ms-uk.org

MS-UK Helpline

0800 783 0518

info@ms-uk.org

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Please note information is accurate at time of publication, please see our online version for the most up to date version.

Check out MS-UK's online activities

Live a happier and healthier life with MS



- ✓ Accessible online exercise classes
- ✓ Chair yoga classes
- ✓ Mindfulness courses
- ✓ Interactive workshops
- ✓ Information sessions
- ✓ Peer Support Service

Don't miss out – sign up for our new online activities today!

Visit www.ms-uk.org or contact us at register@ms-uk.org

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MS-UK
D3 Knowledge Gateway,
Nesfield Road,
Colchester,
Essex, CO4 3ZL

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MS-UK Helpline
0800 783 0518
info@ms-uk.org



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