West of Scotland Cancer Network
Chemotherapy Protocol

Nelarabine for T-cell acute lymphoblastic leukaemia (T-ALL) and T-cell lymphoblastic lymphoma (T-LBL) as a bridge to allogeneic transplantation
(LYMWOS-010/01)

Indication
Treatment of patients with T-ALL and T-LBL whose disease has not responded to, or has relapsed following, treatment with at least two chemotherapy regimens. It is restricted to patients in whom nelarabine is being used as a treatment to bridge to allogeneic stem cell transplant

Eligibility
Inclusion criteria
As Per SMC Guidance Patients must fulfil all three criteria
1. Have a diagnosis of either T-ALL or T-LBL
2. Have failed TWO previous induction regimes i.e. Relapsed or refractory to two separate regimes
3. Have been accepted as Allogeneic HSCT recipient

Absence of CNS disease is a relative requirement. See warnings section

Treatment Intent
Curative

Pre-treatment evaluation
Informed consent, provision of verbal and written information
Assessment of performance status
Height, weight and BSA
Baseline Investigations
• FBC including differential WCC, U+E’s, LFT’s, Urate
• Bone marrow aspirate and trephine
• ECHO to assess cardiac function
• Ideally 24 hour collection for Creatinine Clearance (CrCl) or estimated CrCl via Cockcroft Gault method

Regimen
Adult Dosage: The recommended adult dose of Nelarabine is 1,500 mg/m² administered intravenously over 2 hours on days 1, 3, and 5 repeated every 21 days.

Paediatric Dosage: The recommended paediatric dose of Nelarabine is 650 mg/m² administered intravenously over 1 hour daily for 5 consecutive days repeated every 21 days.

Adolescents: Between 16-21 years old either dosing regime has been adopted. The prescribing physician should consider which regimen is appropriate when treating patients in this age range.
Two cycles of therapy can be administered initially. If patients enter remission then a further two cycles can be administered as consolidation therapy. If the patient is not in remission after two cycles then this should be regarded as a treatment failure.

Nelarabine is not diluted prior to administration. The appropriate dose is transferred into polyvinylchloride (PVC) infusion bags and administered as a two-hour infusion in adult patients and as a one-hour infusion in pediatric patients. Prior to administration, inspect the drug product visually for particulate matter and discoloration.

**Supportive therapy**

Patients receiving nelarabine are recommended to receive intravenous hydration according to standard medical practice for the management of hyperuricemia in patients at risk of tumour lysis syndrome. For patients at risk of hyperuricemia, the use of allopurinol or rasburicase should be considered dependent on disease bulk.

Antimicrobial therapy - as per unit policies for care of neutropenic patients

**Emetogenic Risk**

Moderate (30-90%) Refer to local guideline for management

Is GCSF indicated?

- **Primary prophylaxis** Not recommended
- **Secondary prophylaxis.** GCSF is indicated as supportive therapy in management of febrile neutropenia according to local policy.

**Adverse effects**

Please see SPC for more information.

*Common in adults:* infection, fatigue; gastrointestinal (GI) disorders (nausea, diarrhea, vomiting, and constipation); hematologic disorders (anaemia, neutropenia, and thrombocytopenia); respiratory disorders (cough and dyspnea); nervous system disorders (somnolence and dizziness); and pyrexia.

Neurologic Events: Severe neurologic events have been reported with the use of Nelarabine. These events have included altered mental states including severe somnolence, central nervous system effects including convulsions, and peripheral neuropathy ranging from numbness and paresthesias to motor weakness and paralysis. There have also been reports of events associated with demyelination, and ascending peripheral neuropathies similar in appearance to Guillain-Barré syndrome. Full recovery from these events has not always occurred with cessation of therapy. Close monitoring for neurologic events is essential.

Nelarabine should be discontinued for neurologic events of NCI Common Toxicity Criteria grade 2 or greater.

**Extravasation risk category:**

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<th>Drug</th>
<th>Category</th>
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<td>Nelarabine</td>
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**Contraindications**

History of hypersensitivity to nelarabine or any of its components.

Pregnancy
**Precautions**
Administration with pentostatin or any other adenosine deaminase inhibitors is not recommended – efficacy of nelarabine may be reduced and/or change the adverse event profile of either active substance.

Nelarabine should be administered under the supervision of a physician experienced in the use of antineoplastic therapy.

Barrier contraception should be advised.

**Neurologic Events:**
Nelarabine should be discontinued for neurologic events of NCI Common Toxicity Criteria grade 2 or greater.

Neurotoxicity is the dose-limiting toxicity of Nelarabine. Patients undergoing therapy should be closely observed for signs and symptoms of neurologic toxicity. Common signs and symptoms of nelarabine-related neurotoxicity include somnolence, confusion, convulsions, ataxia, paresthesias, and hypoesthesia. Severe neurologic toxicity can manifest as coma, status epilepticus, craniospinal demyelination, or ascending neuropathy similar in presentation to Guillain-Barré syndrome.

Concurrent CNS therapy is NOT recommended. Patients treated previously or concurrently with intrathecal chemotherapy or previously with craniospinal irradiation may be at increased risk for neurologic adverse events.

**Investigations prior to subsequent cycles**
- FBC including differential WCC, U+E’s, LFT’s, Urate
- performance status
- assessment of toxicity, documented by CTCAE version 3.0
- Weight
- Recalculate BSA if weight has changed by 10% or more from baseline
- Full physical examination including clinical assessment of disease response
- Full neurological assessment

**Dose modifications**

**Haematological**

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<th>Value</th>
<th>Action</th>
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<tr>
<td>Platelets x 10^9/L</td>
<td>&lt; 100</td>
<td>Delay until &gt; 100 – discuss with consultant</td>
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<tr>
<td>Neutrophils</td>
<td>&lt; 1.5</td>
<td>Delay until &gt; 1.5 – discuss with consultant</td>
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**Renal**

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<th>GFR</th>
<th>% of full dose</th>
<th>Comments</th>
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<tr>
<td>&gt; 50 ml/min</td>
<td>100%</td>
<td>Limitation.</td>
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**Hepatic**

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<tr>
<td>Toxicity</td>
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<td>Neurological</td>
<td>NCI CTC 2 or greater</td>
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**Evaluation of response to treatment**

- **Method of evaluation**

  Patients will require bone marrow aspirate and trephine biopsy after each course of therapy. (Morphology, immunophenotyping and cytogenetics)

  In addition, if there was evidence of lymph node involvement, (nodal disease or mediastinal masses), then CT scan will be required.

  All patients are eligible to receive 2 courses of therapy

  1. If not in CR after the initial 2 courses then therapy should be discontinued.

  2. If in CR after 2 courses then allogeneic transplantation should be performed. The patient can receive up to two further cycles while being scheduled for transplantation. In general terms transplant should be performed as soon as possible after CR is achieved. Additional cycles of Nelarabine should not be given if this will delay transplantation in CR.

**References**

1. Scottish Medicines Consortium advice on Nelarabine (454/08), March 2008


5. GlaxoSmithKline product worksheet

Document control

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<tr>
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<th>Dr Andrew Clark</th>
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<tr>
<td>Checked by</td>
<td>Sally McKendrick</td>
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<tr>
<td>Approved by</td>
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