Choices

MS-UK

Disease modifying therapies

Multiple sclerosis information

www.ms-uk.org

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

This Choices leaflet 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 see a box with an icon like this, it is a quote directly from someone affected by multiple sclerosis.

Contents

Disease modifying therapies

Disease modifying therapies (DMTs) are medications which modify the course of multiple sclerosis (MS) and are designed to reduce the amount of relapses. Different DMTs effect the number and severity of relapses in varying degrees. 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. New guidance was issued in 2015 by the Association of British Neurologists (ABN) setting out the eligibility criteria for the prescribing of these drugs. The ABN also states that treatment should start as early as possible in eligible patients, before the person with MS shows any disability or sustains damage to their nerve cells. Some treatments are licensed for use in Clinically Isolated Syndrome (CIS) and these are sometimes given before MS has been made as a definitive diagnosis. The guidelines also state that 'people with MS will face complex choices and must play an active role in treatment decisions' (1).

An MS specialist neurologist should assess your eligibility and suitability for DMTs and should explain the options available to you. You may well have choices over which (if any) you wish to take. Once treatment has started, patients should remain under the supervision of specialist MS 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.

The recommendations for starting disease modifying therapies as stated in the ABN guidance are as follows (1):

Eligible patients will normally be ambulant (maximum EDSS 6.5). There are no treatments licensed for use during pregnancy.

The current list of licensed disease modifying therapies are divided broadly into two classes:

Category 1 – Moderately effective

- Aubagio (Teriflunomide)
- Beta Interferon 1a (Avonex, Rebif and Plegridy)
- Beta Interferon 1b (Betaferon and Extavia)
- Copaxone (Glatiramer acetate)
- Glatiramer acetate (Copaxone and Brabio)
- Mavenclad (Cladribine) – more effective
- Tecfidera (Dimethyl fumerate) – more effective

Category 2 – Highly effective

- Ocrevus (Ocrelizumab)
- Tysabri (Natalizumab)

Treating relapsing remitting multiple sclerosis (RRMS)

Patients with relapsing remitting MS 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 disease modifying therapy.

All people with active relapsing remitting MS should be considered for treatment and most are likely to start treatment with a category 1 drug. There are three drugs in this category that are seen as 'more effective' and all are oral therapies; these are Gilenya, Mavenclad and Tecfidera. Those with active disease may prefer to start with one of these.

Treating more active relapsing remitting MS

Patients may be classified as having more active MS by frequent clinical relapses and/or MRI activity either when untreated or whilst on a category 1 drug (1).

The formal criteria for high-disease activity despite taking Beta Interferon or Glatiramer acetate requires one relapse in the previous year on either drug and:

A) gadolinium enhancing MRI lesions or

B) at least nine T2-hyperintensive lesions on a cranial MRI

For patients with more active disease, a category 2 – highly effective, drug is recommended, either Lemtrada, Ocrevus or Tysabri.

Treating secondary and primary progressive multiple sclerosis (SPMS & PPMS)

Currently, there are no disease modifying therapies recommended in non-relapsing secondary progressive MS or in primary progressive MS. Some people who experience relapsing secondary progressive MS, whereby relapses are their main cause of increasing disability, may benefit from a disease modifying therapy.

There are a number of other drugs in development, some which focus specifically on progressive forms of MS.

Clinically Isolated Syndrome (CIS)

Clinically Isolated Syndrome is used to describe a first neurologic episode that lasts at least 24 hours, and is caused by inflammation/ demyelination in one or more sites in the central nervous system. This is sometimes diagnosed before a formal diagnosis of MS can be made. Those with CIS who show abnormalities on MRI scans within one year, may be offered treatment with a DMT. Currently only Beta interferon and Glatiramer acetate are licensed for clinically isolated syndrome.

People aged under 18 years

The ABN guidance states that minors aged between 16-18 years should be treated according to the above guidelines. 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 (1).

For further information on starting, stopping or changing a disease modifying therapy please speak to your MS Nurse and /or neurologist.

What is a relapse?

The National Institute for Care Excellence (NICE) published guidelines in October 2014 for the management of multiple sclerosis (2). In these guidelines 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 a least one month.’

Disease modifying therapies (DMTs) – a closer look

Aubagio (Teriflunomide)

How does it work?

Aubagio inhibits the function of specific immune cells that have been implicated in MS. It can inhibit a key enzyme required by white blood cells (lymphocytes) – which in turn reduces the T and B immune cells that are active in MS from multiplying.

As well as this, it has shown to have other anti-inflammatory and immune-modulating actions (3) (4).

How can it help?

Studies showed that Aubagio reduced relapses by one-third. In trials a higher dose reduced the risk of disability progression (sustained for 12 weeks) by 30 percent (3) (4).

How is it administered?

Aubagio is taken as a tablet, once a day.

Who manufactures it?

Genzyme

What type of MS is it prescribed for?

Aubagio is a ‘category 1’ drug, licensed for relapsing remitting MS (1).

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, Aubagio can be 'flushed out' of the body by taking activated charcoal or cholestyramine over several days (3) (4).

Beta Interferon 1a (Avonex, Rebif & Plegridy)

How does it work?

Interferons are proteins, produced naturally by the body that help us to fight infection. There are currently three interferon beta 1a DMTs available – Avonex, Rebif and Plegridy.

Interferon beta 1a blocks the action of one type of protein called gamma interferon. It reduces the autoimmune reaction that causes inflammation and destruction of myelin (5) (6) (7) (8).

How can it help?

It has been shown to reduce the rate of relapse by about one-third in people with relapsing remitting MS. It also reduces the severity of relapses that occur (5) (6) (7) (8).

How is it administered?

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

Rebif must be injected under the skin three times per week and should be stored in the fridge. Rebif comes in two dosages – 22mcg and 44mcg (7).

Plegridy must be injected under the skin every 2 weeks and should be stored in the fridge.

Who manufactures it?

Avonex – Biogen

Rebif – EMD Serono

Plegridy – Biogen

What type of MS is it prescribed for?

All types of interferon beta 1a are classed as 'category 1' drugs therefore they are used in those diagnosed with relapsing remitting MS (1).

What are the side effects?

The most common side effect experienced when taking interferon beta 1a is flu-like symptoms after injecting. Injection site irritations may also occur, such as redness, swelling, itching.

Other less common side effects can be mood swings (mainly from Avonex), 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 (5) (6) (7) (8).

Beta Interferon 1b (Betaferon and Extavia)

How does it work?

Both Betaferon and Extavia are thought to block the action of one type of immune cell, called a T-cell and reduce the autoimmune reaction that causes inflammation and destruction of myelin (5) (9) (10).

How can it help?

Both have been shown to reduce the rate of relapse by about one-third in people with relapsing remitting MS and also reduce the severity of relapses that occur (5) (9) (10).

How is it administered?

Betaferon and Extavia must be injected subcutaneously (under the skin, into body fat) every other day. They do not need to be stored in the fridge, but must be mixed before use.

Who manufactures it?

Betaferon – Schering

Extavia – Novaratis

What type of MS is it prescribed for?

Both types of interferon beta 1b are classed as 'category 1' drugs therefore they are used in those diagnosed with relapsing remitting MS (1).

What are the side effects?

The most common side effects experienced with Betaferon and Extavia are flu-like symptoms after injecting and injection site reactions. They can also cause changes in menstruation, blood abnormalities and mood swings; however, these symptoms are less common (5) (9) (10).

Gilenya (Fingolimod)

How does it work?

Gilenya is an immuno-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 less lymphocytes get into the blood stream and fewer reach the central nervous system meaning the potential for immune attack on the cells of the brain and spinal cord is reduced (15) (16).

How can it help?

Gilenya was shown to reduce the risk of relapses by 67 per cent compared to a placebo in trials (17).

How is it administered?

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

Who manufactures it?

Novartis

What type of MS is it prescribed for?

Gilenya is classed a 'category 1' drug although listed as 'more effective', meaning it is slightly more effective than the injectable therapies. It is licensed for adults with highly active relapsing-remitting MS. Such people have a high disease activity as characterised as one relapse in the previous year despite being on another disease modifying therapy, such as an interferon for at least 12 months (1).

In June 2014, NHS England published new guidelines to allow a switch to Fingolimod for those patients with highly active RRMS, if they met the following criteria:

- Patients whose relapse rate is unchanged, or has increased compared to the previous year, while on any of the beta interferons or glatiramer acetate (Copaxone)
- Patients who are receiving natalizumab (Tysabri) and are at a high risk of developing progressive multifocal leukoencephalopathy (PML), a potentially fatal brain infection (18)

Additionally in October 2014 the Scottish Medicines Consortium (SMC) licensed Fingolimod as a first-line treatment for people with rapidly evolving severe relapsing remitting MS (RES RRMS). First-line means it can be offered to people with RES RRMS without them having to have taken any previous medication (19).

What are the side effects?

Possible side effects include changes to liver function, macular edema (an accumulation of fluid in the macular area of the eye (the central area of vision) that sometimes causes blurred vision), headache, respiratory tract infection, shortness of breath, diarrhoea and nausea. Gilenya can cause a decrease in heart rate so your first dose will be monitored in hospital for six hours (13) (14) (15).

Glatiramer acetate (Copaxone and Brabio)

How does it work?

Glatiramer acetate works differently from the interferons in that it is a synthetic combination of four amino acids which resemble the myelin protein. It is thought to work by preventing the production of immune cells that attack myelin (5) (11) (12) (13).

How can it help?

The rate of relapse in people taking Copaxone is generally reduced by one-third (5) (11) (12) (13).

How is it administered?

It needs to be injected subcutaneously (under the skin). There are two doses, 20mg and 40mg, one for daily injections and another for three time a week injections. It needs to be stored in the fridge.

Who manufactures it?

Teva - Copaxone
Mylan - Brabio

What type of MS is it prescribed for?

It is classed as a ‘category 1’ drug and therefore licensed for relapsing remitting multiple sclerosis and some people with clinically isolated syndrome (1).

What are the side effects?

Common side effects are injection-site reactions and lipotrophy (indentations under the skin). Less commonly, it can also cause chest tightness, breathlessness, anxiety, flushing and palpitations after injection (5) (11) (12) (13).

Mavenclad (Cladribine)

How does it work?

Mavenclad is an immuno-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 (20) (21).

How can it help?

Studies have shown that Mavenclad reduces relapse rate significantly and also delays disability progression by reducing brain volume loss, sustained for 6 months compared with placebo (22).

How is it administered?

Mavenclad is taken as a tablet. It is taken in 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 amount of tablets taken in each course is dependent on the individual’s weight.

Who manufactures it?

Merck

What type of MS is it prescribed for?

Mavenclad is a ‘category 1’ drug and therefore it is prescribed for people with RRMS. It is listed as ‘more effective’ meaning it is slightly more effective than the injectable therapies (22).

What are the side effects?

One of the most common side effects from 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, hair loss. If a patient has shingles then Mavenclad may need to be stopped until the infection is treated and cleared (21).

Tecfidera (Dimethyl fumerate)

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 (23) (24).

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 disease (23) (24).

How is it administered?

Tecfidera is taken as a tablet, twice a day.

Who manufactures it?

Biogen

What type of MS is it prescribed for?

Tecfidera is a 'category 1' drug and therefore it is prescribed for people with relapsing remitting MS. It is listed as 'more effective' meaning it is slightly more effective than the injectable therapies (1).

What are the side effects?

Common side effects reported are flushing and feeling hot, headaches, gastrointestinal upset and decreased white blood cell count – increasing risk of infection (23) (24).

Lemtrada (Alemtuzumab, Campath)

How does it work?

Lemtrada was originally licensed for the treatment of leukemia. It is an anti-CD52 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 (25) (26).

How can it help?

In two studies Lemtrada was shown to be effective in reducing the number of relapses in people with relapsing remitting MS. 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.

In the second trial where the drug was again compared to Rebif, in people who had experienced at least one relapse whilst on therapy. Lemtrada reduced the amount of relapses by 49 percent compared to Rebif (27) (28).

How is it administered?

Lemtrada is delivered by two infusions, twelve 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?

Genzyme

What type of MS is it prescribed for?

Lemtrada is listed as a 'category 2' drug and therefore is highly effective when treating more active forms of relapsing remitting MS (1).

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 related to kidney function, reactions at the infusion site and respiratory infections.

More common side effects reported were flu-like symptoms after the infusion was given (25) (26).

Ocrevus (Ocrelizumab)

How does it work?

Ocrevus is a monoclonal antibody which 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 (B cells). These B cells are what attack the immune system are what cause the inflammation and damage. Ocrevus targets these cells to help reduce their activity (29).

How can it help?

Studies have shown that Ocrevus can reduce annual relapse by fifty per cent compared to Rebif. Studies also showed that the drug reduced disability progression and reduced the number of lesions shown on MRI when compared with beta interferon. Brain volume loss was also reduced and no evidence of disease activity (NEDA) was seen in patients taking Ocrevus, again when compared to Rebif (30).

How is it administered?

Ocrevus is administered by infusion every six months. The initial infusion is given in two separate doses, two weeks apart. After that it is one single dose. Each infusion takes around 3-4 hours to complete. At the start of each infusion, a corticosteroid and an antihistamine are given to the patient in order to help prevent any reactions (29).

Who manufactures it?

Roche

What type of MS is it prescribed for?

Ocrevus is listed as a 'category 2' drug and therefore is highly effective when treating more active forms of relapsing remitting MS. It can only be offered if Lemtrada (alemtuzumab) is contraindicated or unsuitable (31).

It is currently under trial for primary progressive MS (PPMS).

What are the side effects?

Infusion reactions are the most frequently reported side effect (itching, rash and difficulty breathing). They are generally short-lived. Additional medications may be given to prevent this and close monitoring during the infusion itself.

Infections are also common, including chest infections, coughs and colds and herpes virus infections (cold sores or shingles) (32).

Tysabri (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 damage (33) (34).

How can it help?

People with relapsing remitting MS 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 disease progression.

Studies also showed that people with rapidly evolving severe relapsing remitting MS (RES RRMS) showed a decrease of 81 per cent in relapses when taking Tysabri (33) (34) (35).

How is it administered?

Tysabri has to be given by intravenous infusion every four weeks at either an infusion centre or a hospital.

Who manufactures it?

Biogen

What type of MS is it prescribed for?

Tysabri is listed as a ‘category 2’ drug and therefore is highly effective when treating more active forms of relapsing remitting MS (1).

What are the side effects?

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

Tysabri increases the risk of developing a serious infection called Progressive Multifocal Leukoencephalopathy (PML), which is a rare but sometimes fatal brain infection that affects the central nervous system. Risk factors associated with an increased risk of 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.

PML is caused by a virus called the JC virus (JCV). Each potential patient is tested to check whether they are positive for JCV as this can help to establish the risk of developing PML.

As the JCV is airborne, patients can develop it at any time. This means that patients who test negative for JCV should be retested regularly.

Patients who have been on immune suppressants prior to treatment also have an increased risk factor. Despite these factors, the benefits of the drug continue to outweigh the risks for many people with highly active relapsing remitting MS (33) (34).

Choosing a disease modifying therapy

> **Do your research very thoroughly indeed 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 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 a number of factors you may want to consider and discuss with your family and neurologist. For example:

- 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 the options with your MS nurse and/or neurologist to come to a decision as to what is the best course of treatment for you.

The MS Trust website has a useful tool called ‘MS Decisions’ with an interactive section that can help compare the different drugs to help you find the one most suitable for you (36).

Side effects

The side effects of these drugs are different with each therapy and vary from person to person. It is important to talk to your MS nurse or neurologist about what side effects the drug may cause. Side effects are generally not severe and there are various ways to manage them.

If you experience flu-like symptoms after injecting, try changing the time of day you take your injection, possibly to just before bedtime so you can sleep through the side-effects. 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 injecting the same area each time. It may also help to ensure the drug is at room temperature and also warming your skin before injecting may also help make your injection more comfortable. If you are on 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 advise you further. Contact the MS-UK Helpline if you need help to find your nearest MS nurse.

I feel the risk of side effects are worth having a better quality of life. I felt my life was over before starting this treatment.

What if I choose not to have medication?

You may be eligible for DMTs and it is your choice whether you wish to take them or not. Should you choose not to take any medications, this is described as being 'drug naïve' by health professionals. Your healthcare team may advise you to use DMTs, however the choice is still yours. If you choose to be drug naïve, it may be useful to keep a symptom diary in case you change your mind in the future.

You have to weigh up the pros and cons personally, but I think taking 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 formed in 1993 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.

MS-UK Counselling

MS-UK Counselling is open to anyone living with MS and is the only service of its kind available in the UK. Whether you want support coming to terms with a diagnosis or to improve your mental wellbeing, our counselling service is focused on helping you.

All of our MS-UK counsellors are BACP registered or accredited with an in depth knowledge of MS.

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Stay in touch

MS-UK
Unsworth House
Hythe Quay
Colchester
Essex, CO2 8JF

www.ms-uk.org

@MSUK6
www.facebook.com/MultipleSclerosisUK
www.youtube.com/c/ms-ukorg
www.linkedin.com/company/ms-uk

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

Registered Company Name:
Multiple Sclerosis-UK Limited, trading as MS-UK
Company Number: 2842023
Registered Charity Number: 1033731
VAT Number: 632 2812 64
Registered Office: Unsworth House, Hythe Quay
Colchester, Essex, CO2 8JF