Tumor Lysis Syndrome (TLS) in Pediatric 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.*

PATIENT PRESENTATION	TREATMENT	MONITORING/FOLLOW UP
Low Risk[1]	• Hydration 1 to 2 L/m^2 per day[2] • Initial management with allopurinol[3] • Sodium, potassium[4], chloride, CO_2, BUN, creatinine, total calcium[5,6], phosphorus[5], uric acid[7], and serum LDH every 12-24 hours throughout chemotherapy treatment, then as clinically indicated post-treatment	Manage fluids and electrolyte abnormalities as clinically indicated (see Appendix B)
Intermediate Risk[1]	• Hydration 2 to 3 L/m^2 per day of IV fluid[2]; 200 mL/kg per day in children weighing ≤ 10 kg • Initial management allopurinol[3] with or without rasburicase[8,9]. Consider rasburicase in patients with pre-existing hyperuricemia (uric acid > 7 mg/dL) or pre-existing renal failure treatment[8,9]. • Sodium, potassium[4], chloride, CO_2, BUN, creatinine, total calcium[5,6], phosphorus[5], uric acid[7], and serum LDH every 6-8 hours throughout chemotherapy treatment, then as clinically indicated post-treatment	
High Risk[1]	• Hydration 2 to 3 L/m^2 per day of IV fluid[2]; 200 mL/kg per day in children weighing ≤ 10 kg • Initial management with rasburicase[8,9] • Transfer to PICU if indicated • Sodium, potassium[4], chloride, CO_2, BUN, creatinine, total calcium[5,6], phosphorus[5], uric acid[7], VBG +, and serum LDH every 6-8 hours throughout chemotherapy treatment, then as clinically indicated post-treatment • Consider Nephrology consult[10]	• Manage fluids and electrolyte abnormalities as clinically indicated (see Appendix B) **and** • Repeat single dose of rasburicase[8,9] for uric acid[7] rise to 7.5 mg/dL or greater

VBG = venous blood gas

Note: These 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 Tumor Lysis Syndrome (TLS).

[1] See Appendix A for stratification based on risk factors

[2] Adequate hydration should be based on clinical judgment and monitoring including urine output. Goal urine output is 4-6 mL/kg/hour if weight ≤ 10 kg and 1-3 mL/kg/hour if weight > 10 kg.

[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 Cancer Center Pharmacy Formulary for a complete list of interactions. Allopurinol should be initiated 24-48 hours prior to chemotherapy when possible.

[4] If potassium > 6 mg/dL, consider verifying results with STAT VBG+ and obtain EKG

[5] If calcium-phosphorus product is ≥ 50 mg^2/dL^2, ensure hydration is maintained. Consider consulting Nephrology service, especially if the calcium-phosphorus product continues to rise above 60 mg^2/dL^2.

[6] If total calcium < 7 mg/dL, check ionized calcium

[7] Blood specimens for uric acid levels should be kept on ice after collection and prior to testing and processed immediately

[8] Rasburicase must be given 4 hours prior to chemotherapy. Rasburicase is given as a single dose of 0.1-0.2 mg/kg. The maximum dose is 6 mg and should be repeated, only if necessary, based on laboratory values and clinical situation.

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

[10] Patients with established TLS or high risk and/or renal insufficiency should be closely monitored and have access to Nephrology service and PICU in case dialysis is required

Department of Clinical Effectiveness V1
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APPENDIX A: Patient Stratification by Risk

DIAGNOSIS/CONDITION	HIGH	INTERMEDIATE	LOW
Lymphoma	Burkitt's lymphoma	Diffuse large B-cell lymphoma	
Acute lymphoid leukemia	White blood count > 100 x 10^9/L	White blood count between 50-100 x 10^9/L	White blood count < 50 x 10^9/L
Acute myeloid leukemia	White blood count > 50 x 10^9/L monblastic	White blood count between 10-50 x 10^9/L	White blood count < 10 x 10^9/L
Other hematologic malignancies (CML) Solid Tumor		Rapid proliferation with expected rapid response to therapy	Remainder of patients
Baseline uric acid	Uric acid ≥ 7.5 mg/dL	Uric acid < 7.5 mg/dL	
Renal injury (new or pre-existing renal disease)	Dehydration, acidosis, acidic urine		

APPENDIX B: Management of Fluid and Electrolyte Abnormalities

Abnormality	Management Recommendations
Acute kidney injury	• Normal Saline 20-60 mL/kg IV bolus then titrate to urine output goal • Consider dialysis in oliguric renal failure unresponsive to IV fluids or with congestive heart failure
Hyperkalemia	
Potassium > 5 mg/dL	• Remove all potassium in IV fluids and discontinue any potassium sparing diuretics • Continuous EKG monitoring • Renal diet
Potassium > 6 mg/dL	All of the above, PLUS: • Consult PICU and Nephrology • Calcium ◦ Calcium chloride 20 mg/kg [maximum dose of 1 gram (13.6 mEq calcium)] IV via central line ◦ Calcium gluconate (if no central access) 100-200 mg/kg/dose [maximum dose 2 grams (9.3 mEq calcium)] IV • Furosemide 0.5-1 mg/kg (maximum single dose of 40 mg) IV ◦ Consider lower dosing in furosemide naïve patients • To temporary shift potassium intracellularly: ◦ Sodium bicarbonate (if carbon dioxide < 17 mEq/L or pH < 7.35)1 mg/kg (maximum 50 mEq per dose) IV via central line ◦ Nebulized Albuterol 2.5 mg/3 mL nebulization - Avoid if tachycardia or in hemodynamically unstable patients ◦ Insulin/glucose 0.1 units/kg regular insulin followed by 1 mL/kg D50W IV via central line - If no central access, may use 10 mL/kg of D10W IV - Repeat POC glucose after 15, 30 and 60 minutes • Dialysis for refractory hyperkalemia

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APPENDIX B: Management of Fluid and Electrolyte Abnormalities - continued

Abnormality	Management Recommendations
Hyperphosphatemia	
Phosphorous > 6.5 mg/dL	• Phosphate binders ◦ Sevelamer dosing based on BSA - BSA ≤ 0.75 m^2: 400 mg PO three times a day with meals - BSA between 0.75-1.2 m^2: 800 mg PO three times a day with meals - BSA ≥ 1.2 m^2: 1,600 mg PO three times a day with meals • Renal diet
Phosphorous > 10 mg/dL **or** Ca-phosphate product > 70 mg^2/dL^2	• Nephrology consult for refractory hyperphosphatemia • Dialysis
Hypocalcemia	
Total calcium < 7 mg/dL or ionized calcium < 0.9 mmol/L	**Do NOT treat hypocalcemia if asymptomatic unless the indication for calcium is also hyperkalemia** (see Page 3) • **Only treat if symptomatic:** EKG changes (prolonged QTc), tetany or seizure • Calcium chloride 20 mg/kg [maximum dose of 1 gram (13.6 mEq calcium)] IV via central line • Calcium gluconate (if no central access) 100-200 mg/kg/dose [maximum dose of 2 grams (9.3 mEq calcium)] IV
Uremia (renal dysfunction)	
BUN > 30 mg/dL	• Strict input/output every 4 hours • Daily weight • Uric acid and phosphate management • Dose adjust medications as indicated • Renal diet • PICU and Nephrology consult • Dialysis if indicated

SUGGESTED READINGS

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