

Disease modifying drug therapy

what you need to know

Multiple
Sclerosis
Trust

MS



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Introduction

There are three main treatment areas in MS: symptomatic treatments; treatments for relapses; and disease modifying drugs. The purpose of this book is to assist you in any decision that is made regarding disease modifying drugs. The difference between disease modifying drugs and drugs that are used to treat symptoms and relapses is that disease modifying drugs affect the long-term course of MS.

The information contained within this book will not be used by everybody in the same way. It may reach people at different stages in the decision-making process or indeed at different stages of their MS or treatment history. However, it should not be used as a substitute for clinical advice. Partnership with your health professionals in the decision-making process is of utmost importance. The more you understand about the drugs, and the better your health professional understands your needs, the more confident you can be in any decision that emerges out of this partnership.

The book is divided into three main sections. The first section aims to provide people who are starting to think about drug treatment with information about the available disease modifying drugs, what they do, and whether they are an option now, in the future, or at all.

The second section of the book is for people who would like to know more about the currently licensed disease modifying drugs, the differences between them, and what to expect from them.

The third section of the book provides some brief information about drugs that are not approved for use in MS, but are sometimes administered to people with MS within a particular context such as a clinical trial.

Section 1

Disease modifying drugs and how they work

i) What are disease modifying drugs?

Disease modifying drugs are used with a view to changing the long-term course of MS. They work by dampening down the inflammatory processes that cause relapses. By reducing the frequency and severity of relapses, some of these drugs have been shown to delay the long-term progression of MS.

Disease modifying drugs are designed to reduce the damage incurred as a result of relapses. For this reason they are only used in relapsing/remitting MS and secondary progressive MS if relapses still occur. Where relapses do not occur, as in primary progressive MS, the current disease modifying drugs have not proven effective.



The different subtypes of MS are characterised as follows:

Relapsing/remitting

Initially, about two thirds of people have relapsing/remitting MS. They experience relapses on average once or twice per year, with good or complete remission in between. However, there is a tendency for symptoms to worsen very gradually over time.

Within this particular subtype of MS a further distinctive form of MS has emerged, rapidly evolving severe relapsing/remitting MS (RES). It is characterised by a high level of disease activity demonstrated by two or more disabling relapses within one year and signs of high disease activity on MRI. Rapidly evolving severe relapsing/remitting MS is also referred to as highly active relapsing/remitting MS.

Secondary progressive

People who start off with relapsing/remitting MS may go on to develop a progressive form of the condition. Studies suggest that half of all people who are diagnosed with relapsing/remitting MS have developed secondary progressive MS after ten years. The severity and frequency of relapses usually decrease, but disability slowly increases. It is only appropriate to use disease modifying drugs in secondary progressive MS if relapses continue to occur.

Primary progressive

About 10% of people experience symptoms right from the start that become progressively worse over a period of years without remission.

Benign

Benign MS is associated with very occasional relapses, with good recovery in between and minimal symptoms over many years; therefore it can only be diagnosed retrospectively.

Clinically Isolated Syndrome (CIS)

In addition to the main subtypes of MS, Clinically Isolated Syndrome (CIS) is also recognised as a distinct presentation of MS. CIS is an individual's first neurological episode lasting at least 24 hours. It is caused by inflammation or damage to the covering of nerves in one or more sites in the central nervous system (brain and spinal cord). Strictly speaking, a clinically isolated syndrome is not a subtype of MS as not everyone who experiences one will go on to develop MS.

In the UK, there are currently 6 licensed disease modifying drugs for the treatment of MS. For ease of discussion they can be divided into two groups: self-administered drugs and a hospital-administered drug.

Self-administered drugs:

- interferon beta – there are two forms of interferon beta: interferon beta 1a (brand names Avonex® and Rebif®); and interferon beta 1b (brand names Betaferon® and Extavia®)
- glatiramer acetate – (brand name Copaxone®)

Hospital-administered drug:

- natalizumab – (brand name Tysabri®)

It is important to recognise that disease modifying drugs are not a cure for MS; they can neither halt the progress of, nor reverse the damage that has already occurred in MS.

Different people will have different priorities and different goals when it comes to managing their condition; meaning that any decision made regarding drug treatment is very individual. While you need to give due consideration to how these drugs fit with your priorities, goals and lifestyle choices, due consideration should also be given to the mounting evidence to suggest that the earlier in the course of

MS treatment commences, the more effective the drugs are. It is also important for any person starting drug treatment to recognise that, while these drugs are a long-term commitment, they are not necessarily a life-long commitment. While these drugs may prove effective over a long period of time, they will not necessarily maintain the same level of effectiveness. Your health professional will regularly review your treatment and advise if and when switching or stopping treatment altogether needs to be considered.

ii) How the drugs work

Self-administered drugs

Interferon beta

Interferons are proteins produced naturally by the human body. They help to fight infections and play an important role in the functioning of the immune system.

There are three types of natural interferon: alpha, beta and gamma. Alpha interferons are used in the treatment of some cancers but have not proven beneficial in the treatment of MS. Gamma interferons are thought to induce MS symptoms. Beta interferons are thought to work by blocking the action of the gamma interferons thereby reducing the autoimmune reaction that results in inflammation and destruction of myelin.

There are two different types of interferon beta used in the treatment of MS: interferon beta 1a (Avonex and Rebif) and interferon beta 1b (Betaferon and Extavia). The differences between them lie in the way they are manufactured.



Glatiramer acetate

Glatiramer acetate (Copaxone) has a different mode of action to interferon beta. It is thought to prevent the production of myelin reactive immune cells – cells responsible for the destruction of myelin – and induce the generation of anti-inflammatory immune cells. This combined effect dampens down the inflammation occurring in the central nervous system, thereby reducing the damage to myelin and nerve fibres.

Hospital-administered drug

Natalizumab

Natalizumab (Tysabri) is a selective adhesion molecule inhibitor (SAMI). It is designed to prevent the passage of immune cells (white blood cells) across the blood-brain barrier. It does so by binding itself to a specific adhesion molecule on the immune cell surface known as alpha-4 integrin, preventing the attraction between the surface of these cells and the surface of the blood-brain barrier. The drug thereby prevents the migration of the immune cells into the central nervous system and the subsequent immune cell activity that leads to nerve damage and destruction.

iii) Eligibility criteria

Because the disease modifying drugs act in different ways, not every person with MS will benefit from, or even respond to, the drugs in the same way. For this reason guidance has been issued setting out the eligibility criteria for the prescribing of the licensed drugs.

Self-administered drugs

Prescribing guidelines

The Association of British Neurologists (ABN) published guidance for the treatment of multiple sclerosis with interferon beta and glatiramer acetate in 2001. The guidance is subject to ongoing review so people considering disease modifying drugs should discuss all issues relating to eligibility with their consultant or MS nurse.

On the basis of the 2001 ABN guidance for the prescribing of interferon beta and glatiramer acetate, in order to start treatment on any one of the self-administered disease modifying drugs an individual must:

- be able to walk at least 10 metres with or without assistance for interferon beta; and at least 100m without assistance for glatiramer acetate;
- have experienced at least two clinically significant relapses in the last two years;
- normally be aged 18 or above.

Licence indications

The ABN guidelines are more prescriptive in their recommendations than the licensing information for each of these drugs. The following is an overview of the products licensed for use in the respective subtypes, or potential presentation of MS in the case of CIS:

- **Relapsing/remitting MS**

The licensed drugs for relapsing/remitting MS are:
Avonex , Betaferon, Rebif, Extavia and Copaxone

- **Secondary progressive MS**

The licensed drugs for secondary progressive MS where relapses are still a feature are:
Betaferon, Extavia and Rebif.

- **Clinically isolated syndrome (CIS)**

Four of the five self-administered disease modifying drugs are licensed for use in clinically isolated syndrome. Current evidence supports early treatment with the drugs to delay progression to clinically definite MS.

The licensed drugs for treatment of clinically isolated syndrome are:
Avonex , Betaferon, Extavia and Copaxone.

Hospital-administered drug

Prescribing guidelines

The National Institute for Health and Clinical Excellence (NICE) for England and Wales and Northern Ireland; and the Scottish Medicines Consortium (SMC) for Scotland, issued guidance for NHS prescription of natalizumab (Tysabri) in 2007. The guidance recommends natalizumab is used only in the treatment of rapidly evolving severe relapsing/remitting multiple sclerosis (RES) as defined by:

- two or more disabling relapses in 1 year, and one or more gadolinium-enhancing lesions on brain magnetic resonance imaging (MRI); or
- a significant increase in T2 lesion load compared with a previous MRI.

Licence indications

Rapidly evolving severe relapsing/remitting MS

Natalizumab is the only disease modifying drug to be licensed for this specific subtype of MS. It is licensed as a single disease modifying drug treatment in highly active relapsing/remitting multiple sclerosis for the following groups:

- patients with high disease activity despite treatment with interferon beta;
- patients with rapidly evolving severe relapsing/remitting MS.



Section 2

What to expect from disease modifying drugs

i) Self-administered drugs

What benefits can I expect from these drugs?

While clinical trials have demonstrated the benefits of these drugs, it is important to remember that just as every individual's experience of MS is unique, each individual's response to the drugs will also be different. In this respect, some people will do better than expected, while others might not do as well.

It is also important to recognise that these drugs are long-term drugs and the benefits they offer will not be seen immediately. As the benefits of the drugs will only be seen over time, stopping and starting them will reduce their effectiveness.

Interferon beta and glatiramer acetate have been used in the UK and the US for over 15 years and have established a very good safety profile. Studies of the effects of these drugs in the treatment of MS have identified two main benefits:

- a reduction in the frequency and severity of relapses; (interferon beta and glatiramer acetate); and
- a reduction in the rate of disease progression (interferon beta only)

Results of clinical trials have also indicated that the disease modifying drugs reduce the accumulation of new MS lesions that are detected using magnetic resonance imaging (MRI).



Frequency and severity of relapses

The four interferon beta drugs (Avonex, Betaferon, Rebif and Extavia) and glatiramer acetate (Copaxone) have been shown to reduce the frequency and severity of relapses by around one-third in patients with relapsing/remitting MS.

Three of the interferon beta drugs (Betaferon, Rebif and Extavia) have also been shown to reduce the frequency and severity of relapses occurring in secondary progressive MS where relapses are still a feature.

People receiving treatment are likely to experience some relapses. However, most people experience fewer relapses than before they started treatment and their relapses are usually less severe.

Disease progression

Clinical trials have provided evidence that the four interferon beta drugs (Avonex, Betaferon, Rebif and Extavia) delay disease progression but there is a lack of clarity about the extent to which they are able to do so.

Clinical trials for glatiramer acetate (Copaxone) have not yet demonstrated an effect on disease progression. Consequently, the drug is not licensed for this particular outcome.

Starting treatment

a) the assessment process

There may be a number of stages to the assessment process. It should involve a series of assessments by a prescribing neurologist as well as a series of meetings and discussions with an MS nurse. You will be involved in every stage of the assessment process and should use it as an opportunity to seek answers to any questions about the drugs that remain unanswered.

You should also use this opportunity to discuss any long-term plans you may have. For instance, if you are planning to start a family, you will need to build this in to any plans to start drug treatment. There is limited information

on the use of these treatments in pregnancy. For this reason you must not start treatment whilst pregnant. If you become pregnant whilst taking one of the treatments you should contact your neurologist and discontinuation of therapy should be considered.

It is not known whether these treatments are excreted in human milk. Because of the potential harm to breastfed infants, you should consult your neurologist in weighing up the risks associated with breastfeeding whilst on drug treatment.

Men who are planning to start a family also need to discuss this with their neurologist and MS nurse.

The assessment process will offer you an opportunity to discuss any concerns you may have over the practicalities of starting treatment and how it will fit in with your lifestyle. For instance, you might work full-time or have to travel frequently and will want to consider how you can fit these drugs into your routine.

b) checking for other conditions

Blood tests will be performed before you start treatment to check for any other problems that might affect how well you do on the drugs. Before starting on these drugs, you should tell the neurologist if you have any pre-existing conditions or have experienced any reactions to previous drugs or treatments. If you do, you may still be able to receive the drugs but may need to start them in a different way.

c) blood tests during treatment

If the neurologist prescribes one of the interferon beta drugs, blood tests may be performed throughout the time you are receiving treatment, to check that your body is tolerating it well. Your blood will be checked on a regular basis during the first year of treatment and assuming you are tolerating the treatment the tests may be reduced to a frequency of every six months, though this may vary between centres.

Should you be prescribed glatiramer acetate you will not be required to have regular blood tests.

Administration and side effects

How are these drugs given?

All of the licensed self-administered drugs are given by injection either under the skin or into the muscle (see table 1 for administration characteristics of each individual drug).

As shown in the table, many of these drugs need to be stored in the fridge. All drugs will need to be at room temperature before they are injected as cold temperatures can make them painful to inject. It is therefore important to follow the storage and administration directions carefully.

People who are anxious about injecting often choose to use autoinjectors. These are available for all the self-administered drugs and work like a pen which holds a needle and syringe inside. Most types of autoinjector allow you to inject without having to see the needle going in.



Side effects

More often than not, the side effects of these drugs are mild and manageable (see table across pages 16 and 17 for more information about side effects). It is often the case that the side effects experienced when on these drugs are worse at the start of treatment and reduce over time as your body gets used to them.

There are various strategies that your MS nurse may recommend in order to reduce the risk of experiencing side effects whilst on these drugs. For instance, if you are prescribed one of the interferon beta drugs, your MS nurse may recommend that you start on a lower dose of the drug and slowly increase the dosage over time to allow your body to adjust to the drug, or where flu-like symptoms after injecting persist, your nurse may recommend that you change the time of day of injection so that you sleep through the worst of your side effects.

It is important to keep your health professionals informed of any new, unusual or persistent symptoms you experience.

Table 1. Characteristics of the self-administered disease modifying drugs

	Interferon beta 1a	Interferon beta 1a	Interferon beta 1b	Interferon beta 1b	Glatiramer acetate
	Avonex	Rebif	Betaferon	Extavia	Copaxone
Manufacturer	Biogen Idec	Merck Serono	Bayer Schering	Bayer Schering/Novartis	Teva Pharmaceuticals
How often is it given?	Once a week	3 times a week	Alternate days	Alternate days	Every day
How is it injected?	Into the muscle	Under the skin	Under the skin	Under the skin	Under the skin
Does the drug come premixed?	Two versions are available: a premixed version (PFS) which comes ready to inject, and a version which must be mixed before use (BIO-SET)	Yes	No	No	Yes
Storage	Premixed version: fridge 2-8°C but a single vial can be kept at room temperature for up to a week*. The BIO-SET version can be kept at room temperature for up to 2 years	In the fridge between 2-8°C*	At room temp 25°C or less	At room temp 25°C or less	In the fridge between 2-8°C or at room temp (15-25°C)* for up to 1 month
Regular blood tests?	Yes	Yes	Yes	Yes	No
Common side effects	Flu like symptoms after injecting	Flu like symptoms after injecting, site reactions	Flu like symptoms after injecting, site reactions	Flu like symptoms after injecting, site reactions	Injection site reactions and lipoatrophy (indentations in the skin)
Less common side effects	Changes in menstruation/ periods, blood abnormalities, neurological symptoms, mood changes	Changes in menstruation/ periods, blood abnormalities, neurological symptoms, mood changes	Changes in menstruation/ periods, blood abnormalities, neurological symptoms, mood changes	Changes in menstruation/ periods, blood abnormalities, neurological symptoms, mood changes	Post injection reaction may present in the form of chest tightness, breathlessness, anxiety, flushing and palpitations. These symptoms typically pass after a few minutes

*See note on page 15 and refer to your health professional for directions on injecting refrigerated products.

Table 1 provides an overview of the main characteristics of the self-administered disease modifying drugs. This information is based on the current product information, but may be subject to change. Always refer to the product information leaflet enclosed with the drugs for the most up-to-date information.

Neutralising antibodies

Antibodies are proteins produced by the immune system to fight foreign substances such as infections. As with drugs that are used in some other conditions such as diabetes, use of interferon beta over a long period of time may result in the production of what are known as 'neutralising antibodies'. These antibodies may reduce the effectiveness of the drug. Over the long-term this may mean that people taking interferon beta receive less benefit from it and start to experience a similar number of relapses as they would have done without taking the drug.

Neutralising antibodies are not associated with any new side effects or long-term safety issues. Most people will not develop neutralising antibodies and in some people the neutralising antibodies will disappear again over time.

The presence of neutralising antibodies alone is not a reason to stop or change drugs.

ii) Hospital-administered drug

Natalizumab (Tysabri)

What benefits can I expect from this drug?

Natalizumab is one of the most recent disease modifying drugs to be approved in the UK for the treatment of multiple sclerosis. Unlike all other disease modifying drugs approved for use in MS, natalizumab is given once every four weeks by infusion in a hospital, clinic or infusion centre.

As discussed in the first section of this book, natalizumab is only approved for use in rapidly evolving severe relapsing/remitting MS.

Studies have shown natalizumab to:

- reduce the occurrence of relapses by around two-thirds;
- significantly reduce the rate of disease progression.



Starting treatment

a) the assessment process

Appropriateness for treatment with natalizumab needs to be established by a neurologist. The neurologist will look for both clinical and MRI evidence of highly active relapsing/remitting MS.

There is limited information on the use of this drug in pregnancy, though animal studies have shown reproductive toxicity. Natalizumab should not be used during pregnancy unless clearly necessary. If you become pregnant while taking natalizumab, inform your neurologist



and discontinuation should be considered. It is not known whether natalizumab is excreted in human milk so mothers should not breastfeed whilst they are receiving treatment.

Men who are planning to start a family need to discuss this with their neurologist and MS nurse. Due consideration needs to be given to the practicalities of starting treatment with natalizumab and how it will fit in with your lifestyle. It is important that you are able to attend appointments every four weeks to receive the infusion. The dose and frequency of administration of natalizumab is designed to ensure that optimum levels of the drug remain in the body at all times so it is important that you do not miss a dose.

b) checking for other conditions

Blood tests will be performed before you start treatment to determine whether it is safe for you to receive this drug. Before starting on natalizumab you should tell the neurologist if you have any pre-existing conditions or have experienced any reactions to previous drugs or treatments.

c) blood tests during treatment

Blood tests will be performed during treatment as part of the monitoring process. Blood samples may be taken to test for the development of neutralising antibodies (see page 23) and to check levels of liver enzymes.

Administration and side effects

How is natalizumab given?

Natalizumab is given as an intravenous infusion (a needle placed in a vein, similar to a drip) once every four weeks. It must be administered in a clinical setting under the supervision of a suitably qualified health professional.

Prior to each infusion, blood pressure, temperature and pulse rates will be taken. A nurse or doctor will monitor the infusion which usually takes one hour and for one hour after the infusion to check for any signs or symptoms of hypersensitivity (allergic) reactions.



What are the side effects?

Natalizumab is designed to treat more active forms of MS and therefore has a more toxic effect in the body. Before starting treatment with natalizumab you will be issued with a patient alert card. The patient alert card is designed to help you identify any potentially serious side effects so they may be addressed in the early stages

The main side effects associated with natalizumab are:

Infusion reactions

Some people experience some discomfort during the infusion which may include the onset of nausea, headache, itchy rash or dizziness. These tend to be mild and last only as long as the infusion. Around 1 in 5 people who receive natalizumab experience an infusion reaction but it does not affect ongoing treatment with the drug.

Hypersensitivity (allergic) reactions

Around 1 in 25 people who receive natalizumab experience an allergic reaction. Symptoms of an allergic reaction include itchy rash (hives), swelling of face, lips or tongue, difficulty breathing. Allergic reactions can occur during the infusion or within an hour of completing the infusion where the patient is still under the supervision of the clinical team. Natalizumab is only administered in centres that have the resources for the management of hypersensitivity reactions. People who experience a hypersensitivity reaction to natalizumab must permanently discontinue treatment.

Serious infections

Natalizumab may increase your chance of getting an unusual or serious infection because it can affect your immune system. People receiving natalizumab must alert their health teams if they develop an infection.

Progressive multifocal leukoencephalopathy (PML)

This is a rare brain infection that can lead to severe disability or even death. PML is a disorder that usually affects individuals with a weakened immune system. It is a very aggressive condition for which there is no known effective treatment. The symptoms of PML may be similar to an MS relapse so it is important to report any new or

worsening symptoms. The estimated risk of developing PML during treatment with natalizumab is about 1 in 1000.

In view of the risks associated with serious infections, particularly PML, individuals undergoing natalizumab treatment are subject to close clinical monitoring.

Liver problems

Liver problems are a rare side effect of natalizumab, affecting less than 1 in 1000. Signs of possible liver problems include yellowing of your skin or the whites of your eyes and unusual darkening of the urine. Blood tests can be done to test for liver damage and where liver damage is detected treatment will be stopped. Liver function generally recovers when treatment is stopped.

Other less serious side effects

A number of other less serious side effects are also associated with natalizumab and are thought to affect fewer than 1 in 10 people receiving the drug. These include: urinary tract infection, sore throat and runny or blocked nose, shivering or fever, itchy rash, headache, dizziness, nausea or vomiting, joint pain and tiredness.

Neutralising antibodies

Antibodies are proteins produced by the immune system to fight foreign substances, such as infections. Sometimes the body's natural defences will develop antibodies against drugs that are entering the body and stop them from working properly. Persistent presence of neutralising antibodies is associated with reduced effectiveness of natalizumab and an increased risk of hypersensitivity reactions. Where the presence of neutralising antibodies is suspected, a blood test may be performed. An individual who tests positive for them will undergo a confirmatory test after six weeks and if the test is positive, treatment will be discontinued.

For further information contact the MS Trust for a factsheet on natalizumab (Tysabri) or download the factsheet from the MS Trust website: www.mstrust.org.uk

iii) Switching and discontinuing

There are two main reasons why people might switch from one disease modifying drug to another, or discontinue treatment altogether. These are:

- lack of effectiveness;
- unmanageable side effects.

Switching

It is important to have realistic expectations about the drugs and what they might achieve for you. The benefits of these drugs may not be immediately evident and may only be seen after time.

However, if after a period of time, your relapses continue at the same rate and with the same severity as before drug treatment, you may be able to switch to another disease modifying drug. Your consultant and MS nurse will advise you of your eligibility and suitability for other disease modifying drugs.

If you are receiving one of the interferon beta drugs, regular blood tests may be carried out to check for neutralising antibodies. The presence of neutralising antibodies alone may not necessarily indicate reduced effectiveness and further signs that the treatment is not working would have to be present in order to warrant switching or discontinuing treatment.

A small number of people find that the side effects of a particular disease modifying drug are unmanageable. If after some time, your side effects have not subsided, and the management techniques advised by your MS nurse have proven ineffective, you may be able to switch to another drug. Again, your consultant and MS nurse will discuss the available alternatives with you.

Discontinuing

While disease modifying drugs are a long-term commitment, for most people this will not mean they are a life-long commitment. Even if the drugs are effective for a period of time, there may come a time in the course of your MS when these drugs are no longer effective.

There are no mandatory stopping criteria that apply in all cases, but the ABN has set guidance on when treatment with self-administered disease modifying drugs should be stopped because they are no longer effective. Generally, the ABN guidelines recommend stopping treatment if:

- the individual experiences two disabling relapses, as defined by the examining neurologist, within a 12 month period;
- the individual develops secondary progressive MS and no longer experiences relapses;
- the individual loses the ability to walk, with or without assistance for at least 6 months.

Your neurologist and MS nurse will discuss the stopping criteria and advise you when it is an appropriate time to discontinue treatment. In some cases, treatment will be gradually withdrawn.

Stopping treatment can often have a greater impact psychologically than physically. It is difficult for some people to accept having something that has helped them completely withdrawn. However, your health professionals will support you throughout the process and help you regain focus in the management of your condition.



Section 3

Other drugs used in MS

The currently licensed disease modifying drugs are the most widely used drugs in the treatment of MS. In the majority of cases one of these licensed drugs will best meet the needs of the person with MS. However, there are certain, rather more exceptional contexts, within which drugs that are not licensed for MS may be given to people with MS.

Unlike the disease modifying drugs licensed for MS, unlicensed drugs do not have recommendations dictating how they should be used. There is a significant difference between these drugs and the currently licensed drugs in terms of the safety and efficacy data that is available for their use in MS. Any recommendations that are made with regards to unlicensed drugs are made on an individual patient basis at the discretion of the prescribing physician.

Unlicensed drugs that are used in MS can be divided into two main groups: drugs that are licensed for use in conditions other than MS; and drugs which are still in development and are therefore not licensed for any condition.

Off-label prescribing

When drugs that are not specifically licensed for MS are prescribed to people with MS, they are used 'off-label'. This means that the medicines regulatory authority has not recommended the use of the drug in MS and there is limited safety or efficacy data relating to its use in the condition. In such cases, the prescribing physician takes full responsibility for the patient's progress on the drug. The prescribing physician will therefore be driving the decision to start treatment and making recommendations regarding the individual's suitability for treatment with the drug.

Because MS is considered to be an autoimmune disease, drugs which are licensed for the treatment of other autoimmune diseases such as

rheumatoid arthritis and psoriasis are occasionally prescribed off-label to people with MS.

A drug that is commonly used in this way in some of the larger neurology centres in the UK is mitoxantrone, a chemotherapy drug. For further information contact the MS Trust for a factsheet on mitoxantrone or download it from the MS Trust website: www.mstrust.org.uk

Clinical trials of unlicensed drugs

Where a drug does not have a licence for use in any condition it is usually because it is still being tested. Every new drug has to go through rigorous testing of its effectiveness and safety through a series of clinical trials usually over a number of years. People who are given these drugs can only receive them by taking part in a clinical trial. If you are considering taking part in a clinical trial it is important to consider the implications and risks associated with taking a drug that is experimental.

In order to be eligible to participate in a clinical trial you must meet the eligibility criteria defined by the trial investigators and a referral from either your neurologist or MS nurse will be required. Your neurologist or MS nurse will base their clinical advice or recommendation on a number of factors including the unique clinical and radiological characteristics of your MS.

Compassionate use

Compassionate use describes the process through which people with debilitating conditions and no satisfactory treatment alternatives, gain access to drugs outside the context of a clinical trial. Only in rare and exceptional circumstances therefore, is this often controversial practice considered for people with MS.

As with off-label prescribing, physicians prescribing drugs on the grounds of compassionate use, take full responsibility for the patient's progress on the drug. In order for a physician to prescribe the drug, it must be in clinical research, preliminary data must exist to indicate that it is likely to be effective and relatively safe, and the drug manufacturer must be actively seeking marketing approval.

A physician will not consider compassionate use of a drug unless you have run out of reasonable treatment options, either with licensed or off-label drugs.

Table 2. Drugs currently in clinical trials

Name of drug	How it is given in MS	Licensed for a different condition	In clinical trials for MS
Alemtuzumab (Campath)	Intravenous infusion	✓	✓
BG-12	Orally	✓	✓
Cladribine (Leustat)	Orally	✓	✓
Daclizumab (Zenapax)	Subcutaneous injection	✓	✓
Fingolimod	Orally		✓
Laquinimod	Orally		✓
MBP8298	Intravenous infusion		✓
Rituximab (Rituxan)	Intravenous infusion	✓	✓
Teriflunomide	Orally		✓
Tovaxin	Subcutaneous injection		✓

Table 2 includes some of the more notable drugs being studied for their safety and effectiveness in MS. Drug development is fast moving and fast changing and it is likely that information in this table will change. To keep abreast of the latest drug developments in MS, visit the research pages of the MS Trust website at:

www.mstrust.org.uk/research



If you are interested in finding out about clinical trials currently recruiting people with MS you can search the Clinical Trials registry online at <http://clinicaltrials.gov> The website is by no means a complete registry of clinical trials in MS and the information provided there should be used only to supplement the advice and information provided by your consultant and MS nurse.

Section 4

Further sources of information and support

Your MS specialist nurse will talk you through the prescription process, offer support while you are getting used to the drugs and throughout the course of treatment.

You should never have unanswered questions about your treatment – there will always be someone who can answer your questions!

MS Decisions website

MS Decisions is a web-based patient decision aid for people considering treatment with a licensed disease modifying drug (interferon beta, glatiramer acetate and natalizumab).

You can access the website at: www.msdecisions.org.uk

MS Trust Information Service

The MS Trust information service is here to answer your questions about MS. To contact us you can:

Phone: 01462 476700
(Lines are open Monday-Friday 9am-5pm)

Email: infoteam@mstrust.org.uk

Write: MS Trust, Spirella Building,
Letchworth Garden City
Herts, SG6 4ET

Website: www.mstrust.org.uk

The MS Trust produces a range of publications and factsheets all of which can be obtained free directly from us or downloaded from our website.

The MS Trust's 'Map of MS Services' may also help you identify your nearest prescribing centre and investigate the availability of MS specialist nurse services. You can access the map online at:

<http://www.mstrust.org.uk/information/maps>.

The MS Trust is a charity working with and for everyone in the UK with multiple sclerosis (MS). Our vision is to enable people with MS to live their lives to the full.

We provide:

- information that is tailored to what people want to know
- education for health professionals about what people with MS need
- research into better management of MS
- support for anyone affected by MS



Multiple Sclerosis Trust,
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