Prescribing Information

▼Hetronifly 10 mg/ml concentrate for solution for infusion

Please refer to the Summary of Product Characteristics (SmPC) before prescribing.

Presentation: Each ml of concentrate for solution for infusion contains 10 mg of serplulimab.

Each vial of 10 ml of concentrate contains 100 mg of serplulimab.

Indications: Hetronifly in combination with carboplatin and etoposide is indicated for the first-line treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC).

Dosage and Administration: Treatment must be initiated and supervised by a physician experienced in the treatment of cancer. *Posology:* Recommended dose is 4.5 mg/kg serplulimab every 3 weeks until disease progression or unacceptable toxicity. *Dose delay or discontinuation*: Dose escalation or reduction is not recommended. Dose withholding or discontinuation may be required based on individual safety and tolerability. Dose withholding for up to 12 weeks for tolerability is acceptable. Serplulimab should be withheld or discontinued to manage adverse reactions, refer to SmPC for further details. *Special populations: Elderly (> 65 years)*: No dose adjustment is needed. *Renal impairment:* No dose adjustment is needed with mild (CRCL=60-89 ml/min) or moderate (CRCL=30-59 ml/min) impairment. Insufficient data and no dose recommendation can be made with severe (CRCL=15-29 ml/min) impairment. *Hepatic impairment:* No dose adjustment is needed with mild (BIL ≤ ULN and AST > ULN or BIL > 1 to 1.5 × ULN and any AST) impairment. There are insufficient data with moderate (BIL > 1.5 to 3 × ULN and any AST) impairment and no data are available in severe (BIL > 3 × ULN and any AST) impairment. No dose recommendation can be made with moderate or severe hepatic impairment. *Paediatric population:* No relevant use in the indication of small cell lung cancer. *Method of administration:* Intravenous use. Initial infusion rate should be set up to 100 ml per hour. If the first infusion is well tolerated, all subsequent infusions may be shortened to 30 minutes (± 10 minutes). When administered in combination with chemotherapy, Hetronifly should be given first followed by chemotherapy on the same day. Use separate infusion bags for each infusion. Must not be administered as an intravenous push or bolus injection. Total dose required should be diluted with sodium chloride 9 mg/ml (0.9%) solution for injection. For instructions on dilution and handling of the medicinal product before administration, refer to SmPC

Contraindications: Hypersensitivity to active substance or to any of the excipients listed in SmPC.

Warnings and Precautions: *Traceability:* Tradename and the batch number of the administered product should be clearly recorded. *Immune-related adverse reactions:* Including severe and fatal cases have occurred. Most occurring during treatment were reversible and managed by withholding treatment, administration of corticosteroids, and/or supportive care. Reactions have also occurred up to 3.6 months after the last dose and can affect more than one body system simultaneously. For suspected reactions, adequate evaluation to confirm aetiology or exclude other causes should be ensured. Based on the severity, treatment should be withheld, and corticosteroid administered. For most Grade 2 and some specific Grade 3 or 4 immune-related adverse reactions, administration should be withheld until recovery or improvement to Grade 1. Serplulimab must be permanently discontinued for any Grade 4 and some specific Grade 3 reactions. For Grade 3, 4 and some specific Grade

2 reactions (e.g., immune-related pneumonitis, immune-related myocarditis), corticosteroid (1-2 mg/kg/day prednisone or equivalent) and other symptomatic treatments should be given according to the clinical symptoms until recovery or improvement to Grade 1. Upon improvement to Grade ≤ 1, corticosteroid taper should be initiated and continued over at least 1 month. Rapid tapering may lead to worsening or recurrence of the adverse reaction. Non-corticosteroid immunosuppressive therapy (e.g., infliximab) should be added if there is worsening or no improvement despite corticosteroid use. *Immune-related lung disease:* Immune-related pneumonitis, including fatal cases, has been reported. Monitor for signs and symptoms, such as radiographic changes (e.g., focal ground glass opacities, patchy filtrates), dyspnoea, and hypoxia. Suspected immune-related pneumonitis should be confirmed with radiographic imaging, and other causes excluded. For treatment modification, refer to SmPC. *Immune-related colitis:* Including fatal cases, has been reported. Monitor for signs and symptoms, such as abdominal pain, diarrhoea, mucus, or blood in stool. Infection and other disease-related aetiologies should be ruled out. For treatment modification, refer to SmPC. The potential risk of gastrointestinal perforation should be taken into consideration and confirmed by radiographic imaging and/or endoscopy if necessary. *Immune-related hepatitis:* Including fatal cases, has been reported. Monitor for changes in liver function and clinical signs and symptoms, such as transaminase and total bilirubin elevations periodically (every month). Infection and diseases-related aetiologies should be ruled out. Frequency of liver function tests should be increased, if immune-related hepatitis occurs. For treatment modification, refer to SmPC. *Immune-related nephritis and renal dysfunction:* Has been reported. Monitor for changes in renal function and clinical signs and symptoms periodically (every month). Frequency of renal function tests should be increased, if immune-related nephritis occurs. Most patients present with asymptomatic increases in serum creatinine. Disease-related aetiologies should be ruled out. For treatment modification, refer to SmPC. *Immune-related endocrinopathies: Thyroid diseases:* Including hyperthyroidism, hypothyroidism, and thyroiditis have been reported. Monitor for changes in thyroid function and clinical signs and symptoms of thyroid disorders. For Grade 2 or 3 symptomatic hypothyroidism, serplulimab should be withheld and thyroid hormone replacement should be initiated as needed. For Grade 2 or 3 symptomatic hyperthyroidism, serplulimab should be withheld and anti-thyroid medicinal product should be initiated as needed. If acute inflammation of the thyroid is suspected, serplulimab should be withheld and hormone therapy initiated. Treatment may be resumed when symptoms of hypothyroidism or hyperthyroidism are controlled, and thyroid function is improved. For life-threatening hyperthyroidism or hypothyroidism, serplulimab must be permanently discontinued. Thyroid function should be monitored continuously to ensure appropriate hormone replacement. *Pituitary disorders:* Hypophysitis has been reported. Monitor for signs and symptoms of hypophysitis, and other causes should be ruled out. For Grade 2 or 3 symptomatic hypophysitis, serplulimab should be withheld, and hormone replacement should be initiated as needed. If acute hypophysitis is suspected, corticosteroids should be initiated. For life-threatening Grade 4 hypophysitis, serplulimab must be permanently discontinued. *Adrenal insufficiency:* Has been reported. Monitor for signs and symptoms, and other causes should be ruled out. For Grade 2 adrenal insufficiency, serplulimab should be withheld and hormone replacement should be initiated as needed. For life-threatening Grade 3 or 4 adrenal insufficiency, serplulimab must be permanently discontinued. Adrenal gland function and hormone levels should be monitored continuously to ensure appropriate hormone replacement. *Hyperglycaemia:* Or type 1 diabetes mellitus has been reported. Monitor for blood glucose level and related clinical signs and symptoms. Insulin replacement therapy should be initiated as needed. For type 1 diabetes mellitus with poor blood glucose control, serplulimab should be withheld, and insulin replacement therapy should be initiated until the symptoms are improved. For life-threatening Grade 4 type 1 diabetes, serplulimab must be permanently discontinued. Blood glucose levels should be monitored continuously to ensure appropriate insulin replacement. *Immune-related adverse skin reactions:* have been reported. For Grade 1 or 2 rash, serplulimab can be continued, and symptomatic treatment or local corticosteroids treatment can be given. For Grade 3 rash, serplulimab should be withheld,

and symptomatic treatment or local corticosteroids treatment should be given. For Grade 4 rash, Stevens-Johnson syndrome (SJS), or toxic epidermal necrolysis (TEN), serplulimab should be permanently discontinued. *Immune-related pancreatitis:* Including increases in serum amylase and lipase levels and fatal cases, has been reported. Monitor for changes in serum lipase and amylase (at the beginning of treatment, periodically during treatment, and as indicated based on clinical evaluation), and clinical signs and symptoms of pancreatitis. Serplulimab should be withheld for Grade 3 or 4 increase in serum amylase or lipase levels, and Grade 2 or 3 pancreatitis. For Grade 4 pancreatitis or recurrent pancreatitis of any grade, serplulimab should be permanently discontinued. *Immune-related myocarditis:* Including fatal cases, has been reported. Monitor for clinical signs and symptoms of myocarditis. Suspected immune-mediated myocarditis should be confirmed with myocardial enzyme examinations, and other causes excluded. For Grade 2 myocarditis, serplulimab should be withheld, and corticosteroid treatment should be given. The safety of restarting treatment previously experiencing immune-related myocarditis is unclear. A multidisciplinary discussion is recommended before restarting with previous Grade 2 myocarditis, and the decision should be based on various clinical factors, including the degree of cardiac recovery, oncological response to the treatment, availability of alternative oncology treatments and prognosis. For Grade 3 or 4 myocarditis, serplulimab must be permanently discontinued and corticosteroids therapy should be initiated. Once a diagnosis of myocarditis is established, serplulimab should be withheld or permanently discontinued. Myocardial enzymes and cardiac function should be monitored closely for any grade myocarditis. *Immune-related uveitis:* If uveitis and other immune-mediated adverse reactions occur at the same time, such as Vogt-Koyanagi-Harada syndrome, systemic corticosteroids should be given to prevent permanent blindness. *Other immune-related adverse reactions:* Given the mechanism of action, other potential immune-related adverse reactions may occur. Other fatal and life-threatening immune-mediated adverse reactions have been observed in clinical trials across doses and tumour types: thrombocytopenia, acute coronary syndrome, myocardial infarction and immune-mediated encephalitis. For other suspected reactions, adequate evaluation should be performed to confirm aetiology and exclude other causes. Based on the severity of adverse reactions, serplulimab should be withheld for Grade 2 or 3 immune-related adverse reactions which occur for the first time. For recurrent Grade 3 (except endocrinopathies) and Grade 4 immune-related adverse reactions, serplulimab must be permanently discontinued. Corticosteroids can be initiated as clinically indicated. *Infusion-related reactions:* Monitor for clinical signs and symptoms. Patients with Grade 1 infusion-related reactions may continue administration under close monitoring. The rate of infusion should be reduced, or treatment should be interrupted in patients with Grade 2 infusion-related reactions. Antipyretic and antihistamines may be considered. Treatment may be resumed under close monitoring when Grade 2 infusion-related reactions are controlled. For Grade ≥ 3 infusion-related reactions, infusion should be stopped immediately, treatment should be permanently discontinued, and appropriate treatment should be given. *Patients excluded from clinical trials:* Following conditions were excluded: history of active or prior documented autoimmune disease, patients with active tuberculosis or hepatitis B or C or HIV infection or patients receiving live attenuated vaccine within 28 days prior to serplulimab administration, patients with any active infection requiring systemic anti-infective therapy within 14 days prior to the first dose, history of pneumonitis or interstitial lung disease, patients with active brain metastases, history of significant cardiovascular disease (e.g. myocardial infarction within half a year), a history of hypersensitivity to another monoclonal antibody, systemic immunosuppressive medicinal products within 2 weeks prior to receiving serplulimab. *Excipients:* Contains 0.98 mmol (or 22.5 mg) sodium per 10 ml vial, equivalent to 1.1% of the WHO recommended maximum daily intake of 2 g sodium for an adult. *Patient card:* Prescriber must discuss the risks. Patient will be provided with the patient card with each prescription. *Effects on ability to drive and use machines:* has minor influence. Because of potential adverse reactions such as fatigue, should be advised to use caution when driving or operating machinery until they are certain that serplulimab does not adversely affect them.

Fertility, Pregnancy & Lactation: *Women of childbearing potential/contraception:* Should use effective contraception during treatment and for at least 6 months after the last dose. *Pregnancy:* No data on the use. Therefore, not recommended. *Breastfeeding:* Unknown whether excreted in human milk. The risk to breast-fed infants cannot be excluded, could be used if clinically needed. *Fertility:* Studies have not been performed, effect on male and female is unknown.

Adverse Events include: *Adverse events which could be considered serious:* Neutropenia, leukopenia, anaemia, thrombocytopenia, pneumonia, hyperglycaemia, diabetes mellitus, hyperthyroidism, immune-related lung disease, immune-related colitis, platelet count decrease, urinary tract infection, respiratory tract infection, septic shock, skin infection, enteritis infectious, meningoencephalitis herpetic, coagulation function test abnormal, granulocytopenia, lymphadenitis, infusion-related reaction, anaphylactic reaction, hypothyroidism, thyroiditis, adrenal insufficiency, other thyroid disorder, hyperadrenocorticism, hypophysitis, hypoglycaemia, lipoprotein abnormal, paraesthesia, neuropathy peripheral, immune-mediated encephalitis, neurotoxicity, vision blurred, arrhythmia, sinus tachycardia, sinus bradycardia, cardiac failure, cardiomyopathy, myocardial ischaemia, pericardial effusion, myocardial necrosis marker increased, myocarditis, hypertension, vasculitis, pneumonitis, dyspnoea, diarrhoea, vomiting, dysphagia, gastrointestinal disorder, stomatitis, enteritis, gastritis, immune-mediated pancreatitis, hyperbilirubinaemia, liver injury, pruritus, dermatitis, autoimmune myositis, arthritis, myositis, renal injury, pyrexia, oedema, immune-related lung disease, immune-related colitis, immune-related hepatitis, immune-related nephritis and renal dysfunction, immune-related endocrinopathies, adrenal gland disorders, pituitary disorders, immune-related skin adverse reactions, immune-related pancreatitis, immune-related myocarditis, immune-related uveitis, acute coronary syndrome, myocardial infarction, cardiac failure acute, cardiotoxicity, respiratory failure, proctitis, cholangitis acute, sepsis, infusion-related reactions, rash, thyroiditis.

Other Very Common adverse events: Lymphopenia, hyperlipidaemia, decreased appetite, hypoproteinaemia, hyperuricaemia, electrolyte imbalance, insomnia, cough, nausea, constipation, abdominal pain, alanine aminotransferase increased, aspartate aminotransferase increased, gamma-glutamyltransferase increased, alopecia, musculoskeletal pain, asthenia, blood alkaline phosphatase increased.

Other Common adverse events: Coagulation function test abnormal, thyroid function test abnormal, weight decreased, headache, dizziness, conduction defects, N-terminal prohormone brain natriuretic peptide increased, chest pain, flatulence, dyspepsia, hyperhidrosis, arthralgia, pain in extremity, musculoskeletal discomfort, blood urea increased, protein urine present, haematuria, renal injury, blood creatinine increased, glycosuria, white blood cells urine positive, fatigue, malaise, myoglobin blood increased, blood creatine phosphokinase increased, troponin increased. See SmPC for details of other adverse events.

Presentation and Price: 1 x vial £1321.83

Legal Category: POM

Further information is available from:
Accord-UK Ltd, Whiddon Valley, Barnstaple, Devon, EX32 8NS.

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Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard
Adverse events should also be reported to Accord-UK LTD on 01271 385257 or email medinfo@accord-healthcare.com