Prescribing Information: AUBAGIO® 14 mg (teriflunomide) film-coated tablets
Please refer to the Summary of Product Characteristics (SmPC) before prescribing.

Presentation: Each film-coated tablet contains 14 mg of teriflunomide.
Indication: AUBAGIO is indicated for the treatment of adult patients and paediatric patients aged 10 years and older with relapsing remitting multiple sclerosis (MS).
Dosage and administration: The treatment should be initiated and supervised by a physician experienced in the management of MS. In adults, the recommended dose of teriflunomide is 14 mg once daily. In paediatric patients (10 years of age and above), the recommended dose is 14mg once daily with body weight >40 kg. AUBAGIO should be taken orally and swallowed whole with some water. AUBAGIO can be taken with or without food. *Elderly (≥65 years):* AUBAGIO should be used with caution due to insufficient data on safety and efficacy. *Renal impairment:* No dose adjustment is necessary for patients with mild, moderate or severe renal impairment not undergoing dialysis. *Hepatic impairment:* No dose adjustment is necessary for patients with mild and moderate hepatic impairment. *Paediatric:* The safety and efficacy in children aged below 10 years have not been established. No data are available.
Contraindications: Hypersensitivity to the active ingredient or excipients. Patients with severe hepatic impairment (Child-Pugh class C). Pregnant women, or women of childbearing potential not using reliable contraception during treatment and thereafter as long as plasma levels are above 0.02 mg/l. Breastfeeding women. Pregnancy must be excluded before start of treatment. Patients with severe immunodeficiency states, e.g. AIDS. Significantly impaired bone marrow function or significant anaemia, leucopoenia, neutropenia or thrombocytopenia. Severe active infection until resolution. Severe renal impairment undergoing dialysis, because insufficient clinical experience is available in this patient group. Severe hypoproteinaemia, e.g. in nephrotic syndrome.
Warnings and precautions: *Monitoring: Before starting treatment*: blood pressure, alanine aminotransferase (ALT/SGPT), complete blood cell count (CBC) including differential white blood cell (WBC) and platelet count. Pregnancy should be excluded. *During treatment* the following should be monitored: blood pressure periodically, ALT/SGPT assessed at least every 4 weeks for the first 6 months of treatment and regularly thereafter. Consider additional monitoring when AUBAGIO is given in patients with pre-existing liver disorders, given with other potentially hepatotoxic drugs or as indicated by clinical symptoms such as unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine. Liver enzymes should be assessed every 2 weeks during the first 6 months of treatment, and at least every 8 weeks thereafter for at least 2 years from initiation of treatment. For ALT (SGPT) elevations between 2- and 3-fold the upper limit of normal, monitoring must be performed weekly. CBC should be performed based on clinical signs and symptoms. *Accelerated elimination procedure (AEP):* Without an AEP, it takes an average of 8 months to reach plasma concentrations less than 0.02 mg/l and may take up to 2 years. An AEP can be used at any time after discontinuation of teriflunomide. *Hepatic effects:* Elevations of liver enzymes have been observed in patients receiving teriflunomide. These elevations occurred mostly within the first 6 months of treatment. Cases of drug-induced liver injury (DILI) have been observed during treatment with teriflunomide, sometimes life-threatening. Most cases of DILI occurred with time to onset of several weeks or several months after treatment initiation of teriflunomide, but DILI can also occur with prolonged use. The risk for liver enzyme increases and DILI with teriflunomide might be higher in patients with pre-existing liver disorder, concomitant treatment with other hepatotoxic drugs, and/or consumption of substantial quantities of alcohol. Patients should be closely monitored for signs and symptoms of liver injury. Teriflunomide therapy should be discontinued and accelerated elimination procedure considered if liver injury is suspected. If liver enzymes are confirmed as >3x ULN, teriflunomide therapy should be discontinued. In case of treatment discontinuation, liver tests should be pursued until normalisation of transaminase levels. *Infections:* Patients receiving AUBAGIO should be instructed to report symptoms of infections to a physician. Patients with active acute or chronic infections should not start treatment with AUBAGIO until the infection(s) is resolved. Patients tested positive in tuberculosis screening should be treated by standard medical practice prior to therapy. *Respiratory reactions:* Interstitial lung disease (ILD) as well as cases of pulmonary hypertension have been reported with teriflunomide in the post-marketing setting. The risk might be increased in patients with a history of ILD. Due to the potential risk of ILD, pulmonary symptoms, such as persistent cough and dyspnoea, may be a reason for discontinuation of the therapy and for further investigation, as appropriate. *Haematological effects*: A mean decrease of <15% from baseline affecting WBC counts have been observed. Obtain CBC including differential white blood cell count and platelets prior to initiation of treatment, thereafter CBC should be assessed as indicated by clinical signs and symptoms. Patients with pre-existing cytopenias may have a higher risk of haematological disorders. In cases of severe haematological reactions, including pancytopenia, AUBAGIO and all concomitant myelosuppressive treatment must be discontinued and the AEP be considered. *Skin reactions:* Cases of serious skin reactions, sometimes fatal, including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) and drug reaction with eosinophilia and systemic symptoms (DRESS), have been reported with AUBAGIO. If skin and /or mucosal reactions (ulcerative stomatitis) are observed which raise the suspicion of severe generalised major skin reactions, teriflunomide must be discontinued and an accelerated procedure initiated immediately. New onset of psoriasis (including pustular psoriasis) and worsening of pre-existing psoriasis have been reported during the use of teriflunomide. Treatment withdrawal and initiation of an AEP may be considered. *Peripheral neuropathy:* Discontinuing AUBAGIO therapy and performing the AEP should be considered. *Vaccination*: Live attenuated vaccines should be avoided. *Interference with determination of ionised calcium levels:* The measurement of ionised calcium levels might show falsely decreased values under treatment with teriflunomide. The plausibility of observed values should be questioned and in case of doubtful measurements, it is recommended to determine the total albumin adjusted serum calcium concentration. *Immunosuppressive/Immunomodulating therapies:* Co-administration with leflunomide is not recommended. Co-administration with antineoplastic or immunosuppressive therapies has not been evaluated. *SWITCHING to/from AUBAGIO:* No waiting period is required when initiating teriflunomide after interferon beta or glatiramer acetate. Due to the risk of concomitant immune effects for up to 2-3 months, caution is required when switching patients immediately from natalizumab to teriflunomide. To avoid concomitant immune effects when switching from fingolimod, 10-14 weeks is needed for lymphocytes to return to the normal range. If a decision is made to stop treatment with AUBAGIO, during the interval of 5 half-lives (approximately 3.5 months, although may be longer in some patients), starting other therapies will result in concomitant exposure to AUBAGIO. This may lead to an additive effect on the immune system and caution is, therefore, indicated. Paediatric population: Cases of pancreatitis have been observed. Clinical symptoms included abdominal pain,

nausea and/or vomiting. Serum amylase and lipase were elevated in these patients. The time to onset ranged from a few months up to three years. Patients should be informed of the characteristic symptoms of pancreatitis. If pancreatitis is suspected, pancreatic enzymes and related laboratory parameters should be obtained. If pancreatitis is confirmed, teriflunomide should be discontinued and an accelerated elimination procedure should be initiated. *Lactose:* Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption, should not take this medicinal product. *Sodium:* This medicine contains less than 1 mmol sodium (23 mg per tablet), that is to say essentially "sodium free". *Interactions:* Rifampicin and other known potent CYP and transporter inducers; medicinal products metabolised by CYP1A2 or CYP2C8; substrates of OAT3; substrates of BCRP and the OATP family, especially HMG-Co reductase inhibitors, should be used with caution during the treatment with teriflunomide. Patients should be closely monitored for signs and symptoms of excessive exposure to the medicinal products and reduction of the dose of these medicinal products should be considered. Co-administration with cholestyramine or activated charcoal is not recommended unless an accelerated elimination is desired. Whilst the interaction of teriflunomide is not expected to adversely impact the efficacy of oral contraceptives, it should be considered when selecting or adjusting oral contraceptive treatment. A 25% decrease in peak international normalised ratio (INR) was observed when teriflunomide was co-administered with warfarin as compared with warfarin alone. Close INR follow-up and monitoring is recommended. **Pregnancy and lactation:** Women of childbearing potential must use effective contraception during treatment and after treatment as long as teriflunomide plasma concentration is >0.02 mg/l. Female children and/or parents/caregivers of female children should be informed about the need to contact the treating physician once the female child under AUBAGIO treatment experiences menses. Counselling should be provided to the new patients of child-bearing potential about contraception and the potential risk to the foetus. Referral to a gynaecologist should be considered. Plans to stop or change contraception, or in the case of suspected pregnancy, patient must discontinue AUBAGIO and notify the physician immediately. In case of pregnancy, the physician and patient must discuss the risk to the pregnancy and the AEP. In women wishing to become pregnant, teriflunomide should be stopped and an AEP is recommended. Please see SmPC for more details. Lactation is contraindicated.

Adverse effects: ***Very common (≥1/10):*** Headache, diarrhoea, nausea, alopecia and ALT increase. ***Common (≥1/100 to <1/10):*** Influenza, upper respiratory tract infection, urinary tract infection, bronchitis, sinusitis, pharyngitis, cystitis, gastroenteritis viral, oral herpes, tooth infection, laryngitis, tinea pedis, neutropenia, anaemia, mild allergic reactions, anxiety, paraesthesia, sciatica, carpal tunnel syndrome, palpitations, hypertension, pancreatitis in the paediatric population, upper abdominal pain, vomiting, toothache, Gamma-glutamyltransferase increase, aspartate aminotransferase increase, rash, acne, musculoskeletal pain, myalgia, arthralgia, pollakiuria, menorrhagia, pain, asthenia, weight decrease, neutrophil count decrease, WBC decrease and blood creatine phosphokinase increase. ***Uncommon (≥1/1000 to <1/100):*** Severe infections including sepsis, mild thrombocytopenia (platelets <100G/l), hypersensitivity reactions (immediate or delayed) including anaphylaxis and angioedema, hyperaesthesia, neuralgia, peripheral neuropathy, interstitial lung disease, pancreatitis in the adult population, stomatitis, colitis, dyslipidaemia, nail disorders psoriasis (including pustular), severe skin reactions and post-traumatic pain. ***Rare:*** (≥1/10,000 to <1/1,000): Acute hepatitis. ***Frequency not known:*** Pulmonary hypertension, drug-induced liver injury (DILI. Please see SPC for full details.

Legal Classification: POM. **List Price: GB:** £1037.84 (28x tablets). **Marketing authorisation number:** PLGB 04425/0819. **Marketing authorisation holder:** Aventis Pharma Ltd, 410 Thames Valley Park Drive, Reading, Berkshire, RG6 1PT, UK. **For more information please contact:** Medical Information, Sanofi, 410 Thames Valley Park Drive, Reading, Berkshire, RG6 1PT, UK. Or uk-medicalinformation@sanofi.com.

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Adverse events should be reported. Reporting forms and information can be found at: In the UK: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to the Sanofi drug safety department on Tel: 0800 0902314. Alternatively, send via email to UK-drugsafety@sanofi.com