LEUSTAT® (cladribine) 1 mg/ml Injection Prescribing Information

Please consult the full Summary of Product Characteristics (SmPC) before Prescribing

Presentation: Each vial contains 10 mg (1 mg/ml) of cladribine for dilution. **Indications:** For the primary or secondary treatment of patients with Hairy Cell Leukaemia (HCL). For the treatment of patients with B-cell chronic lymphocytic leukaemia (CLL) who have not responded to, or whose disease has progressed during or after, treatment with at least one standard alkylating-agent-containing regimen. **Dosage and administration**: *Usual dose:* Adults and elderly: *HCL:* The recommended treatment is a single course of LEUSTAT given by continuous intravenous infusion for 7 consecutive days at a dose of 0.09 mg/kg/day (3.6 mg/m^2/day). Deviations from this dosage regimen are not advised. Physicians should consider delaying or discontinuing the drug if neurotoxicity or renal toxicity occurs. *CLL:* The recommended treatment consists of a continuous intravenous infusion of LEUSTAT for 2 hours on days 1 to 5 of a 28 day cycle at a dose of 0.12 mg/kg/day (4.8 mg/m^2/day). The patient's response to therapy should be determined every 2 cycles of treatment. It is recommended that LEUSTAT be administered in responding patients for 2 cycles after maximum response has occurred, up to a maximum of 6 cycles. Therapy should be discontinued after 2 cycles in non-responding patients. Response for this treatment decision is defined as a lymphocyte reduction of 50% or more, i.e. if lymphocyte count decreases by 50% or more, administer 2 more cycles and re-evaluate response for decision whether to continue with 2 more cycles up to a maximum of 6 cycles. Children: Safety and efficacy in children have not been established. Preparation and administration of intravenous solutions: Must be diluted with the designated diluent prior to administration with aseptic technique and proper environmental precautions. Please refer to SmPC for details. **Contraindications:** Hypersensitivity to cladribine or other components. **Special warnings and precautions**: LEUSTAT is a potent antineoplastic agent with potentially significant toxic side effects. It should be administered under the supervision of a qualified physician experienced in the use of antineoplastic therapy. CLL: Patients whose disease has progressed while treated with fludaribine are unlikely to respond to treatment with LEUSTAT Injection and therefore use is not recommended in such patients. Serious (e.g., respiratory infection, pneumonia and viral skin infections), including fatal infections (e.g., sepsis) have been reported. Active infection should be treated prior to therapy with LEUSTAT. Patients who are or who become Coombs' positive should be monitored carefully for potential haemolysis. Patients should be monitored closely for infections. Those presenting with herpes infections should be treated with acyclovir. For those on sodium free regimens the salt content of LEUSTAT should be taken into consideration (38.2 mg of sodium per vial). Elderly patients should be treated by individual assessment, with careful monitoring of blood counts, renal and hepatic function. Patients with high tumour burden or at risk for the development of hyperuricaemia resulting from tumour breakdown should receive appropriate prophylactic treatment. Allopurinol and adequate hydration should be considered for patients with initially high WBC, to alleviate potential tumour lysis syndrome side effects. *Progressive multifocal leukoencephalopathy (PML):* Cases of PML, including fatal cases, have been reported with cladribine, 6 months to several years after treatment. An association with prolonged lymphopenia has been reported. Physicians should consider PML in the differential diagnosis in patients with new or worsening neurological, cognitive or behavioural signs or symptoms. Patients with suspected PML should not receive further treatment with cladribine. *Bone Marrow Suppression:* Suppression of bone marrow function should be anticipated, is usually reversible and appears to be dose dependent. Proceed carefully in patients with severe bone marrow impairment of any aetiology. Secondary malignancies are a potential risk. Primary haematological malignancies are also a risk factor for secondary malignancies. HCL: Careful haematological monitoring, especially during the first 4 to 8 weeks after treatment with LEUSTAT is recommended. CLL: Careful haematological monitoring is recommended throughout administration of LEUSTAT. *Neurotoxicity:* Serious neurological toxicity (including irreversible paraparesis and quadraparesis) has been reported in patients who received LEUSTAT by continuous infusion at high doses (4 to 9 times the recommended dose for HCL) and reported rarely with the recommended dose. Physicians should consider delaying or discontinuing therapy if neurotoxicity occurs. *Fever/Infection:* HCL: Fever (≥ 37.8°C) was associated with the use of LEUSTAT in approximately 72% (89/124) of patients, most episodes during the first month. Although 70% of patients were treated empirically with parenteral antibiotics, less than a third of febrile events were associated with documented infection. CLL: Pyrexia was reported in 22-24% of CLL patients during Cycle 1 of therapy with LEUSTAT, and in less than 3% of patients during subsequent cycles. Forty of 123 patients (32.5%) reported at least one infection during Cycle 1. Majority of fevers occurred in neutropenic patients, patients should be closely monitored during the first month of treatment and empirical antibiotics should be initiated as clinically indicated. Given the known myelosuppressive effects of LEUSTAT, practitioners should carefully evaluate the risks and benefits of administering this drug to patients with active infections. Since fever may be accompanied by increased fluid loss, patients should be kept well hydrated. *Rare cases of tumour lysis syndrome have been reported in patients with haematological malignancies having a high tumour burden. Effect on Renal and Hepatic Function:* Caution is advised when administering the drug to patients with known or suspected renal or hepatic insufficiency. Monitoring of renal and hepatic function should be performed as clinically indicated, especially in patients with underlying kidney or liver dysfunction. Physicians should consider delaying or discontinuing therapy if renal toxicity occurs. LEUSTAT injection must be diluted in a designated intravenous solution prior to administration. *Laboratory Tests:* During and following treatment, the patient's haematological profile should be monitored regularly to determine the degree of haematopoietic suppression. HCL: bone marrow aspiration and biopsy should be performed to confirm response to treatment with LEUSTAT after peripheral counts have normalised. Febrile events should be investigated with appropriate laboratory and radiological studies. *Interactions:* Caution if administering following or in conjunction with other

drugs known to cause myelosuppression. Not recommended to administer live attenuated vaccines to patients receiving LEUSTAT. Simultaneous administration of nucleoside analogues with cladribine is not advisable. Medicinal products undergoing intracellular phosphorylation, such as antiviral agents, or with inhibitors of adenosine uptake (e.g. didanosine, tenofovir, adefovir) are likely to cause interaction, therefore concomitant use with cladribine is not recommended. **For further information on special warnings, precautions and interactions please refer to SmPC. Pregnancy and lactation:** Should not be given during pregnancy. Women of childbearing potential must use effective contraception during and for 6 months after treatment with LEUSTAT. Men being treated with LEUSTAT should be advised not to father a child up to 6 months after the last LEUSTAT dose. Breastfeeding should not be undertaken during treatment with LEUSTAT injection and for 6 months after the last LEUSTAT dose. **Undesirable effects:** HCL: *Very common (1/10);* headache, nausea, rash, administration site reaction, fatigue and pyrexia. *Common (1/100 to <1/10);* septic shock, secondary malignancies, primary haematological malignancies, haemolytic anaemia, anaemia, febrile neutropenia, hypersensitivity, confusion, anxiety, insomnia, dizziness, conjunctivitis, tachycardia, myocardial ischaemia, pulmonary interstitial infiltrates, breath sounds abnormal, cough, dyspnoea, rales, abdominal pain, constipation, diarrhoea, flatulence, vomiting, urticaria, ecchymosis, hyperhidrosis, petechiae, pruritus, arthralgia, myalgia, pain, renal failure, asthenia, chills, decreased appetite, malaise, muscular weakness, oedema peripheral and contusion. CCL: *Very common (1/10);* headache, administration site reaction, fatigue and pyrexia. *Common (1/100 to <1/10);* septic shock, bacteraemia, cellulitis, localised infection, pneumonia, secondary malignancies, primary haematological malignancies, haemolytic anaemia, anaemia, thrombocytopenia (with bleeding or petechiae), hypersensitivity, confusion, conjunctivitis, phlebitis , pulmonary interstitial infiltrates, breath sounds abnormal, cough, dyspnoea, rales, diarrhoea, nausea, vomiting, urticaria, hyperhidrosis, purpura, rash, pain, renal failure, asthenia, crepitations, localised oedema, muscular weakness, oedema and oedema peripheral. **Legal category**: POM. **Presentation and cost:** 10 ml vial £159.70. **Marketing authorisation holder and number**: Atnahs Pharma UK Limited, Sovereign House, Miles Gray Road, Basildon SS14 3FR, UK. PL 43252/0030. **Date of last revision:** February 2022

Adverse events should be reported. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme 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 Atnahs Pharma UK Limited on +44 (0) 1279 406759 or by email to atnahspv@diamondpharmaservices.com