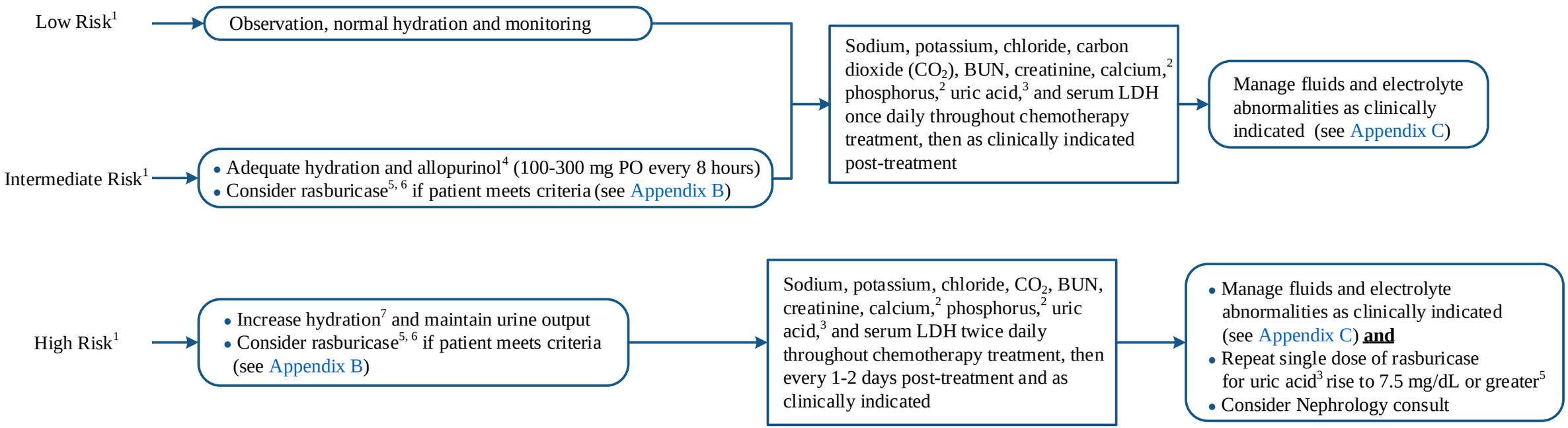
Tumor Lysis Syndrome (TLS) in Adult Patients

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.*



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 disease type

[2] If calcium-phosphorus product is greater than or equal to 50 mg^2/dL^2, ensure hydration is maintained and alkalinization is discontinued. Consider consulting renal service, especially if the calcium-phosphorus product continues to rise above 60 mg^2/dL^2.

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

[4] 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.

[5] Rasburicase must be given 4 hours prior to chemotherapy. For adult patients, it 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.

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

[7] Patients with established TLS or high risk and/or renal insufficiency should be closely monitored and have access to renal team and ICU unit in case dialysis is required

Department of Clinical Effectiveness V2
Approved by The Executive Committee of the Medical Staff on 11/27/2018

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APPENDIX A: Risk Assessment Based on Disease Type

Low Risk (less than 1% risk of tumor lysis):

- AML with WBC less than 25 K/microliter and serum LDH level less than two times the upper limit of normal
- CLL with a WBC less than 50 K/microliter and treated with alkylating agents only
- Multiple myeloma
- CML chronic-phase
- Adult intermediate-grade Non-Hodgkin's, Hodgkin's, small lymphocytic, follicular, marginal zone B-cell, mantle cell (non-blastoid variant), and cutaneous T-cell lymphomas, and serum LDH level within normal limits
- Most solid tumors

Intermediate Risk (1-5% risk of tumor lysis):

- Adult T-cell lymphoma, peripheral T-cell lymphoma, diffuse large B-cell lymphoma, transformed lymphoma, or mantle cell lymphoma with serum LDH level above the upper limit of normal, but without bulky disease
- Early stage Burkitt's lymphoma/leukemia and lymphoblastc lymphomas with serum LDH level less than two times the upper limit of normal
- ALL with WBC less than 100 K/microliter and serum LDH level less than two times the upper limit of normal
- AML with WBC at least 25 K/microliter, but less than 100 K/microliter
- AML with WBC less than 25 K/microliter and LDH greater than or equal to two times the upper limit of normal
- Early stage lymphoblastic lymphoma with serum LDH level less than two times the upper limit of normal
- CLL treated with targeted and biological therapies (fludarabine or rituximab) and/or those with high WBC (greater than or equal to 50 K/microliter)
- CLL treated with venetoclax (dependent upon tumor size and absolute lymphocyte count)[1]
- Patients with lymphoma/leukemia with low-risk disease with renal dysfunction and/or renal involvement
- Rare bulky solid tumors that are sensitive to chemotherapy (such as neuroblastoma, germ cell cancer)

High Risk (greater than 5% risk of tumor lysis):

- Advanced stage Burkitt's lymphoma/leukemia or early stage Burkitt's lymphoma/leukemia with serum LDH two or more time the upper limit of normal
- ALL with WBC greater than or equal to 100 K/microliter and/or serum LDH greater than or equal to two times the upper limit of normal
- AML with WBC greater than or equal to 100 K/microliter
- Stage III or IV lymphoblastic lymphoma or early stage lymphoblastic lymphoma with serum LDH level two or more times the upper limit of normal
- Any adult T-cell lymphoma, peripheral T-cell lymphoma, diffuse large B-cell lymphoma, transformed lymphoma, mantle cell lymphoma with serum LDH level above the upper limit of normal with a bulky tumor mass, or myeloma with extra medullary disease
- Stage III or IV diffuse large B-cell lymphoma with serum LDH level greater than or equal to two times the upper limit of normal
- CLL treated with venetoclax (dependent upon tumor size and absolute lymphocyte count)[1]
- Plasma cell leukemia

[1] See venetoclax prescribing information for further details

APPENDIX B: Rasburicase Criteria for Use[1]

Criteria for Use	Risk Factors
• Serum uric acid greater than 7.5 mg/dL plus at least two risk factors • Serum uric acid less than or equal to 7.5 mg/dL plus at least three risk factors	• High risk disease (see Appendix A) • Serum creatinine greater than 1.3 mg/dL or greater than 50% increase from baseline • White blood cell count greater than 50 K/uL • 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

Abnormality	Management Recommendations
Hyperphosphatemia	
Moderate (greater than or equal to 6 mg/dL)	• Restrict phosphorus intake (avoid IV and PO phosphorus; limit dietary sources) • Administer phosphate binder: ◦ Sevelamer (Renagel®, Renvela®) 800-1,600 mg PO three times a day with meals ◦ Lanthanum carbonate (Fosrenol®) 500-1,000 mg PO three times a day with meals ◦ Aluminum hydroxide 300-600 mg PO three times a day with meals (avoid with renal dysfunction)
Severe	Dialysis may be needed in severe cases
Hypocalcemia (calcium less than or equal to 7 mg/dL or ionized calcium less than or equal to 0.8 mmol/L)	
Asymptomatic	No therapy To avoid calcium phosphate precipitation, asymptomatic patients with acute hypocalcemia and hyperphosphatemia should not be given calcium repletion until phosphorous level has normalized
Symptomatic	Calcium gluconate 1 gram via slow IV infusion with EKG monitoring

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APPENDIX C: Suggested Guide for Management of Electrolyte Abnormalities - continued

Abnormality	Management Recommendations
Hyperkalemia	
Moderate (6 mEq/L – 7 mEq/L) **and** asymptomatic	• Restrict potassium intake (avoid IV and PO potassium; limit dietary intake) • EKG and cardiac rhythm monitoring • Sodium polystyrene sulfonate (Kayexalate®) ◦ Give 15-30 grams PO ◦ Repeat every 4 or 6 hours depending upon follow-up potassium levels
Severe (greater than 7 mEq/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 - Give 10 units of regular insulin in 500 mL of $D_{10}W$ IV infused over 60 minutes - Monitor blood glucose closely ◦ Sodium bicarbonate - Give 50 mEq via slow IV infusion - Can be used if patient is acidemic; however sodium bicarbonate and calcium should not be administered through the same lumen ◦ Albuterol - Give 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
Uremia (renal dysfunction)	
	• Fluid and electrolyte management • Uric acid and phosphate management • Adjust doses for renally excreted medications • Dialysis

SUGGESTED READINGS

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