Tumor Lysis Syndrome (TLS) in Adult Patients

Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson's specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care. This algorithm should not be used to treat pregnant women.

**RISK LEVEL**

- **Low Risk**
  - Observation, normal hydration and monitoring

- **Intermediate Risk**
  - Adequate hydration
  - Allopurinol (100-300 mg PO every 8 hours)
  - Consider rasburicase if patient meets criteria (see Appendix B)

- **High Risk**
  - Increase hydration and maintain urine output
  - Consider rasburicase if patient meets criteria (see Appendix B)

**TREATMENT**

- **Low Risk**
  - Observation, normal hydration and monitoring

- **Intermediate Risk**
  - Allopurinol (100-300 mg PO every 8 hours)
  - Consider rasburicase if patient meets criteria (see Appendix B)

- **High Risk**
  - Increase hydration and maintain urine output
  - Consider rasburicase if patient meets criteria (see Appendix B)

**MONITORING/FOLLOW UP**

- **Low Risk**
  - Sodium, potassium, chloride, carbon dioxide (CO₂), BUN, creatinine, calcium², phosphorus², uric acid³, and LDH at least daily throughout chemotherapy treatment, then as clinically indicated post-treatment

- **Intermediate Risk**
  - Sodium, potassium, chloride, CO₂, BUN, creatinine, calcium, phosphorus, uric acid, and LDH at least daily and at least twice daily monitoring of potassium, creatinine, calcium, phosphorus, uric acid, and LDH throughout chemotherapy treatment, then every 1-2 days post-treatment and as clinically indicated

- **High Risk**
  - Manage fluids and electrolyte abnormalities as clinically indicated (see Appendix C)
  - Repeat single dose of rasburicase for uric acid rise to ≥ 7.5 mg/dL
  - Consult Nephrology

**Notes:**

- High Risk patients should NOT be on electrolyte replacement protocols. Use of sodium bicarbonate for alkalinization of urine is currently not recommended for prevention and treatment of TLS.

- Intermediate Risk patients should be on adequate hydration and have the option of getting rasburicase if criteria are met.

- Low Risk patients should be monitored for electrolyte abnormalities and managed as clinically indicated.

- Blood specimens for uric acid levels should be kept on ice after collection and processed immediately.

- Allopurinol dose needs to be adjusted in renal failure. Maximum daily dose of allopurinol is 800 mg/day. Dose adjustments may be necessary if allopurinol is used with other drugs (e.g., mercaptopurine, azathioprine, cyclophosphamide, thiazide and loop diuretics, and warfarin) – Refer to MD Anderson Formulary for a complete list of interactions. Allopurinol should be initiated 24-48 hours prior to chemotherapy when possible.

- Rasburicase must be given 4 hours prior to chemotherapy. For adult patients, rasburicase is to be given at a fixed dose of 3 mg per institutional formulary restrictions; repeat doses are permitted if patient meets restrictions based on repeat lab values prior to each dose.

- Rasburicase is contraindicated in glucose-6 phosphate dehydrogenase deficient patients, known hypersensitivity reactions, hemolytic anemia or methemoglobinemia. Allopurinol should be substituted in these patients.

- Patients with established TLS or high risk and/or renal insufficiency should be closely monitored and have access to Nephrology service and Intensive Care Unit (ICU) in the event that dialysis is required.

---

1. See Appendix A for stratification based on disease type
2. If calcium-phosphorus product ≥ 50 mg²/dL², ensure hydration is maintained and alkalinization is discontinued. Consider consulting Nephrology service, especially if the calcium-phosphorus product continues to rise > 60 mg²/dL².
3. Allopurinol dose needs to be adjusted in renal failure. Maximum daily dose of allopurinol is 800 mg/day. Dose adjustments may be necessary if allopurinol is used with other drugs (e.g., 6-mercaptopurine, azathioprine, cyclophosphamide, thiazide and loop diuretics, and warfarin) – Refer to MD Anderson Formulary for a complete list of interactions. Allopurinol should be initiated 24-48 hours prior to chemotherapy when possible.
4. Rasburicase must be given 4 hours prior to chemotherapy. For adult patients, rasburicase is to be given at a fixed dose of 3 mg per institutional formulary restrictions; repeat doses are permitted if patient meets restrictions based on repeat lab values prior to each dose.
5. Rasburicase is contraindicated in glucose-6 phosphate dehydrogenase deficient patients, known hypersensitivity reactions, hemolytic anemia or methemoglobinemia. Allopurinol should be substituted in these patients.
6. Patients with established TLS or high risk and/or renal insufficiency should be closely monitored and have access to Nephrology service and Intensive Care Unit (ICU) in the event that dialysis is required.
## APPENDIX A: Risk Assessment Based on Disease Type

<table>
<thead>
<tr>
<th>LOW RISK</th>
<th>INTERMEDIATE RISK</th>
<th>HIGH RISK</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Leukemia</strong></td>
<td><strong>Leukemia</strong></td>
<td><strong>Leukemia</strong></td>
</tr>
<tr>
<td>● CLL receiving only alkylating agents</td>
<td>● AML with WBC &lt; 25 K/microliter</td>
<td>● ALL</td>
</tr>
<tr>
<td>● CML (excluding blast crisis)</td>
<td>● CLL receiving targeted and/or biological therapies</td>
<td>● AML with WBC ≥ 25 K/microliter</td>
</tr>
<tr>
<td><strong>Lymphoma</strong></td>
<td><strong>Lymphoma</strong></td>
<td><strong>Lymphoma</strong></td>
</tr>
<tr>
<td>● Anaplastic large-cell lymphoma</td>
<td>● DLBCL with LDH greater than upper limit of normal (non-bulky)</td>
<td>● Burkitt’s leukemia</td>
</tr>
<tr>
<td>● DLBCL with LDH within normal limits (WNL)</td>
<td>● Mantle cell lymphoma (blastoid variants) with LDH greater than upper limit of normal (non-bulky)</td>
<td>● CML-BC</td>
</tr>
<tr>
<td>● Mantle cell lymphoma (blastoid variants) with LDH WNL</td>
<td>● Peripheral T-cell lymphoma with LDH greater than upper limit of normal (non-bulky)</td>
<td>● CLL treated with venetoclax and ALC ≥ 25 K/microliter or bulky lymph nodes</td>
</tr>
<tr>
<td>● Peripheral T-cell lymphoma with LDH WNL</td>
<td>● T-cell lymphoma with LDH greater than upper limit of normal (non-bulky)</td>
<td>● Anaplastic large-cell lymphoma</td>
</tr>
<tr>
<td>● T-cell lymphoma with LDH WNL</td>
<td>● Transformed lymphoma with LDH greater than upper limit of normal (non-bulky)</td>
<td>● DLBCL with LDH greater than upper limit of normal (bulky)</td>
</tr>
<tr>
<td>● Transformed lymphoma with LDH WNL</td>
<td>● Cutaneous T-cell lymphoma</td>
<td>● Mantle cell lymphoma (blastoid variants) with LDH greater than upper limit of normal (bulky)</td>
</tr>
<tr>
<td>● Cutaneous T-cell lymphoma</td>
<td>● Follicular lymphoma</td>
<td>● Peripheral T-cell lymphoma with LDH greater than upper limit of normal (bulky)</td>
</tr>
<tr>
<td>● Follicular lymphoma</td>
<td>● Hodgkin lymphoma</td>
<td>● Transformed lymphoma with LDH greater than upper limit of normal (bulky)</td>
</tr>
<tr>
<td>● Mantle cell lymphoma (non-blastoid variants)</td>
<td>● Marginal zone B-cell lymphoma</td>
<td>● Early stage lymphoblastic lymphoma with LDH less than 2 times upper limit of normal</td>
</tr>
<tr>
<td>● Marginal zone B-cell lymphoma</td>
<td>● Small lymphocytic lymphoma</td>
<td>● Advanced Stage lymphoblastic lymphoma</td>
</tr>
<tr>
<td>● Small lymphocytic lymphoma</td>
<td></td>
<td>● Burkitt’s lymphoma</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td><strong>Other</strong></td>
<td><strong>Other</strong></td>
</tr>
<tr>
<td>● Solid tumors (excluding neuroblastomas, germ-cell tumors, and small cell lung cancer)</td>
<td>● Neuroblastoma</td>
<td>● Myeloma with extramedullary disease and LDH greater than upper limit of normal</td>
</tr>
<tr>
<td>● Multiple myeloma</td>
<td>● Germ-cell tumors</td>
<td>● Myelofibrosis - Intermediate-2 risk or High-risk disease</td>
</tr>
<tr>
<td>● MDS</td>
<td>● Small cell lung cancer</td>
<td>● Plasma cell leukemia</td>
</tr>
</tbody>
</table>

---

**Notes:**

1. Renal dysfunction elevates the patient to the next risk level.
2. Bulky disease is defined as any mass ≥ 7.5 cm.
## APPENDIX B: Rasburicase Criteria for Use

<table>
<thead>
<tr>
<th>Criteria for Use</th>
<th>Risk Factors</th>
</tr>
</thead>
</table>
| • Uric acid > 7.5 mg/dL plus at least two risk factors or  
  • Uric acid ≤ 7.5 mg/dL plus at least three risk factors | • High risk disease (see Appendix A)                                         |
|                                               | • Creatinine > 1.3 mg/dL or > 50% increase from baseline                     |
|                                               | • WBC > 50 K/microliter                                                    |
|                                               | • Lactate dehydrogenase greater than 2 times the upper limit of normal (ULN)|

1 Criteria based on MD Anderson Formulary Restriction
### APPENDIX C: Suggested Guide for Management of Electrolyte Abnormalities

<table>
<thead>
<tr>
<th>Abnormality</th>
<th>Management Recommendations</th>
</tr>
</thead>
</table>
| **Hyperphosphatemia**             | • Restrict phosphorus intake (avoid IV and PO phosphorus; limit dietary sources)  
• If tolerating oral intake, administer phosphate binder (select one):  
  ○ Sevelamer (Renagel®, Renvela®) 800-1,600 mg PO three times a day with meals  
  ○ Aluminum hydroxide 300-600 mg PO three times a day with meals (avoid with renal dysfunction)  
| Moderate (phosphorus ≥ 6 mg/dL)   | Dialysis may be needed in severe cases                         |
| Severe                            | No therapy                                                    |
| **Hypocalcemia** (calcium ≤ 7 mg/dL or ionized calcium ≤ 0.8 mmol/L) | To avoid calcium phosphate precipitation, asymptomatic patients with acute hypocalcemia and hyperphosphatemia should not be given calcium repletion until phosphorous level has normalized |
| Asymptomatic                      | No therapy                                                    |
| Symptomatic                       | Calcium gluconate 1 gram via slow IV infusion with EKG monitoring |
| **Uremia (elevated BUN with altered mental status)** | Fluid and electrolyte management  
  • Uric acid and phosphate management  
  • Adjust doses for renally excreted medications  
  • Dialysis |

Continued on next page
### Hyperkalemia

**Moderate (potassium 5-6 mmol/L) and asymptomatic**
- Restrict potassium intake (avoid IV and PO potassium; limit dietary intake)
- EKG and cardiac rhythm monitoring
- If tolerating oral intake, administer potassium binder<sup>1</sup>
  - Sodium polystyrene sulfonate (Kayexalate®)
    - 15-30 grams PO; repeat every 4 or 6 hours depending upon follow-up potassium levels
  - Patiromer sorbitex calcium (Veltassa®)
    - 8.4 grams once daily PO; may increase frequency based on potassium levels; adjust dose at ≥ 1-week intervals in increments of 8.4 grams (maximum dose: 25.2 grams/day)
  - Sodium zirconium cyclosilicate (Lokelma®)<sup>2</sup>
    - 10 grams 3 times daily PO for up to 48 hours; adjust dose by 5 grams daily at 1-week intervals as needed based on potassium (maximum maintenance dose: 15 grams/day)

**Severe (potassium > 6 mmol/L) and/or symptomatic**
- Same as moderate, plus:
  - Concurrent EKG changes: calcium gluconate 1 gram via slow IV infusion; may be repeated after 5-10 minutes if EKG changes persist
  - To temporarily shift potassium intracellularly
    - IV insulin and dextrose
      - 0.1 units/kg of regular insulin IV followed by 25-50 grams of D50W IV based on pre-treatment glucose. Hold D50W if glucose > 250 mg/dL. See IP Hyperkalemia order set.
    - Monitor blood glucose closely
    - Sodium bicarbonate
      - 50 mEq via slow IV infusion
      - Can be used if patient is acidemic (arterial pH < 7.35); however sodium bicarbonate and calcium should not be administered through the same lumen
    - Albuterol
      - 10-20 mg in 4 mL saline via nebulizer over 20 minutes or 10-20 puffs via MDI over 10-20 minutes
      - Avoid in patients with acute coronary disease

---

<sup>1</sup> Risk for use includes intestinal necrosis. High risk patient populations for intestinal necrosis include those with post-operative bowel motility disorders or with ileus, small or large bowel obstruction, or ulcerative colitis.

<sup>2</sup> Avoid sodium zirconium cyclosilicate (Lokelma®) in patients with volume overload; may worsen heart failure and/or pulmonary edema.


Tumor Lysis Syndrome (TLS) in Adult Patients

Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson’s specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient’s care. This algorithm should not be used to treat pregnant women.

DEVELOPMENT CREDITS

This practice consensus statement is based on majority opinion of the Tumor Lysis workgroup at the University of Texas MD Anderson Cancer Center for the patient population. These experts included:

Core Development Team Leads
Sandra B. Horowitz, PharmD (Pharmacy Clinical Programs)
Nicholas J. Short, MD (Leukemia)

Workgroup Members
Ala Abudayyeh, MD (Nephrology)
Janine Douglas, PharmD (Pharmacy Medication Management & Informatics)
Olga N. Fleckenstein, BS*
Stacey M. Sobocinski, PharmD (Pharmacy)
Mary Lou Warren, DNP, APRN, CNS-CC*

*Clinical Effectiveness Development Team