This document contains PI for Avonex® (interferon beta-1a), Plegridy™ (peginterferon beta-1a), Tecfidera® (dimethyl fumarate), Tysabri™ (natalizumab) and Vumerity® (diroximel fumarate)

Prescribing information: AVONEX® (interferon beta-1a) 30 micrograms/0.5ml solution for injection and pre-filled pen

Please refer to the Summary of Product Characteristics (SmPC) for further information. Indication(s): Treatment of patients with relapsing multiple sclerosis (MS), or patients with a single demyelinating event with an active inflammatory process, if it is severe enough to warrant treatment with intravenous corticosteroids, if alternative diagnoses have been excluded, and if they are determined to be at high risk of developing clinically definite multiple sclerosis. **Dosage and administration:** Treatment should be initiated under the supervision of a physician experienced in the treatment of MS. Recommended dose of 30 micrograms (µg) injected intramuscularly once a week. Safety and efficacy in children below 10 years of age have not yet been established. No data are available. There is limited data available in children and adolescents ages 10 to less than 18 years old. **Contraindications:** History of hypersensitivity to natural or recombinant interferon beta or to any of the excipients; current severe depression and/or suicidal ideation. **Special warnings and precautions:** To improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded. Caution in patients with previous or current depressive disorders, a history of seizures, or those receiving treatment with anti-epileptics, particularly if their epilepsy is not adequately controlled. Use with caution and monitor closely in patients with cardiac disease, severe renal or hepatic failure or severe myelosuppression. Patients should be monitored for signs of hepatic failure and caution exercised if other medicinal products associated with hepatic injury are used concomitantly. Cases of nephrotic syndrome and thrombotic microangiopathy (TMA) have been reported during treatment with interferon-beta products. If clinical features of TMA are observed, further testing is recommended. If TMA is diagnosed, prompt treatment is required and immediate discontinuation of AVONEX is recommended. If nephrotic syndrome is diagnosed, prompt treatment is required and discontinuation of AVONEX should be considered. Periodic assessment of renal function, routine periodic blood chemistry and haematology tests are recommended during treatment. Development of neutralizing antibodies to AVONEX may decrease efficacy. Cases of injection site necrosis have been reported. To minimise the risk of injection site reactions, patients should be advised to use an aseptic injection technique and rotate the injection sites with each dose. The procedure for the self-administration by the patient should be reviewed periodically especially if injection site reactions have occurred. If the patient experiences any break in the skin, which may be accompanied by swelling or drainage of fluid from the injection site, the patient should be advised to speak with their doctor. Whether to discontinue therapy following a single site of necrosis is dependent on the extent of necrosis. For patients who continue therapy with AVONEX after injection site necrosis has occurred, avoid administration of AVONEX into the affected area until it is fully healed. If multiple lesions occur, change injection site, or discontinue therapy until healing occurs. **Drug interactions:** No formal interaction studies have been conducted in humans. Corticosteroids or ACTH can be given concomitantly during relapses. Caution should be exercised when combining AVONEX with products with a narrow therapeutic index and largely dependent on cytochrome P450 for clearance. **Pregnancy and lactation:** If clinically needed, the use of AVONEX may be considered during pregnancy. AVONEX can be used during breast-feeding. **Undesirable effects:** The most commonly reported side effects in adults are flu-like symptoms: myalgia, fever, chills, sweating, asthenia, headache and nausea. Very common side effects in children were myalgia, pain in extremity, fatigue and arthralgia. Other common events include: Investigations: decreased lymphocyte, white blood cell, and neutrophil counts; decreased haematocrit and increased blood potassium and blood urea nitrogen. Nervous system: muscle spasticity, hypoesthesia. Respiratory, thoracic and mediastinal: rhinorrhoea. Gastrointestinal: vomiting, diarrhoea. Skin and subcutaneous tissue: rash, increased sweating, contusion. Musculoskeletal and connective tissue: muscle cramp, neck pain, arthralgia, pain in extremity, back pain, muscle stiffness, musculoskeletal stiffness. Metabolism and nutrition: anorexia. Vascular: flushing. General disorders and administration site conditions: injection site pain, injection site erythema, injection site bruising, pain, fatigue, malaise, night sweats. Psychiatric disorders: depression, insomnia. Other serious side effects of rare or unknown frequency include: cardiomyopathy, congestive heart failure, anaphylactic reaction, hepatic failure, seizures, suicide, systemic lupus erythematosus, pancytopenia and thrombocytopenia. Cases of pulmonary arterial hypertension have been reported with interferon beta products up to several years after starting treatment. See SmPCs for full list of side effects. **Legal classification:** POM. **Pack size and basic NHS price:** Box containing four injections £654; box containing twelve injections £1962. **Package quantities:** AVONEX 30 µg/0.5 ml solution for injection: 1 box containing 4 or 12 trays. Each tray contains 1 ml pre-filled syringe containing 0.5 ml of solution (30 µg dose of interferon beta-1a) and 1 needle. AVONEX 30 µg/0.5 ml solution for injection, in pre-filled pen (30 µg dose of interferon beta-1a): 1 box containing 4 or 12 cartons. Each carton contains a single-use AVONEX pen with 1 injection needle and a pen cover. **Marketing Authorisation number:** *Ireland/Northern-Ireland* EU/1/97/033/003-006. *Great Britain*: Avonex Pen: PLGB 22407/0014, Avonex PFS: PLGB 22407/0029. **Marketing Authorisation Holder:** Biogen Netherlands B.V., Prins Mauritslaan 13, 1171 LP Badhoevedorp, The Netherlands. **Date of last revision of Prescribing Information:** July 2023

Adverse events should be reported.
For Ireland, reporting forms and information can be found at www.hpra.ie.For the UK, reporting forms and information can be found at https://yellowcard.mhra.gov.uk/ or via the Yellow Card app available from the Apple App Store or Google Play Store.
Adverse events should also be reported to Biogen Idec Ltd MedInfoUKI@biogen.com **UK: 0800 008 7401 (Ireland 1800 812 719) Fax: +44 (0) 1628 501010.**

Prescribing Information: Plegridy™ (peginterferon beta-1a) solution for injection in pre-filled pen/pre-filled syringe

Please refer to the Summaries of Product Characteristics (SmPCs) for further information.
Indication(s): Treatment of adult patients with relapsing remitting multiple sclerosis (MS). **Dosage and administration:** Treatment should be initiated under the supervision of a physician experienced in the treatment of MS. Recommended dose of 125 micrograms (µg) injected subcutaneously or intra-muscularly every 2 weeks. It is generally recommended that patients start treatment with 63 µg on day 0, increasing to 94 µg at day 14, reaching the full dose of 125 µg by day 28 and every 2 weeks (14 days) thereafter. **Contraindications:** Hypersensitivity to natural or recombinant interferon beta or peginterferon or to any of the excipients; current severe depression and/or suicidal ideation. **Special warnings and precautions**: To improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded. Caution in patients with previous or current depressive disorders, a history of seizures, or those receiving treatment with anti-epileptics, particularly if their epilepsy is not adequately controlled. Patients should be advised to immediately report any symptoms of depression and/or suicidal ideation to their prescribing physician. Serious hypersensitivity reactions have been reported as rare complications of treatment with interferon beta including Plegridy. If anaphylaxis or severe hypersensitivity occurs Plegridy should be discontinued, immediate medical attention sought and treatment with Plegridy not restarted. Discontinuation should also be considered if injection site necrosis occurs, depending on the extent of necrosis. Aseptic injection technique should be used to minimise risk of injection site reactions. Use with caution and monitor closely in patients with significant cardiac disease, severe renal impairment or myelosuppression. Patients should be monitored for signs of hepatic injury. Cases of nephrotic syndrome and thrombotic microangiopathy (TMA) have been reported during treatment with interferon-beta products (class effects). If clinical features of TMA are observed, further testing is recommended. If TMA is diagnosed, prompt treatment is required and immediate discontinuation of Plegridy is recommended. If nephrotic syndrome is diagnosed, prompt treatment is required and discontinuation of Plegridy should be considered. Complete and differential blood cell counts, platelet counts and blood chemistries including LFTs are recommended prior to treatment initiation and at regular intervals. In the absence of clinical symptoms, periodic assessment of renal and hepatic function, routine periodic blood chemistry and haematology tests are recommended. Regular thyroid function tests are recommended in patients with a history of thyroid dysfunction. Development of neutralising antibodies to Plegridy may decrease efficacy. Caution should be used in patients with a history of seizures, to those receiving treatment with anti-epileptics, particularly if their epilepsy is not adequately controlled with anti-epileptics. **Drug interactions:** No formal interaction studies have been conducted in humans. Corticosteroids can be given concomitantly during relapses. Caution should be exercised when combining Plegridy with products with a narrow therapeutic index and largely dependent on cytochrome P450 for clearance. **Pregnancy and lactation:** If clinically needed, the use of Plegridy may be considered during pregnancy. Experience with exposure during the second and third trimester is very limited. Plegridy can be used during breast-feeding. **Undesirable effects:** The most commonly reported side effects are injection site erythema, influenza-like illness, pyrexia, headache, myalgia, chills, injection site pain, asthenia, injection site pruritus and arthralgia. Other common events include: Gastrointestinal: nausea, vomiting. Skin and subcutaneous tissue: alopecia, pruritus. General disorders and administration site conditions: hyperthermia, pain, and injection site reactions including; oedema, warmth, haematoma, rash, swelling, discolouration and inflammation. Investigations: increased body temperature, increased ALT, AST, GGT, decreased haemoglobin, decreased WBC counts. Psychiatric disorders: depression. Cases of pulmonary arterial hypertension have been reported with interferon beta products up to several years after starting treatment. Paediatric population: The safety and efficacy of peginterferon beta 1a in children and adolescents aged 10 to less than 18 years have not been fully established in multiple sclerosis. The following adverse events which are very common in the adult population were also reported as very common in the paediatric population (aged 10 to less than 18 years): injection site erythema, influenza like illness, headache and pyrexia. See SmPCs for full list of side effects. **Legal classification:** POM.

Price: Available on request. **Package quantities:** SC: The Plegridy Pen Initiation Pack contains one 63 µg pre-filled pen (orange labelled pen, first dose) and one 94 µg pre-filled pen (blue labelled pen, second dose) in a protective plastic tray. Recommended Dose Pack sizes: Box of two 125 µg pre-filled pens (grey labelled pens) in a protective plastic tray. Multipacks containing 6 (3 packs of 2) 125 µg pre-filled pens (grey labelled pens). The pack contains 3 inner cartons. Each inner carton contains 2 pens in a protective plastic tray. IM: Box of two 125 microgram pre-filled syringes in sealed plastic trays. **Marketing Authorisation numbers:** *Ireland*: EU/1/14/934/002, 005, 006, 007. *United Kingdom*: PLGB 22407/0016, 0017 and 0019. **Marketing Authorisation Holder:** Biogen Netherlands B.V., Prins Mauritslaan 13, 1171 LP Badhoevedorp, The Netherlands. **Date of last revision of Prescribing Information**: March 2026.

Adverse events should be reported.
For Ireland, reporting forms and information can be found at www.hpra.ie.
Adverse events should also be reported to Biogen Idec on medinfouki@biogen.com 1800 812 719 in Ireland and 0800 008 7401 in the UK.

Prescribing Information: Tecfidera® (dimethyl fumarate) 120 mg and 240 mg gastro-resistant hard capsules

Please refer to the Summary of Product Characteristics (SmPC) for further information. Indication(s): Treatment of adult patients with relapsing remitting multiple sclerosis (MS). **Dosage and administration**: Treatment should be initiated under the supervision of a physician experienced in the treatment of MS. Starting dose 120 mg twice a day, increased to recommended maintenance dose 240 mg twice a day after 7 days. Capsules must be swallowed whole and taken with food. Temporary dose reduction to 120 mg twice a day for up to one month may reduce flushing and gastrointestinal events. **Contraindications:** Hypersensitivity to dimethyl fumarate or to any of the excipients. Suspected or confirmed Progressive Multifocal Leukoencephalopathy (PML) **Special warnings and precautions:** PML has been reported in patients treated with Tecfidera. Cases of progressive multifocal leukoencephalopathy (PML) have occurred in the setting of lymphopaenia. PML is caused by the JC virus (JCV) and may be fatal or result in severe disability. JCV testing has not been studied in Tecfidera-associated lymphopaenia. At first sign/symptom suggestive of PML, withhold Tecfidera and perform appropriate diagnostic evaluations (e.g. immediate MRI, determination of JCV DNA in CSF). If a patient develops PML, Tecfidera must be permanently discontinued. No studies have been performed evaluating use of Tecfidera when switching patients from disease modifying therapies (DMTs). PML cases have occurred in patients previously treated with natalizumab or prior immunomodulatory treatment. When switching from another DMT to Tecfidera, half-life and mode of action of prior therapy should be considered. Exercise caution in patients with pre-existing lymphopaenia. If lymphocyte count is low, alternative causes of lymphopaenia should be considered. Tecfidera may cause lymphopaenia, including severe and prolonged lymphopaenia. Tecfidera should not be initiated in patients with severe lymphopenia (lymphocyte counts < 0.5 × 10^9/L). A current complete blood count, including lymphocytes, should be available prior to initiating treatment and must be repeated every 3 months. Discontinue therapy if lymphocyte counts < 0.5 × 10^9/L persist for > 6 months. Evaluation of benefit/risk of continued therapy should be taken as the risk of an opportunistic infection (including PML) cannot be ruled out. If therapy is discontinued, lymphocyte counts should be followed until recovery and a decision to restart should be based on clinical judgement. Re-assess the benefit/risk in patients with lymphocyte counts ≥ 0.5 × 10^9/L and < 0.8 × 10^9/L for 6 months. In patients with lymphocyte counts below the lower limit of normal, regular monitoring of absolute lymphocyte counts is recommended. Baseline MRI should be available prior to treatment initiation. Further scanning should be considered as part of increased vigilance in patients considered at increased risk of PML. Changes in renal laboratory tests have been seen in trial subjects treated with Tecfidera. Renal function assessments are recommended prior to initiating treatment, after 3 and 6 months of treatment, every 6 to 12 months thereafter and as clinically indicated. Drug-induced liver injury, including liver enzyme (≥ 3 times ULN) and total bilirubin (≥ 2 × ULN) increases can result from treatment with Tecfidera. Assessment of serum aminotransferases and total bilirubin levels are recommended prior to initiation and during treatment as clinically indicated. Use with caution in patients with severe renal or hepatic impairment, or patients with severe active gastrointestinal disease. Prescribers and patients should be alert to the possibility of hypersensitivity or anaphylactoid reactions in the event of severe flushing reactions. Cases of anaphylaxis have been reported generally after the first dose. Treatment should be discontinued and patients should seek immediate medical care. Consider treatment suspension in the event of serious infection; reassess benefit/risk prior to resuming therapy. Cases of herpes zoster have occurred with Tecfidera including serious and non-serious cases including disseminated herpes zoster, herpes zoster ophthalmicus, herpes zoster oticus, herpes zoster infection neurological, herpes zoster meningoencephalitis and herpes zoster meningomyelitis have been reported and may occur at any time during treatment. Monitor patients taking Tecfidera for signs and symptoms of herpes zoster, especially when concurrent lymphocytopenia is reported, although cases may also occur during periods of normal lymphocyte count. If herpes zoster occurs, administer appropriate treatment. Consider withholding Tecfidera treatment in patients with serious infections until the infection has resolved. Treatment should be started gradually to reduce flushing and gastrointestinal adverse reactions. Cases of Fanconi syndrome have been reported with products containing fumaric acid esters. Early diagnosis of Fanconi syndrome and discontinuation of dimethyl fumarate treatment are important to prevent the onset of renal impairment and osteomalacia, as the syndrome is usually reversible. The most important signs are: proteinuria, glucosuria (with normal blood sugar levels), hyperaminoaciduria and phosphaturia (possibly concurrent with hypophosphatemia). Importantly, Fanconi syndrome can occur without elevated creatinine levels or low glomerular filtration rate. In case of unclear symptoms Fanconi syndrome should be considered and appropriate examinations should be performed. This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium free'. **Drug interactions:** Concomitant use of Tecfidera with a short course of IV corticosteroids was not associated with an increase in infection. IM interferon beta-1a, glatiramer acetate and oral acetylsalicylic acid did not alter the pharmacokinetic profile of dimethyl fumarate. Simultaneous use of other fumaric acid derivatives should be avoided during treatment with Tecfidera. Concurrent therapy with nephrotoxic medicines may increase the potential of renal adverse reactions in patients taking Tecfidera. **Pregnancy and lactation:** A moderate amount of data on pregnant women are available (between 300-1,000 pregnancy outcomes), based on a pregnancy registry and post-marketing spontaneous reports. In the Tecfidera pregnancy registry, prospectively collected pregnancy outcomes were documented in patients with MS who were exposed to dimethyl fumarate. The median duration of exposure to dimethyl fumarate was 4.6 gestational weeks with limited exposure after the sixth gestational week. Exposure to dimethyl fumarate during such early pregnancy indicates no malformative or foeto/neonatal toxicity compared to the general population. The risk of longer dimethyl fumarate exposure or exposure in later stages of pregnancy is not known. As a precautionary measure, it is preferable to avoid the use of Tecfidera during pregnancy. It is unknown whether dimethyl fumarate or its metabolites are excreted in human milk; a risk to newborns/infants cannot be excluded. The benefits of breastfeeding for the child and therapy for the woman should be considered when deciding whether or not to discontinue Tecfidera therapy. **Undesirable effects:** The most commonly (≥1/10) reported sides effects are flushing, diarrhoea, nausea, abdominal upper pain and abdominal pain and ketone measured in the urine. Other common side effects (≥1/100 to <1/10) include gastroenteritis, lymphopenia, leucopenia, burning sensation, hot flushes, vomiting, dyspepsia, gastritis, gastrointestinal disorder, aspartate aminotransferase and alanine aminotransferase increase, pruritus, rash, erythema, alopecia, proteinuria, feeling hot, albumin urine present and white blood cell count decrease. See special warnings and precautions for other serious side effects. See SmPC for full list of side effects. **Legal classification:** POM. **Pack size and basic NHS price:** 120 mg capsules x 14 £343.00; 240 mg capsules x 56 £1373.00**. Marketing Authorisation numbers:** *Ireland/Northern Ireland:* EU/1/13/837/001-002; *Great Britain:* PLGB 22407/0012, PLGB 22407/0013. **Marketing Authorisation Holder:** Biogen Netherlands B.V., Prins Mauritslaan 13, 1171 LP Badhoevedorp, The Netherlands. **Date of last revision of Prescribing Information: November 2023**.

Adverse events should be reported.
For Ireland, reporting forms and information can be found at www.hpra.ie.
For the UK, reporting forms and information can be found at https://yellowcard.mhra.gov.uk/ or via the Yellow Card app available from the Apple App Store or Google Play Store.

Adverse events should also be reported to Biogen Idec Ltd MedInfoUKI@biogen.com UK: 0800 008 7401 (Ireland 1800 812 719) Fax: +44 (0) 1628 501010.

Prescribing information: Tysabri™ (natalizumab) 300mg concentrate for solution for infusion / 150mg solution for injection in pre-filled syringe

Please refer to the Summary of Product Characteristics (SmPC) for further information. Indication: Single disease modifying therapy (DMT) in adult patients with highly active relapsing remitting multiple sclerosis (rapidly evolving disease or highly active disease despite a full and adequate course of at least one DMT). **Dosage and administration:** 300 mg Tysabri is administered by IV infusion or SC injection every 4 weeks at specialist centres with timely access to MRI. 150mg Tysabri can be administered by a healthcare professional, patient or carer via subcutaneous (SC) injection only. It is not intended for intravenous (IV) infusion. Patients should be observed for hypersensitivity reactions as per the SmPC. Any switch from IV to SC should be made 4 weeks after the previous dose. Tysabri is not recommended for use in patients over 65 years. Natalizumab injections administered by a healthcare professional outside a clinical setting (e.g. at home) or self-administration by the patient or administration by a caregiver may be considered for patients who have previously tolerated at least six doses of natalizumab well, i.e. who have not experienced hypersensitivity reactions. The decision should be made after evaluation and recommendation by the specialised physician. Patients or caregivers must administer at least two doses via SC route (two injections each) under the guidance of a healthcare professional. They must be instructed to read the patient alert card and review the Pre-Administration Checklist prior to each dose. Patients or caregivers must be advised to remain vigilant for the early signs and symptoms of PML and if a hypersensitivity reaction occurs, to stop administration and seek medical attention immediately. After a treatment gap of 3 months or more, the six subsequent doses must be administered under the supervision of a healthcare professional because of the concern for hypersensitivity reaction.

Contraindications: Hypersensitivity to natalizumab or to any of the excipients; progressive multifocal leukoencephalopathy (PML); patients with increased risk of opportunistic infections, including immunocompromised patients; combination with other DMTs; known active malignancies except for patients with cutaneous basal cell carcinoma. **Special warnings and precautions:** Traceability: To improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded. PML; Use of Tysabri has been associated with increased risk of PML (opportunistic infection caused by John Cunningham virus (JCV)) which may be fatal or result in severe disability. Patients must be monitored at regular intervals for early signs and symptoms of PML. JCV also causes JCV GCN (granule cell neuronopathy), which is similar to PML (i.e. cerebellar syndrome). PML should be considered as a differential diagnosis in any MS patient taking Tysabri presenting with neurological symptoms and/or new brain lesions in MRI. If PML or JCV GCN is suspected, further dosing must be suspended until PML has been excluded. Presence of anti-JCV antibodies, treatment duration (especially beyond 2 years) and prior immunosuppressant use are risk factors for PML. Anti-JCV antibody testing provides supportive information for risk stratification of Tysabri treatment. Please refer to the SmPC and Physician Information and Management Guidelines for information on quantification and stratification of PML risk; monitoring of anti-JCV antibodies; MRI monitoring and management of suspected PML. Patients and physicians should continue to be alert for signs or symptoms suggestive of PML for approximately 6 months following treatment discontinuation. IRIS: Immune Reconstitution Inflammatory Syndrome occurs in almost all Tysabri PML patients after Tysabri removal, which can be fatal. Infections including opportunistic infections: Tysabri increases the risk of encephalitis and meningitis caused by herpes simplex and varicella zoster viruses. Rare cases of acute retinal necrosis have also been observed and can be potentially blinding. Patients with eye symptoms should be referred for retinal screening. Other opportunistic infections may occur. If suspected, Tysabri should be suspended until such an infection can be excluded. Educational guidance: Physicians intending to prescribe Tysabri must be familiar with the Physician Information and Management Guidelines. Physicians must discuss benefits and risks with patients, counsel on the importance of uninterrupted dosing (particularly in the early months), and provide an Alert Card. Patients and caregivers should be instructed on early signs and symptoms of PML and to inform their physician of any infection. Healthcare professionals administering natalizumab subcutaneous injection outside a clinical setting (OCS), e.g. at home or patients/carers self-administering must complete the Pre-Administration Checklist for each patient prior to each administration. Hypersensitivity reactions have been associated with Tysabri, including serious systemic reactions. If a hypersensitivity reaction occurs, patients or caregivers should be advised to stop administration and seek medical attention immediately. Prior treatment with immunosuppressive DMTs: care should be taken in order to avoid additive immune effects. Immunogenicity: in the case of disease exacerbations or infusion related events, the presence of antibodies should be evaluated. Treatment should be discontinued if persistent antibodies develop. Hepatic events: serious cases of liver injury have been reported. Patients should be monitored for liver impairment and Tysabri discontinued if serious liver injury occurs. Anaemia: Rare, serious cases of anaemia and haemolytic anaemia have been reported. Thrombocytopenia and immune thrombocytopenic purpura (ITP) have been reported with uncommon frequency. Patients should be instructed to report any signs of unusual or prolonged bleeding, petechiae, or spontaneous bruising immediately. Stopping therapy: if therapy is discontinued the physician needs to be aware that Tysabri has pharmacodynamic effects for approximately 12 weeks. **Fertility, pregnancy and lactation:** In case of pregnancy, consider discontinuation. Patients receiving Tysabri should not breastfeed. It is unlikely that Tysabri will affect fertility. **Undesirable effects:** The most commonly reported side effects are urinary tract infection, nasopharyngitis, herpes infection, hypersensitivity, anaemia, hepatic enzyme increased, drug specific antibody present, infusion related reaction, dyspnoea, vomiting, nausea, fatigue, pyrexia, chills, infusion/injection site reaction, pruritus, rash, urticaria, flushing, dizziness, headache and arthralgia. See special warnings and precautions for serious side effects. See SmPC for full list of side effects. **Legal classification:** POM. **Pack size and price:** 1 vial of concentrate for solution for IV infusion/pack or 2 pre-filled syringes for SC injection/pack: Ireland: Price available on request. UK: £1130. **Marketing Authorisation number:** Ireland: EU/1/06/346/001-002, UK: PLGB 22407/0010-0011. **Marketing Authorisation Holder:** Biogen Netherlands B.V., Prins Mauritslaan 13, 1171 LP Badhoevedorp, The Netherlands. **Date of last revision of Prescribing Information:** August 2025.

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For the UK, reporting forms and information can be found at https://yellowcard.mhra.gov.uk/ or via the Yellow Card app available from the Apple App Store or Google Play Store.

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Prescribing information: Vumerity ® (diroximel fumarate) 231 mg gastro-resistant hard capsules

Please refer to the Summary of Product Characteristics (SmPC) for further information. Indication: Treatment of adult patients with relapsing remitting multiple sclerosis. **Dosage and administration:** Treatment should be initiated under supervision of a physician experienced in the treatment of multiple sclerosis. The starting dose is 231 mg twice a day, orally with or without food. After 7 days, the dose should be increased to the recommended maintenance dose of 462 mg twice a day. Temporary dose reductions to 231 mg twice a day may reduce the occurrence of flushing and gastrointestinal adverse reactions. Within 1 month, the recommended dose of 462 mg twice a day should be resumed. Treatment should be started gradually to reduce the occurrence of flushing and gastrointestinal adverse reactions. **Contraindications:** Hypersensitivity to the active substance, to any of the excipients or other fumaric acid esters. Suspected or confirmed PML **Special warnings and precautions:** Diroximel fumarate and dimethyl fumarate are metabolised to monomethyl fumarate upon oral administration. The risks associated with diroximel fumarate are expected to be similar to those reported for dimethyl fumarate, because the exposure of monomethyl fumarate was demonstrated to be bioequivalent. Blood/laboratory tests: Assessment of renal function (e.g. creatinine, blood urea nitrogen and urinalysis) is recommended prior to treatment initiation with Vumerity, after 3 and 6 months of treatment, every 6 to 12 months thereafter and as clinically indicated. Assessment of serum aminotransferases and total bilirubin levels are recommended prior to treatment initiation and during treatment as clinically indicated. Patients treated with diroximel fumarate may develop lymphopenia. Prior to initiating treatment, a current complete blood count, including lymphocytes, must be performed. If the lymphocyte count is found to be below the normal range, a thorough assessment of possible causes should be completed prior to initiation of treatment. Treatment should not be initiated in patients with severe lymphopenia (lymphocyte counts <0.5 x 10^9/L). After starting therapy, complete blood counts, including lymphocytes, must be performed every 3 months. MRI: Before initiating treatment, a baseline MRI should be available (usually within 3 months) as a reference. The need for further MRI scanning should be considered in accordance with national and local recommendations. PML: PML cases have occurred with dimethyl fumarate and other medicinal products containing fumarates in the setting of lymphopenia. Prolonged moderate to severe lymphopenia appears to increase the risk of PML with dimethyl fumarate, however, risk cannot be excluded in patients with mild lymphopenia. If a patient develops PML, Vumerity must be permanently discontinued. At the first sign or symptom suggestive of PML, Vumerity should be withheld and appropriate diagnostic evaluations, including determination of JCV DNA in cerebrospinal fluid (CSF) by quantitative polymerase chain reaction (PCR) methodology, need to be performed. Prior treatment with immunosuppressive or immunomodulating therapies: No studies have been performed evaluating the efficacy and safety of diroximel fumarate when switching patients from other disease modifying therapies. The contribution of prior immunosuppressive therapy to the development of PML is possible. **Severe renal and hepatic impairment and active GI disease:** Diroximel fumarate has not been studied in patients with severe renal impairment, severe hepatic impairment and severe active gastrointestinal disease. Therefore, caution should be used when considering treatment in these patient. Flushing: In dimethyl fumarate pivotal clinical trials, 3 patients out of a total of 2,560 patients treated with dimethyl fumarate experienced serious flushing symptoms that were probable hypersensitivity or anaphylactoid reactions. Prescribers and patients should be alert to this possibility in the event of severe flushing reactions with Vumerity. Anaphylactic reactions: Cases of anaphylaxis/anaphylactoid reaction have been reported following dimethyl fumarate administration in the post-marketing setting. Reactions can occur after the first dose, but may also occur at any time during treatment, and may be serious and life threatening. Patients should be instructed to discontinue Vumerity and seek immediate medical care if they experience signs or symptoms of anaphylaxis. Treatment should not be restarted. Infections: Diroximel fumarate exerts immunomodulatory properties. Patients receiving Vumerity should be instructed to report symptoms of infections to a physician. If a patient develops a serious infection, suspending treatment should be considered and the benefits and risks should be reassessed prior to re-initiation of therapy. If Vumerity therapy is continued in the presence of moderate to severe prolonged lymphopenia, the risk of an opportunistic infection, including PML, cannot be ruled out. Herpes zoster infections: Cases of herpes zoster have occurred with diroximel fumarate and dimethyl fumarate. These events may occur at any time during treatment. Patients should be monitored for signs and symptoms of herpes zoster especially when concurrent lymphocytopenia is reported. Withholding treatment should be considered in patients with serious infections until the infection has resolved. Fanconi syndrome**:** Cases of Fanconi syndrome have been reported for a medicinal product containing dimethyl fumarate in combination with other fumaric acid esters. Early diagnosis of Fanconi syndrome and discontinuation of Vumerity treatment are important to prevent the onset of renal impairment and osteomalacia, as the syndrome is usually reversible. **Fertility**, **pregnancy and lactation:** There are no or limited amount of data from the use of diroximel fumarate in pregnant women. Vumerity should be used during pregnancy only if clearly needed and if the potential benefit justifies the potential risk to the foetus. It is unknown whether diroximel fumarate or its metabolites are excreted in human milk. A risk to the newborns/infants cannot be excluded. A decision must be made whether to discontinue breast feeding or to discontinue Vumerity therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman. **Undesirable effects:** The common (≥ 1/10) and very common (≥ 1/100 to < 1/10) incidence of the adverse reactions reported in dimethyl fumarate treated patients are: Gastroenteritis, Lymphopenia (Lymphopenia was reported with the frequency “very common” in a phase 3, open-label, uncontrolled study with diroximel fumarate), Leukopenia, Burning sensation, Flushing, Hot flush, Diarrhoea, Nausea, Upper abdominal pain, Abdominal pain, Vomiting, Dyspepsia, Gastritis, Gastrointestinal disorder, AST/ALT increased, Pruritus, Rash, Erythema, Alopecia, Proteinuria, feeling hot, Ketones in urine, Albuminin in urine, White blood cell count decreased. See special warnings and precautions for serious side effects. See SmPC for full list of side effects. **Legal classification:** POM. **Pack size and price:** Pack of 120 (1 bottle) gastro-resistant hard capsules.; £1,471.07. **Marketing Authorisation number:** *Ireland/Northern Ireland:* EU/1/21/1585/001; *Great Britain*: PLGB 22407/0026. **Marketing Authorisation Holder:** Biogen Netherlands B.V., Prins Mauritslaan 13, 1171 LP Badhoevedorp, The Netherlands. **Date of last revision of Prescribing Information:** May 2022.

Adverse events should be reported.

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https://yellowcard.mhra.gov.uk/ or via the Yellow Card app available from the Apple App Store or Google Play Store.

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