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Living with MS

Treatment options for RRMS

This booklet was created by Biogen. The information has been put together with great care, but it is not a substitute for the opinion, diagnosis or advice of a treating physician.

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1. Introduction

The information series “Living with MS” provides more information about the condition called MS: the various symptoms, the possible treatments, and what you can do to make life with MS as easy as possible.

Biogen developed this series of booklets with the help of specialists and experts. The booklets can help you prepare yourself, know what to expect and manage your life with MS.

This is booklet 3 in a series of five booklets:

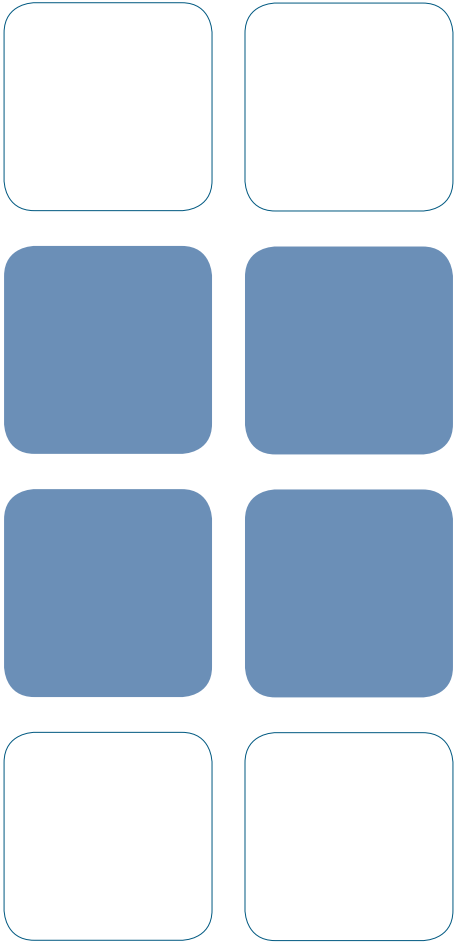
Booklet 1: What is MS

Booklet 2: MS and daily life

Booklet 3: Treatment options for RRMS

Booklet 4: MS, sexuality and parenthood

Booklet 5: MS and cognitive function



The booklet "Treatment options for RRMS"

The diagnosis MS raises a lot of questions. The first two booklets explained what MS is, the effect the disease may have on your daily life, and the most effective, practical way to deal with it.

This third booklet talks about the available options for the treatment of relapsing remitting MS (RRMS). There is no cure yet for this disease, but fortunately there are different treatments now available.

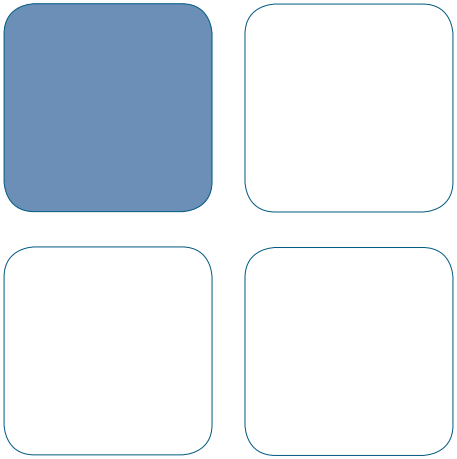
For example, there are medications that can inhibit the disease process (immunomodulation) and medications that can alleviate the symptoms of RRMS (symptomatic treatment). This booklet lists these medications and explains what they do and who can take them.

2. Goal of the treatment

The treatment of RRMS has two objectives:

a. Inhibiting the disease process

Inhibition of the disease process is also referred to as immunomodulation by means of immunomodulating therapy. The aim is to reduce the number of relapses and to inhibit the progression of the disease. Immunomodulating therapy does this by preventing inflammation in the central nervous system, which in turn prevents damage to the nervous system and can inhibit worsening of the disease.



b. Reducing the signs and symptoms of the disease

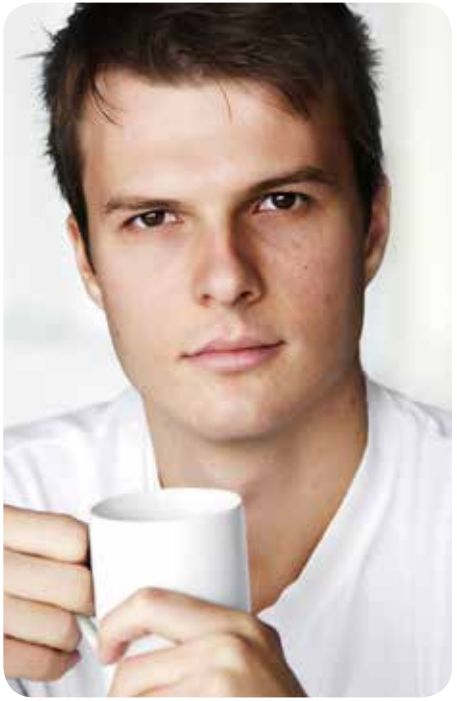
Reducing the signs and symptoms of the disease is focused on reducing the pain or discomfort you experience. However, these treatments are not designed to fight the disease RRMS itself, and they don't take away the cause of the symptoms.

Who will treat me?

RRMS is a disease of the central nervous system; the main treating physician is a neurologist (a specialist in the field of central nervous system disorders). RRMS can cause a wide variety of symptoms, which may occur anywhere in the body. For the treatment of these symptoms, your neurologist may refer you to a specialist in that particular field, like a urologist or an ophthalmologist.

3. Early, effective treatment

Various studies have shown that early, effective treatment of RRMS has significant benefits for the patient.[1,2] For example, it may limit neurological damage in the long term, which in turn may prevent the resulting physical limitations (disability). Another important argument for starting effective (immunomodulating) treatment on time is that once nerve damage occurs, it cannot be reversed. Early treatment prevents this type of damage as much as possible. Treatments may vary in terms of effectiveness and side effects, so make sure you are well-informed about these differences.



4. Medications aimed at slowing down the disease progression (immunomodulation)

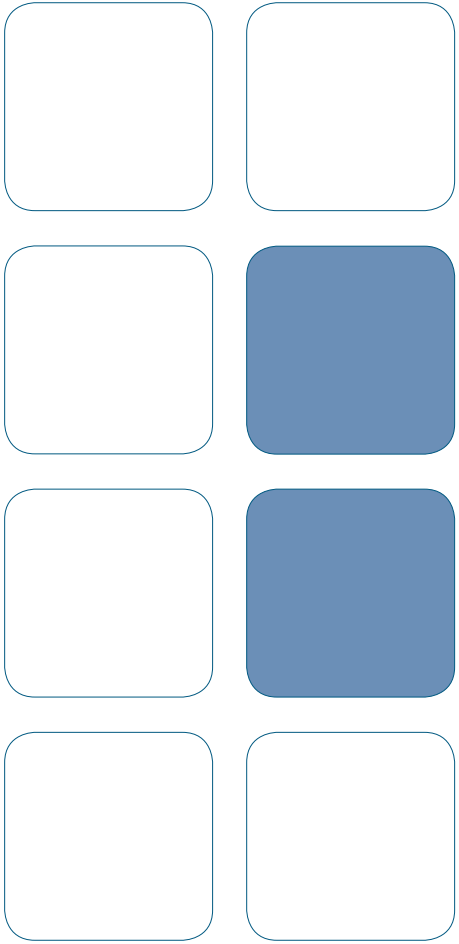
RRMS is not curable yet. Fortunately, a lot of effective treatments have become available during the past few years, and MS can now be treated much more effectively than ever before.

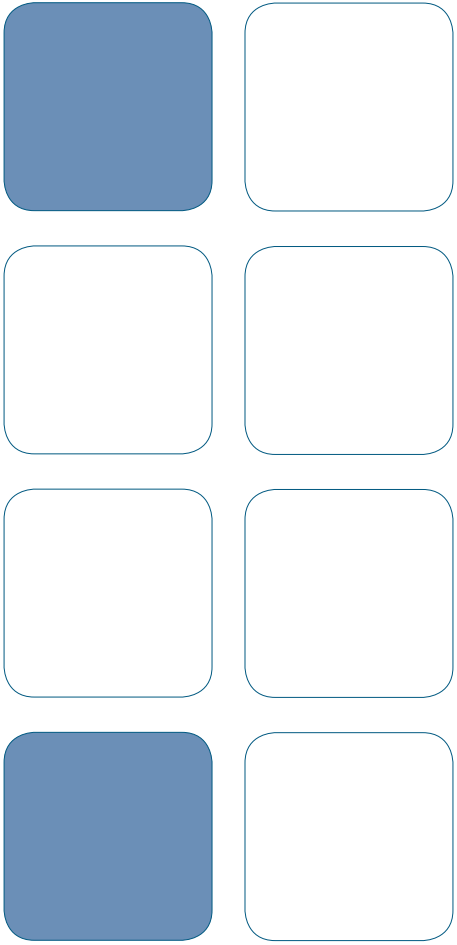
Immunomodulating treatment focuses on the immune system (defence system) of the patient. The immune system of people with MS does not work as it should: it has to be adjusted. This adjustment is a very precise, continual process.

This means that the use of immunomodulating treatment:

- follows the doctor's instructions
- is long-term (chronic)
- is not associated with symptoms.

In practice, this means that you won't notice any immediate effects from the treatment. Nevertheless, it's important that you continue the treatment as instructed by your neurologist, because this treatment reduces the risk of new flare-ups and it may also minimise the risk of further, permanent worsening.





4.1 What are the available immunomodulating medications for the treatment of RRMS?

RRMS is often described as the disease of a thousand faces. This is because the disease can manifest itself in countless different ways. We're not just talking about differences between patients, but also about different manifestations in the same patient over time.

This is why it's a good thing that a range of different medications is available, so every patient can receive the right medication at the right time. The medications may vary in effectiveness and side effects. Another difference is that some medication have a longer effect on the body (the immune system) than others. One of the benefits of this is that the dosing frequency is lower than medications that have a short term effect on your body (immune system), but there are disadvantages as well with

regard to potential side effects. In that case you will have to wait until the effects of the medication have worn off before you can switch to a different therapy.

Talk to your neurologist to determine which medication is most suitable for your situation. A choice is made based on your signs and symptoms, but your stage of life plays a part as well. For example, you can continue to use some of these medications if you are trying to conceive or you are pregnant, but there are others that you would have to stop taking.
Talk to your neurologist about your expectations, preferences and experiences. Make sure you are well-prepared for this conversation; write down your questions and bring them with you.

The following pages contain an overview of the available medications in alphabetical order:

a. Aubagio® (teriflunomide)[3]

Teriflunomide inhibits the increase of certain white blood cells (lymphocytes), which helps to protect against attacks from the immune system against the central nervous system. This reduces the inflammation which results in RRMS-related nerve damage.

b. Avonex® (interferon bèta-1a)[4]; Bètaferon® (interferon bèta-1b)[5]; Plegridy® (peginterferon bèta-1a)[11]; Rebif® (interferon bèta-1a)[12]

These medications belong to a group called "interferons". Interferons are natural substances that are produced by the body to fight attacks, such as viral infections, more effectively. We don't fully understand yet how interferons work in RRMS, but interferon bèta appears to calm down the immune system and prevent RRMS relapses.

c. Copaxone® (glatiramer acetate)[6]

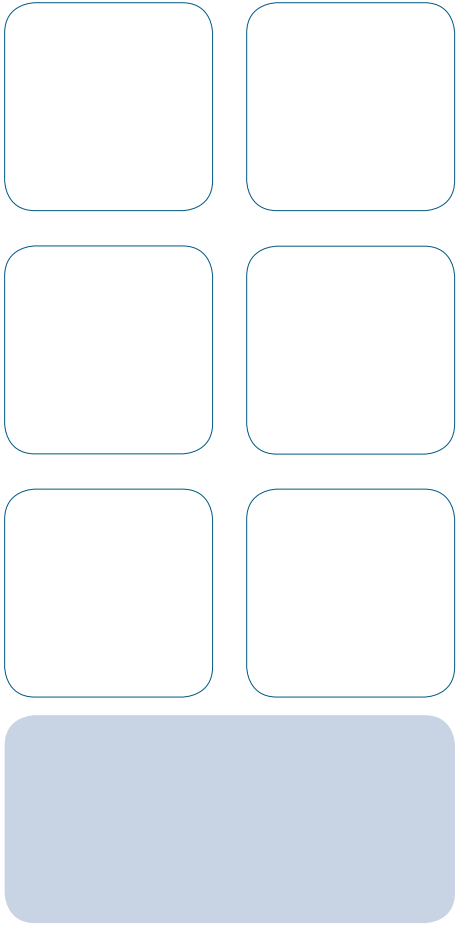
Glatiramer suppresses the immune system and reduces inflammation.

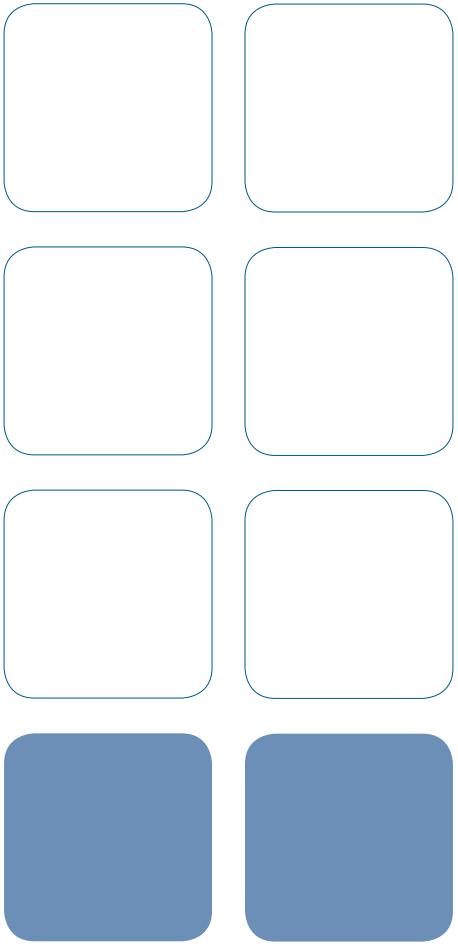
d. Gilenya® (fingolimod)[7]

Fingolimod helps to protect against attacks from the immune system against the central nervous system by affecting the ability of certain white blood cells (lymphocytes) to move around freely in the body and by making sure that they can't reach the brain or the spinal cord.

e. Lemtrada® (alemtuzumab)[8]

When alemtuzumab binds to white blood cells (lymphocytes), they die and are replaced by new lymphocytes. We don't fully understand yet how alemtuzumab works in RRMS,





but we think that it reduces the damaging effect of the immune system by killing existing lymphocytes, allowing them to be replaced by new ones.

f. Mavenclad® (cladribine)[9]

Cladribine is a cytotoxic (cell-killing) substance which acts primarily on lymphocytes. These are cells in the immune system that play a part in inflammation.

g. Ocrevus® (ocrelizumab)[10]

Ocrelizumab binds to specific B cells, a type of white blood cells (lymphocytes) that are part of the immune system and play a part in RRMS. Ocrelizumab reduces the number of these cells.

h. Tecfidera® (dimethyl fumarate)[13]

One of the ways in which dimethyl fumarate works is by activating a protein called “Nrf2”, which regulates certain “antioxidant” genes that help protect cells against damage. Studies have shown that dimethyl fumarate reduces inflammation and modulates the activity of the immune system.

i. Tysabri (natalizumab)[14]

Natalizumab prevents the cells that cause the inflammation (lymphocytes) from entering your brain. This reduces the nerve damage caused by RRMS.

What choices need to be made?

What can you expect from the treatment?

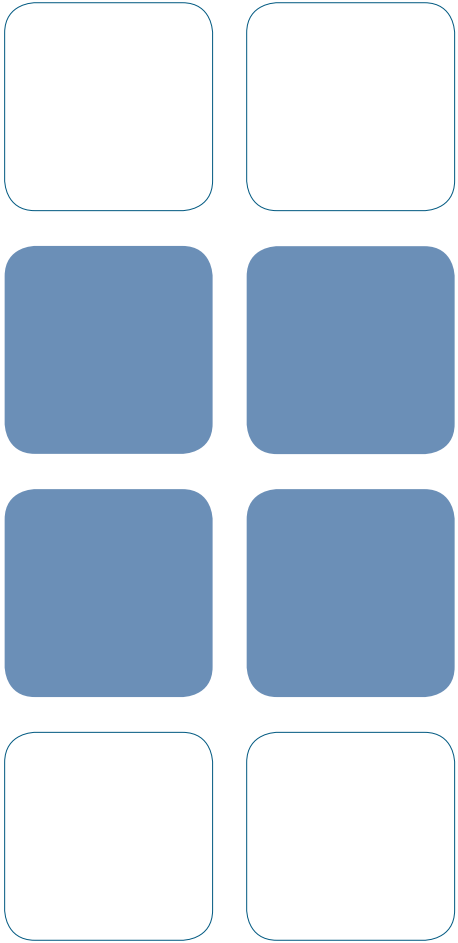
Your neurologist or MS nurse is the best person to explain the flood of information available on the internet and in all kinds of brochures. He/she will be able to talk to you in depth about the questions that concern you personally and help you choose the medication that is most suitable for you.

5. Treatment of symptoms

RRMS can lead to all kinds of symptoms, which may come and go. Symptomatic treatments are targeted treatments to alleviate a specific symptom you are experiencing. For example, there are medications for alleviating pain, bladder and intestinal problems, or stiffness, spasticity and mobility problems. Your neurologist or MS nurse will be able to tell you more about this.

Treatment of an MS attack

An MS attack (flare-up, exacerbation) can last 24 hours to several weeks. There may be a rapid succession of new symptoms, or old symptoms that were gone may come back. These symptoms must not be related to a fever, an infection or the start or end of a treatment. It's not always easy to know if it's an actual flare-up or “just” a fever and/or an infection.



The symptoms may also be related to the start or end of treatment with an MS medication, or they may be part of slow changes in the pattern of symptoms; neither of these are flare-ups.

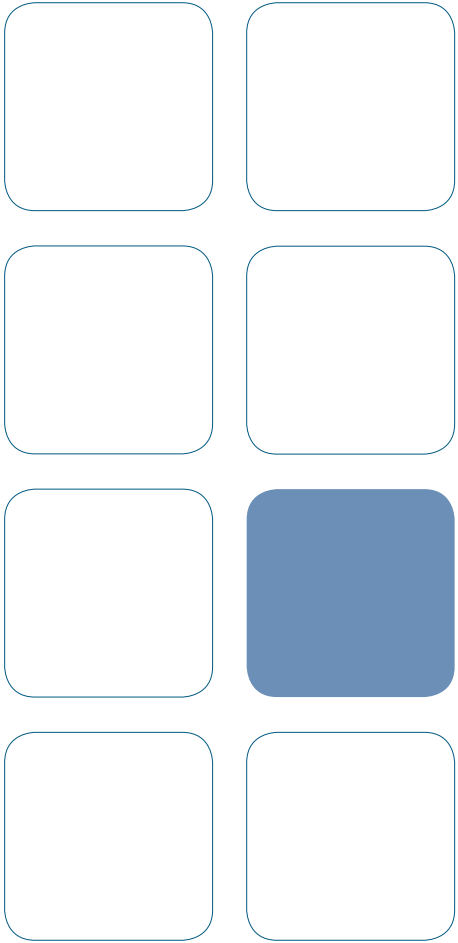
Corticosteroids

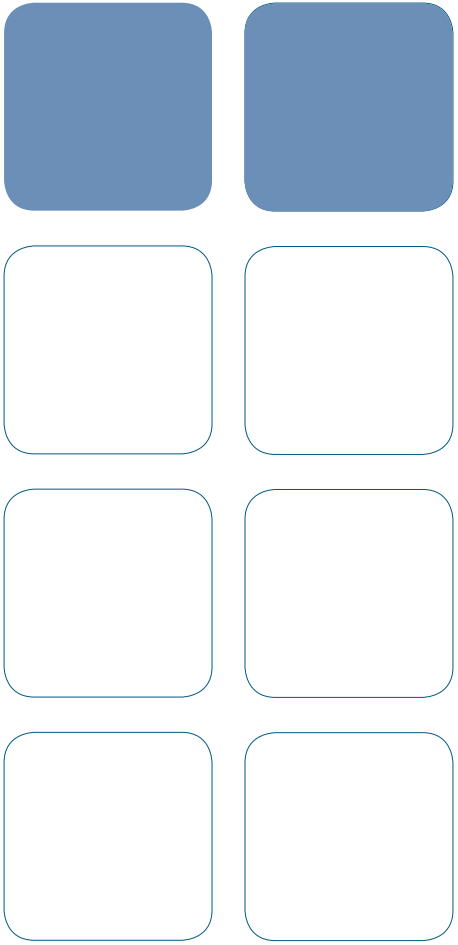
A flare-up is a sign of acute inflammation in one or more places in the central nervous system.

Corticosteroids are often used as treatment. These are anti-inflammatory medications that can shorten the duration of MS attacks. They can be administered in several different ways. This is usually done by infusion, so the medication enters the bloodstream directly. You will be hospitalised for a few days, usually three to five days. You may also receive corticosteroids in tablet form.

Treatment of mild relapses

Flare-ups are not always treated with corticosteroids. For mild attacks you are often advised to rest more and to wait for things to get better. Corticosteroids are often more effective for loss of muscle strength or vision problems than for sensory problems or balance issues. Because of the potential side effects, these medications are not suitable for maintenance treatment. Prolonged use leads to an increased risk of problems like osteoporosis, diabetes and high blood pressure.





6. Useful addresses

Stichting MS Research (MS Research Foundation)
Postbus 200
2250 AE Voorschoten
t +31 71 560 0500
e info@msresearch.nl

Nationaal MS Fonds (National MS Fund)
Mathenesserlaan 378
3023 HB Rotterdam
t +31 10 591 9839
e info@nationaalmsfonds.nl

Multiple Sclerose Vereniging Nederland (MSVN, Dutch MS Society)
De Corridor 5c
3621 ZA Breukelen
t +31 88 374 8585
e info@msvereniging.nl

Would you like to know more?
You can find more information about MS at
www.toekomstmetms.nl
(in Dutch)

For more information about medications you can consult
www.ema.europe.eu

References
1. Noyes K. Impact of diagnosis and early treatment on the course of multiple sclerosis. Am J Manag Care. 2013 Nov;19(17 Suppl):s321-31.
2. Mori F, et al. Early treatment with high-dose interferon bèta-1a reverses cognitive and cortical plasticity deficits in multiple sclerosis. Funct Neurol. 2012 Jul-Sep;27(3):163-8.
3. Aubagio: European public assessment report (EPAR) Summary for the public at www.ema.europa.eu
4. Avonex: European public assessment report (EPAR) Summary for the public at www.ema.europa.eu
5. Bètaferon: European public assessment report (EPAR) Summary for the public at www.ema.europa.eu
6. Copaxone: European public assessment report (EPAR) Summary for the public at www.ema.europa.eu
7. Gilenya: European public assessment report (EPAR) Summary for the public at www.ema.europa.eu
8. Lemtrada: European public assessment report (EPAR) Summary for the public at www.ema.europa.eu
9. Mavenclad: European public assessment report (EPAR) Summary for the public at www.ema.europa.eu
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11. Plegridy: European public assessment report (EPAR) Summary for the public at www.ema.europa.eu
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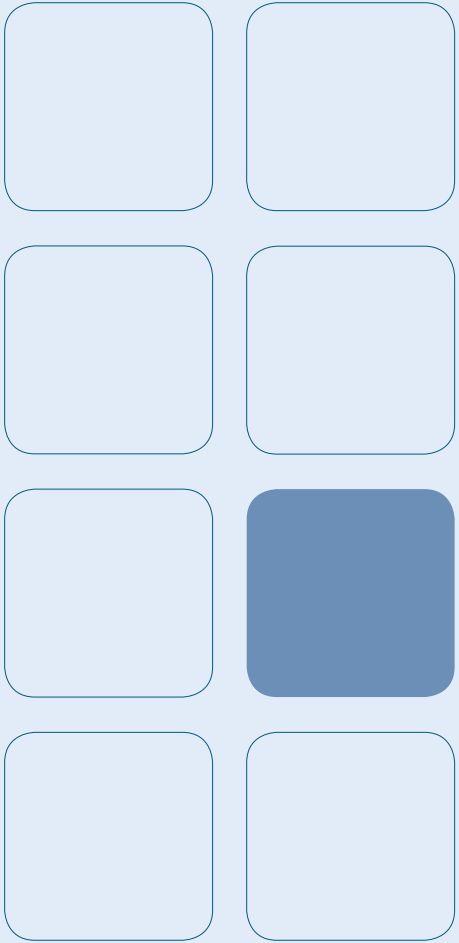
13. Tecfidera: European public assessment report (EPAR) Summary for the public at www.ema.europa.eu
14. Tysabri: European public assessment report (EPAR) Summary for the public at www.ema.europa.eu



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