Bijsluiter: informatie voor de patiënt

Ditagfenda 120 mg harde maagsapresistente capsules
Ditagfenda 240 mg harde maagsapresistente capsules
dimethyl fumarate

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Ditagfenda is and what it is used for

What Ditagfenda is
Ditagfenda is a medicine that contains the active substance **dimethyl fumarate**.

What Ditagfenda is used for
Ditagfenda is used to treat relapsing-remitting multiple sclerosis (MS) in patients aged 13 years and older.

MS is a long-term condition that affects the central nervous system (CNS), including the brain and the spinal cord. Relapsing-remitting MS is characterised by repeated attacks (relapses) of nervous system symptoms. Symptoms vary from patient to patient, but typically include walking difficulties, feeling off balance and visual difficulties (e.g. blurred or double vision). These symptoms may disappear completely when the relapse is over, but some problems may remain.

How Ditagfenda works
Ditagfenda seems to work by stopping the body's defence system from damaging your brain and spinal cord. This may also help to delay future worsening of your MS.

2. What you need to know before you take Ditagfenda

Do not take Ditagfenda
- **if you are allergic to dimethyl fumarate** or any of the other ingredients of this medicine (listed in section 6).
- **if you are suspected to suffer from a rare brain infection called progressive multifocal leukoencephalopathy (PML) or if PML has been confirmed.**

Warnings and precautions
Ditagfenda may affect your **white blood cell counts**, your **kidneys** and **liver**. Before you start Ditagfenda, your doctor will do a blood test to count the number of your white blood cells and will

check that your kidneys and liver are working properly. Your doctor will test these periodically during treatment. If your number of white blood cells decreases during treatment, your doctor may consider additional analytic measures or discontinue your treatment.

Talk to your doctor before taking Ditagfenda if you have:
- severe **kidney** disease
- severe **liver** disease
- a disease of the **stomach** or **bowel**
- a serious **infection** (such as pneumonia)

Herpes zoster (shingles) may occur with Ditagfenda treatment. In some cases, serious complications have occurred. **You should inform your doctor** immediately if you suspect you have any symptoms of shingles.

If you believe your MS is getting worse (e.g. weakness or visual changes) or if you notice any new symptoms, talk to your doctor straight away because these may be the symptoms of a rare brain infection called progressive multifocal leukoencephalopathy (PML). PML is a serious condition that may lead to severe disability or death.

A rare but serious kidney disorder (Fanconi syndrome) has been reported for a medicine containing dimethyl fumarate, in combination with other fumaric acid esters, used to treat psoriasis (a skin disease). If you notice you are passing more urine, are more thirsty and drinking more than normal, your muscles seem weaker, you break a bone, or just have aches and pains, talk to your doctor as soon as possible so that this can be investigated further.

Children and adolescents
The warnings and precautions listed above also apply to children. Dimethyl fumarate can be used in children and adolescents aged 13 years and above. No data are available in children below 10 years of age.

Other medicines and Ditagfenda
Tell your doctor or pharmacist if you are taking, have recently taken or might take any medicines, in particular:
- medicines that contain **fumaric acid esters** (fumarates) used to treat psoriasis
- **medicines that affect the body's immune system** including **other medicines used to treat MS**, such as fingolimod, natalizumab, teriflunomide, alemtuzumab, ocrelizumab or cladribine, or some commonly used cancer treatments (rituximab or mitoxantrone).
- **medicines that affect the kidneys including** some **antibiotics** (used to treat infections), "**water tablets**" (diuretics), **certain types of painkillers** (such as ibuprofen and other similar anti-inflammatories and medicines purchased without a doctor's prescription) and medicines that contain **lithium**
- taking this medicine with certain types of vaccines (live vaccines) may cause you to get an infection and should, therefore, be avoided. Your doctor will advise whether other types of vaccines (non-live vaccines) should be given.

Ditagfenda with alcohol
Consumption of more than a small quantity (more than 50 ml) of strong alcoholic drinks (more than 30% alcohol by volume, such as spirits) should be avoided within an hour of taking Ditagfenda, as alcohol can interact with this medicine. This could cause inflammation of the stomach (gastritis), especially in people already prone to gastritis.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

<u>Pregnancy</u>
Do not use Ditagfenda if you are pregnant unless you have discussed this with your doctor.

Breast-feeding
It is not known whether the active substance of this medicine passes into breast milk. Ditagfenda should not be used during breast-feeding. Your doctor will help you decide whether you should stop breast-feeding or stop using Ditagfenda. This involves balancing the benefit of breast-feeding for your child, and the benefit of therapy for you.

Driving and using machines
The effect of this medicine on the ability to drive or use machines is not known. This medicine is not expected to affect your ability to drive and use machines.

3. How to take Ditagfenda

Always take this medicine exactly as your doctor has told you. Check with your doctor if you are not sure.

Starting dose
120 mg twice a day.
Take this starting dose for the first 7 days, then take the regular dose.

Regular dose
240 mg twice a day.

Ditagfenda is for oral use

Swallow each capsule whole, with some water. Do not divide, crush, dissolve, suck or chew the capsule as this may increase some side effects.

Take Ditagfenda with food – it may help to reduce some of the very common side effects (listed in section 4).

If you take more Ditagfenda than you should
If you have taken too many capsules, **talk to your doctor straight away**. You may experience side effects similar to those described below in section 4.

If you forget to take Ditagfenda
If you forget or miss a dose, **do not take a double dose** to make up for the forgotten dose.

You may take the missed dose if you leave at least 4 hours between the doses. Otherwise wait until your next planned dose.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious effects
Ditagfenda may lower lymphocyte counts (a type of white blood cell). Having a low white blood cell count can increase your risk of infection, including the risk of a rare brain infection called progressive multifocal leukoencephalopathy (PML). PML may lead to severe disability or death. PML has occurred after 1 to 5 years of treatment and so your physician should continue to monitor your white blood cells throughout your treatment, and you should remain observant of any potential symptoms of PML as described below. The risk of PML may be higher if you have previously taken a medicine impairing the functionality of your body’s immune system.

The symptoms of PML may be similar to an MS relapse. Symptoms may include new or worsening weakness on one side of the body; clumsiness; changes in vision, thinking, or memory; or confusion or personality changes, or speech and communication difficulties lasting for more than several days. Therefore, if you believe your MS is getting worse or if you notice any new symptoms while you are on Ditagfenda treatment, it is very important that you speak to your doctor as soon as possible. Also speak with your partner or caregivers and inform them about your treatment. Symptoms might arise that you might not become aware of by yourself.
Call your doctor straight away if you experience any of these symptoms.

Severe allergic reactions
The frequency of severe allergic reactions cannot be estimated from the available data (not known).

Reddening of the face or body (*flushing*) is a very common side effect. However, should flushing be accompanied by a red rash or hives **and** you get any of these symptoms:
- swelling of the face, lips, mouth or tongue (*angioedema*)
- wheezing, difficulty breathing or shortness of breath (*dyspnoea, hypoxia*)
- dizziness or loss of consciousness (*hypotension*)

then this may represent a severe allergic reaction (*anaphylaxis*)
Stop taking Ditagfenda and call a doctor straight away

Very common side effects
These may affect *more than 1 in 10 people*:
- reddening of the face or body feeling warm, hot, burning or itchy (flushing)
- loose stools (diarrhoea)
- feeling sick (nausea)
- stomach pain or stomach cramps

Taking your medicine with food can help to reduce the side effects above

Substances called ketones, which are naturally produced in the body, very commonly show up in urine tests while taking dimethyl fumarate.

Talk to your doctor about how to manage these side effects. Your doctor may reduce your dose. Do not reduce your dose unless your doctor tells you to.

Common side effects
These may affect *up to 1 in 10 people*:
- inflammation of the lining of the intestines (*gastroenteritis*)
- being sick (*vomiting*)
- indigestion (*dyspepsia*)
- inflammation of the lining of the stomach (*gastritis*)
- gastrointestinal disorder
- burning sensation
- hot flush, feeling hot
- itchy skin (*pruritus*)
- rash
- pink or red blotches on the skin (*erythema*)
- hair loss (alopecia)

<u>Side effects which may show up in your blood or urine tests</u>
- low levels of white blood cells (*lymphopenia, leucopenia*) in the blood. Reduced white blood cells could mean your body is less able to fight an infection. If you have a serious infection (such as pneumonia), talk to your doctor immediately
- proteins (*albumin*) in urine
- increase in levels of liver enzymes (*ALT, AST*) in the blood

Uncommon side effects
These may affect *up to 1 in 100 people:*
- allergic reactions (*hypersensitivity*)
- reduction in blood platelets

Not known (frequency cannot be estimated from the available data)
- liver inflammation and increase in levels of liver enzymes (*ALT or AST in combination with bilirubin*)
- herpes zoster (*shingles*) with symptoms such as blisters, burning, itching or pain of the skin, typically on one side of the upper body or the face, and other symptoms, like fever and weakness in the early stages of infection, followed by numbness, itching or red patches with severe pain
- runny nose (*rhinorrhoea*)

Children (13 years of age and above) and adolescents
The side effects listed above also apply to children and adolescents.
Some side effects were reported more frequently in children and adolescents than in adults, e.g, headache, stomach pain or stomach cramps, being sick (vomiting), throat pain, cough, and painful menstrual periods.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Ditagfenda

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the blister, bottle label and the carton after "EXP". The expiry date refers to the last day of that month.

This medicine does not require any special temperature storage conditions
Store in the original package in order to protect from light.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to dispose of medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Ditagfenda contains
The active substance is dimethyl fumarate.

Ditagfenda 120 mg hard gastro-resistant capsules
Each hard gastro-resistant capsule contains 120 mg of dimethyl fumarate.

Ditagfenda 240 mg hard gastro-resistant capsules
Each hard gastro-resistant capsule contains 240 mg of dimethyl fumarate.

The other ingredients are:
- Capsule content: cellulose, microcrystalline, crospovidone, talc, povidone, silica colloidal anhydrous, magnesium stearate, triethyl citrate, methacrylic acid/ethylacrylate copolymer (1:1), hypromellose, titanium dioxide (E 171), triacetin.

- Capsule shell: gelatin, titanium dioxide (E 171), brilliant blue FCF-FD&C Blue 1 (E 133), yellow iron oxide (E 172)
- Capsule printing ink: shellac, potassium hydroxide, propylene glycol (E 1520), black iron oxide (E 172), strong ammonia solution.

What Ditagfenda looks like and contents of the pack
Ditagfenda 120 mg hard gastro-resistant capsules (gastro-resistant capsules): green cap and white body, capsule shell of 21.4 mm, imprinted in black ink with "DMF 120" on the body containing white to off-white minitablets
Ditagfenda 240 mg hard gastro-resistant capsules (gastro-resistant capsules): green cap and body, capsule shell of 23.2 mm, imprinted in black ink with "DMF 240" on the body containing white to off-white minitablets.

HDPE bottles with PP/HDPE caps with seal and silica gel desiccant cannister.
Do not swallow the desiccant.
OPA/Alu/PVC//Alu blisters or OPA/Alu/PVC//Alu unit dose blister.

Ditagfenda 120 mg hard gastro-resistant capsules
14 capsules (blisters)
14 X 1 capsules (unit dose perforated blisters)
100 capsules (bottle)

Ditagfenda 240 mg hard gastro-resistant capsules
56 capsules (blisters)
56 X 1 capsules (unit dose perforated blisters)
100 capsules (bottle)

Not all pack sizes may be marketed.

Houder van de vergunning voor het in de handel brengen en fabrikant

Vergunninghouder:
Adalvo Limited
Malta Life Science Park,
Level 4, Building 1,
Sir Temi Zammit Buildings,
San Gwann, SGN 3000,
Malta

Fabrikant:
Pharmadox Healthcare Limited
KW20A Kordin Industrial Park
Paola, PLA 3000
Malta

Adalvo Limited
Malta Life Science Park,
Level 4, Building 1
Sir Temi Zammit Buildings,
San Gwann, SGN 3000,
Malta

KeVaRo GROUP Ltd
9 Tzaritza Elenora Str. Office 23
Sofia 1618
Bulgarije

Dit medicijn is in het register ingeschreven onder:

Ditagfenda 120 mg: RVG 129392
Ditagfenda 240 mg: RVG 129393

Dit medicijn is geregistreerd in lidstaten van de Europese Economische Ruimte onder de volgende namen:

België	Ditagfenda 120 mg, 240 mg maagsapresistente capsules, hard
Kroatië	Ditagfenda 120mg, 240 mg tvrde želučanootporne kapsule
Ierland	Ditagfenda 120 mg, 240 mg hard gastro-resistant capsules
IJsland	Ditagfenda 120 mg, 240 mg magasýruþolin hörð hylki
Nederland	Ditagfenda 120 mg, 240 mg harde maagsapresistente capsules
Portugal	Ditagfenda
Roemenië	Ditagfenda 120 mg, 240 mg capsule gastrorezistente
Slovenië	Ditagfenda 120 mg, 240 mg gastrorezistentne trde kapsule

Deze bijsluiter is voor het laatst goedgekeurd in juni 2023.