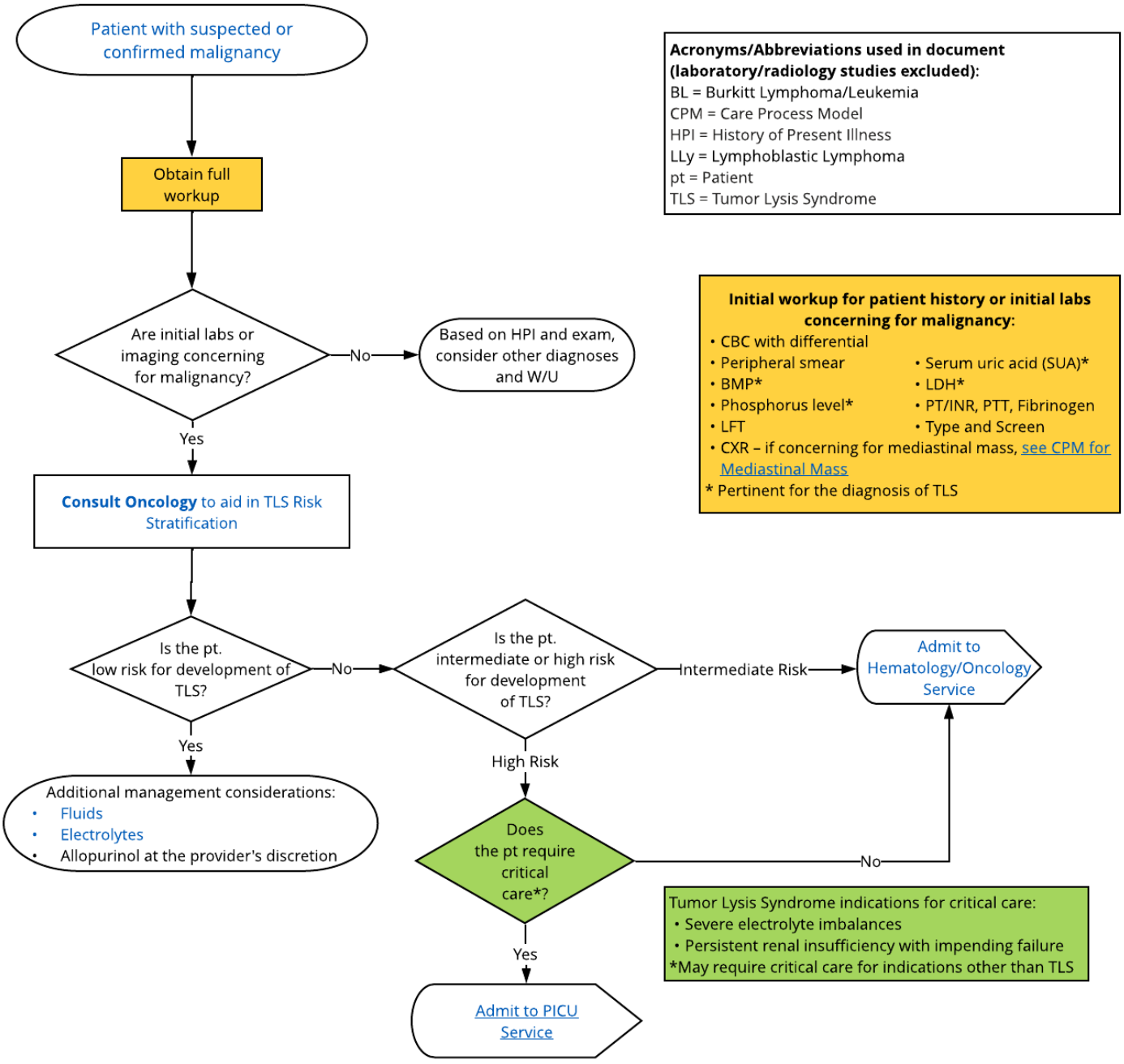
Tumor Lysis Syndrome (TLS)
Clinical Practice Guideline Committee

Algorithm: TLS Risk Stratification



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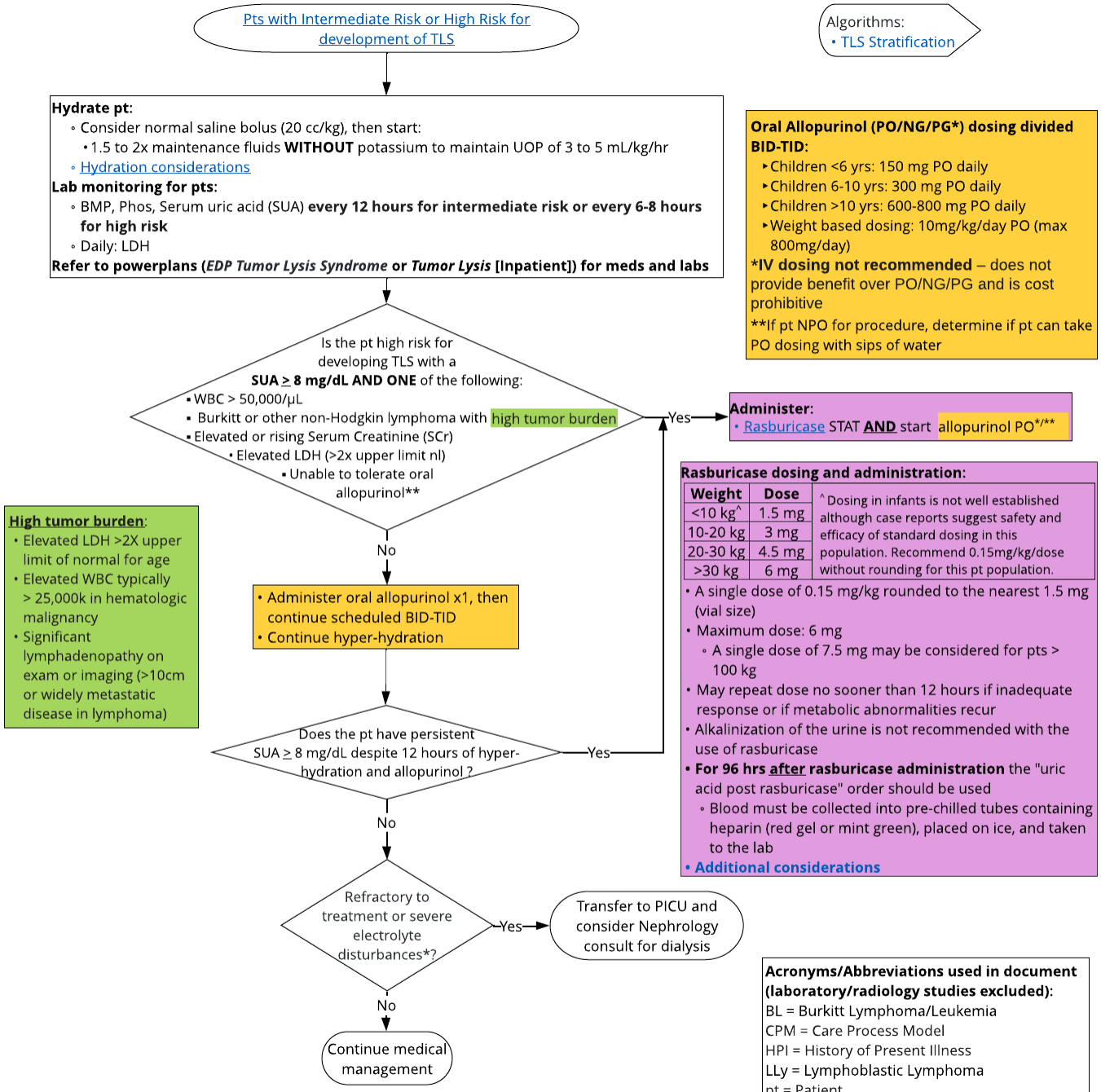
Algorithm TLS Intermediate/High Risk



Acronyms/Abbreviations used in document (laboratory/radiology studies excluded):
BL = Burkitt Lymphoma/Leukemia
CPM = Care Process Model
HPI = History of Present Illness
LLy = Lymphoblastic Lymphoma
pt = Patient
TLS = Tumor Lysis Syndrome
UOP = Urine output

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Clinical Practice Guideline (CPG) Objective

The objective of this CPG is to improve and standardize the care of children with newly diagnosed and newly relapsed malignancies at risk of tumor lysis syndrome (TLS).

Background

Tumor Lysis Syndrome (TLS) is a life-threatening oncologic emergency. Patients at highest risk for TLS include those with bulky disease, high tumor burden, chemo-sensitive malignancies, and those with pre-existing metabolic derangements. Patients with newly diagnosed and newly relapsed hematologic malignancies, such as leukemia and lymphoma, are at the highest risk. TLS causes metabolic derangements and hyperuricemia that can lead to subsequent renal compromise. Treatment of TLS includes aggressive fluid hydration, allopurinol, and at times rasburicase. Rasburicase is costly and may be avoided in patients without other metabolic derangements or renal compromise. Stratification of patients into low, moderate, and high risk for the development of tumor lysis allows for standardized management strategies.

Target Users

- Emergency Medicine, Urgent Care, Pediatric Intensive Care and Oncology providers
- Oncology Fellows
- House Staff
- Pediatric Nurse Practitioners

Target Population

Guideline Inclusion Criteria

- Patients with suspected or newly diagnosed or newly relapsed malignancy should be screened for TLS.

Guideline Exclusion Criteria

- Non oncologic diagnoses associated with hyperuricemia (i.e., hemolytic uremic syndrome, chronic renal failure, etc.)

AGREE

Two international guidelines (Jones et al., 2015; New South Wales Government, 2018) and one national guideline (Cairo et al., 2010) provided guidance to the Tumor Lysis CPG Committee. See Tables 1-3 for AGREE II.

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Table 1.
AGREE II[a] Summary for the British Committee for Standards in Haematology (Jones et al., 2015)

Domain	Percent Agreement	Percent Justification
Scope and purpose	100%	The aim of the guideline, the clinical questions posed and target populations **were** identified.
Stakeholder involvement	54%	The guideline **did not** describe who created the guideline nor were the views/preferences of the target population.
Rigor of development	46%	Search strategy was weak, GRADE was not used to identify strengths and limitations of the evidence, an explicit link between the evidence and the recommendations was not included, unable to ascertain if guideline is currently used or obsolete.
Clarity and presentation	93%	The guideline recommendations **are** clear, unambiguous, and easily identified.
Applicability	41%	The guideline **did not** provide how it should be disseminated or implemented; nor were facilitators or barriers discussed. Treatment monitoring recommendations **were** identified.
Editorial independence	92%	COI and funding sources were stated; however, it is **unclear** if the recommendations were biased by competing interests.
Committee's recommendation for guideline use	Yes	

Note: Four EBP Scholars completed the AGREE II on this guideline.

Table 2.
AGREE II[a] Summary for the New South Wales Guideline (New South Wales Government, 2018)

Domain	Percent Agreement	Percent Justification
Scope and purpose	56%	The aim of the guideline **was** identified. The clinical questions posed and target populations **were not** found in the guideline.
Stakeholder involvement	15%	The guideline **did not** identify the authors nor were the viewpoints of the intended user sought.
Rigor of development	28%	Search strategy found on website, evidence selection/strength/limitations not described, formation of recommendations not described, linkage between evidence and recommendations not discussed; external review process not discussed; guideline update process is not detailed
Clarity and presentation	93%	The guideline recommendations, with specific dosing, **are** clear, unambiguous, and easily identified.
Applicability	46%	The guideline **did not** provide how it should be disseminated or implemented; nor were facilitators or barriers discussed. Treatment monitoring recommendations **were** identified.
Editorial independence	6%	COI and funding sources **were not** stated.
Committee's recommendation for guideline use	Yes	

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Table 3.
AGREE II[a] Summary for the Recommendations for the Evaluation of Risk and Prophylaxis of Tumour Lysis Syndrome (Cairo et al., 2010)

Domain	Percent Agreement	Percent Justification
Scope and purpose	88%	The aim of the guideline **was** identified. The clinical questions posed **was not** found in the guideline.
Stakeholder involvement	71%	The guideline group **was** comprised of either adult or pediatric hematologists/oncologists with one internal medicine representative. There **does not** appear to be representatives from nephrology, emergency medicine or patient/family.
Rigor of development	42%	Search strategies/engines employed **were not** discussed, how the evidence selection occurred **was not** discussed, Oxford level of evidence used (gold standard at time), majority of the guideline focused on risk stratification while prophylactic care is within the discussion, linkage between evidence and recommendations **were not** explicitly stated, external review **was not** described, guideline review update **not** disclosed.
Clarity and presentation	93%	The guideline recommendations, with specific dosing, **are** clear, unambiguous, and easily identified.
Applicability	18%	The guideline **did not** provide how it should be disseminated or implemented; facilitators and or barriers **were not** discussed nor were treatment monitoring recommendations identified.
Editorial independence	25%	COI and funding sources **were not** stated.
Committee's recommendation for guideline use	Yes	

Note: Four EBP Scholars completed the AGREE II on this guideline.

Care Questions Answered
No clinical questions were posed for this review.

Measures
In coordination with the Hematology, Oncology and Blood and Marrow Transplantation Service the following measures are being monitored:

- Adherence to rasburicase administration and dosing guidelines.
- Prompt administration of allopurinol following rasburicase to avoid re-accumulation of uric acid.
- Appropriate usage of post-rasburicase laboratory order.
- Others?

Practice Recommendations
Children's Mercy TLS CPG Committee adopted the practice recommendations made by Cairo et al (2010) and substantiated by the two international guidelines (Jones et al., 2015; New South Wales Government, 2018).

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Cost Implications

The following potential improvements may reduce costs and resource utilization for healthcare facilities and reduce healthcare costs. Except for IV allopurinol, rasburicase administration involves a greater cost when compared with other preventative strategies, with no associated reduction in mortality or the need for renal support. Rasburicase costs $2,441 for a 4.5mg dose at our institution. IV allopurinol costs $7,067 for two 150mg doses. Oral allopurinol costs less than a dollar a day.

- Decreased risk of overdiagnosis
- Decreased risk of overtreatment
- Decreased frequency of admission
- Decreased inpatient length of stay
- Decreased unwarranted variation in care

Organizational Barriers

- Variability of acceptable level of risk among providers

Organizational Facilitators

- Collaborative engagement across care settings in CPG development
- Standardized order set for Emergency Department and Inpatient stay

Order Sets

- Inpatient plan: *Tumor Lysis* (See Appendix A)
- EDP Powerplan (See Appendix B)

Guideline Preparation

This guideline was prepared by the Evidence Based Practice (EBP) Department in collaboration with subject matter experts at Children's Mercy Kansas City. The development of this guideline supports the Service and Performance Excellence initiative to promote care standardization that builds a culture of quality and safety that is evidenced by measured outcomes. If a conflict of interest is identified, the conflict will be disclosed next to the committee member's name.

Additional Review & Feedback

- The CPG was presented to each division or department represented on the CPG committee as well as other appropriate stakeholders. Feedback was incorporated into the final product.
- The CPG was reviewed by an internal and external reviewer using the AGREE II instrument (see Appendix C).

Implementation & Follow-Up

Once approved, the guideline and power plans were presented to appropriate care teams and implemented. Care measurements will be assessed and shared with appropriate care teams to determine if changes need to occur. This guideline is scheduled for revision in 2025.

Committee Members and Representation

- Nicole Wood, DO | Department of Hematology, Oncology and Blood and Marrow Transplantation | Committee Chair
- Keith August, MD, MS | Department of Hematology, Oncology and Blood and Marrow Transplantation | Committee member
- Jay Rilinger, MD | Department of Critical Care Medicine | Committee member
- Allison Hadley, MD | Department of Emergency Medicine | Committee member
- Mary Haywood, DO | Department of Emergency Medicine | Committee member

MIT Committee Members

- George Abraham, MD | Emergency Medicine, Medical Informatics
- Tammy Frank, RPh, CPHIMS | Medical Informatics - Pharmacy

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- Brandan Kennedy, MD | Hospital Medicine, Human Factors Collaborative, Medical Informatics
- Amber Lanning | Medical Informatics – general inpatient
- Tracy Taylor | Medical Informatics – ED, UCC

EBP Committee Members

- Todd Glenski, MD, MSHA, FASA | Department of Anesthesiology and Department of Evidence Based Practice
- Jacqueline A. Bartlett, PhD, RN | Department of Evidence Based Practice

Guideline Development Funding

The development of this guideline was underwritten by the Department of EBP and the divisions of Hematology, Oncology and Blood and Marrow Transplantation, Critical Care Medicine, and Emergency Medicine.

Approval Process

This guideline was reviewed and approved internally by Hematology, Oncology and Blood and Marrow Transplantation, Critical Care Medicine, Emergency Medicine, the TLS CPG Committee, the EBP Department, Medical Executive, and other appropriate hospital committees deemed suitable for this guideline's intended use. Guidelines are reviewed and updated as necessary every 3 years within the EBP Department at CMKC. Content expert committees will be involved with every review and update.

Approval Obtained

Department/Unit	Date Approved
Hem/Onc	April 13, 2022
PICU	June 22, 2022
Emergency Medicine	July 6, 2022
Medical Executive Committee	August 3, 2022

Version History

Date	Comments
8/2022	Version one: Established a guideline using the British Committee for Standards in Haematology (Jones et al., 2015), the New South Wales Guideline (New South Wales Government, 2018), and the Summary for the Recommendations for the Evaluation of Risk and Prophylaxis of Tumour Lysis Syndrome (Cairo et al., 2010) as foundational guidelines.

Disclaimer

When evidence is lacking or inconclusive, options in care are provided in the guideline and the power plans that accompany the guideline.

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Planned Review Date:

8/2025

References

Cairo, M. S., Coiffier, B., Reiter, A., & Younes, A. (2010). Recommendations for the evaluation of risk and prophylaxis of tumour lysis syndrome (TLS) in adults and children with malignant diseases: an expert TLS panel consensus. *Br J Haematol*, *149*(4), 578-586. https://doi.org/10.1111/j.1365-2141.2010.08143.x

Jones, G. L., Will, A., Jackson, G. H., Webb, N. J., Rule, S., & British Committee for Standards in, H. (2015). Guidelines for the management of tumour lysis syndrome in adults and children with haematological malignancies on behalf of the British Committee for Standards in Haematology. *Br J Haematol*, *169*(5), 661-671. https://doi.org/10.1111/bjh.13403

New South Wales Government. (2018, May 25, 2018). https://www.eviq.org.au/clinical-resources/side-effect-and-toxicity-management/prophylaxis-and-treatment/108-prevention-and-management-of-tumour-lysis-synd#:~:text=The%20best%20management%20of%20TLS,monitoring%20for%20low%2Drisk%20patients.

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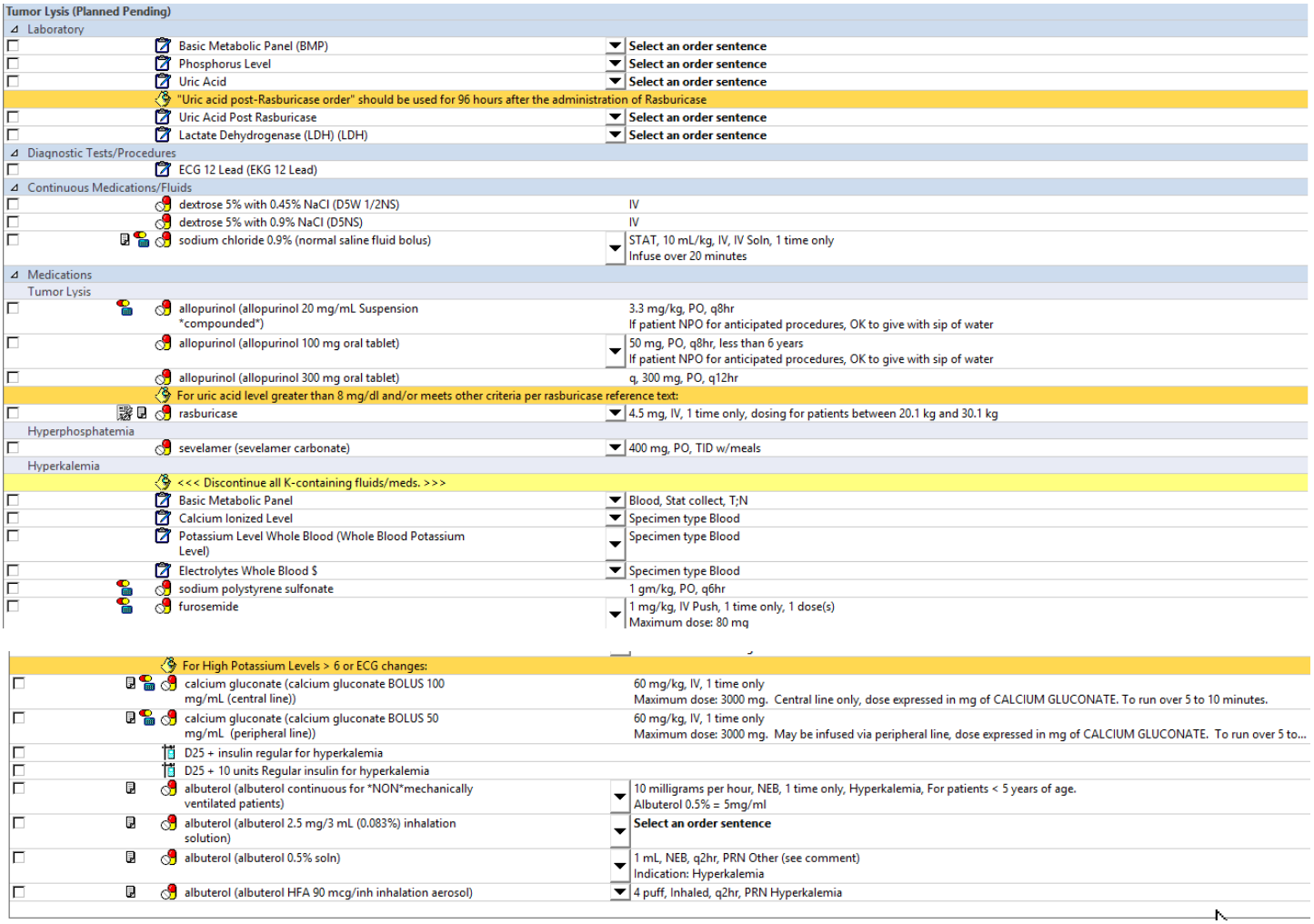
Appendix A: Inpatient Stay: Tumor Lysis



Tumor Lysis (Planned Pending)	
Laboratory	
Basic Metabolic Panel (BMP)	**Select an order sentence**
Phosphorus Level	**Select an order sentence**
Uric Acid	**Select an order sentence**
"Uric acid post-Rasburicase order" should be used for 96 hours after the administration of Rasburicase	
Uric Acid Post Rasburicase	**Select an order sentence**
Lactate Dehydrogenase (LDH) (LDH)	**Select an order sentence**
Diagnostic Tests/Procedures	
ECG 12 Lead (EKG 12 Lead)	
Continuous Medications/Fluids	
dextrose 5% with 0.45% NaCl (D5W 1/2NS)	IV
dextrose 5% with 0.9% NaCl (D5NS)	IV
sodium chloride 0.9% (normal saline fluid bolus)	STAT, 10 mL/kg, IV, IV Soln, 1 time only Infuse over 20 minutes
Medications	
Tumor Lysis	
allopurinol (allopurinol 20 mg/mL Suspension *compounded*)	3.3 mg/kg, PO, q8hr If patient NPO for anticipated procedures, OK to give with sip of water
allopurinol (allopurinol 100 mg oral tablet)	50 mg, PO, q8hr, less than 6 years If patient NPO for anticipated procedures, OK to give with sip of water
allopurinol (allopurinol 300 mg oral tablet)	q, 300 mg, PO, q12hr
For uric acid level greater than 8 mg/dl and/or meets other criteria per rasburicase reference text:	
rasburicase	4.5 mg, IV, 1 time only, dosing for patients between 20.1 kg and 30.1 kg
Hyperphosphatemia	
sevelamer (sevelamer carbonate)	400 mg, PO, TID w/meals
Hyperkalemia	
<<< Discontinue all K-containing fluids/meds. >>>	
Basic Metabolic Panel	Blood, Stat collect, T;N
Calcium Ionized Level	Specimen type Blood
Potassium Level Whole Blood (Whole Blood Potassium Level)	Specimen type Blood
Electrolytes Whole Blood $	Specimen type Blood
sodium polystyrene sulfonate	1 gm/kg, PO, q6hr
furosemide	1 mg/kg, IV Push, 1 time only, 1 dose(s) Maximum dose: 80 mg
For High Potassium Levels > 6 or ECG changes:	
calcium gluconate (calcium gluconate BOLUS 100 mg/mL (central line))	60 mg/kg, IV, 1 time only Maximum dose: 3000 mg. Central line only, dose expressed in mg of CALCIUM GLUCONATE. To run over 5 to 10 minutes.
calcium gluconate (calcium gluconate BOLUS 50 mg/mL (peripheral line))	60 mg/kg, IV, 1 time only Maximum dose: 3000 mg. May be infused via peripheral line, dose expressed in mg of CALCIUM GLUCONATE. To run over 5 to...
D25 + insulin regular for hyperkalemia	
D25 + 10 units Regular insulin for hyperkalemia	
albuterol (albuterol continuous for *NON*mechanically ventilated patients)	10 milligrams per hour, NEB, 1 time only, Hyperkalemia, For patients < 5 years of age. Albuterol 0.5% = 5mg/ml
albuterol (albuterol 2.5 mg/3 mL (0.083%) inhalation solution)	**Select an order sentence**
albuterol (albuterol 0.5% soln)	1 mL, NEB, q2hr, PRN Other (see comment) Indication: Hyperkalemia
albuterol (albuterol HFA 90 mcg/inh inhalation aerosol)	4 puff, Inhaled, q2hr, PRN Hyperkalemia

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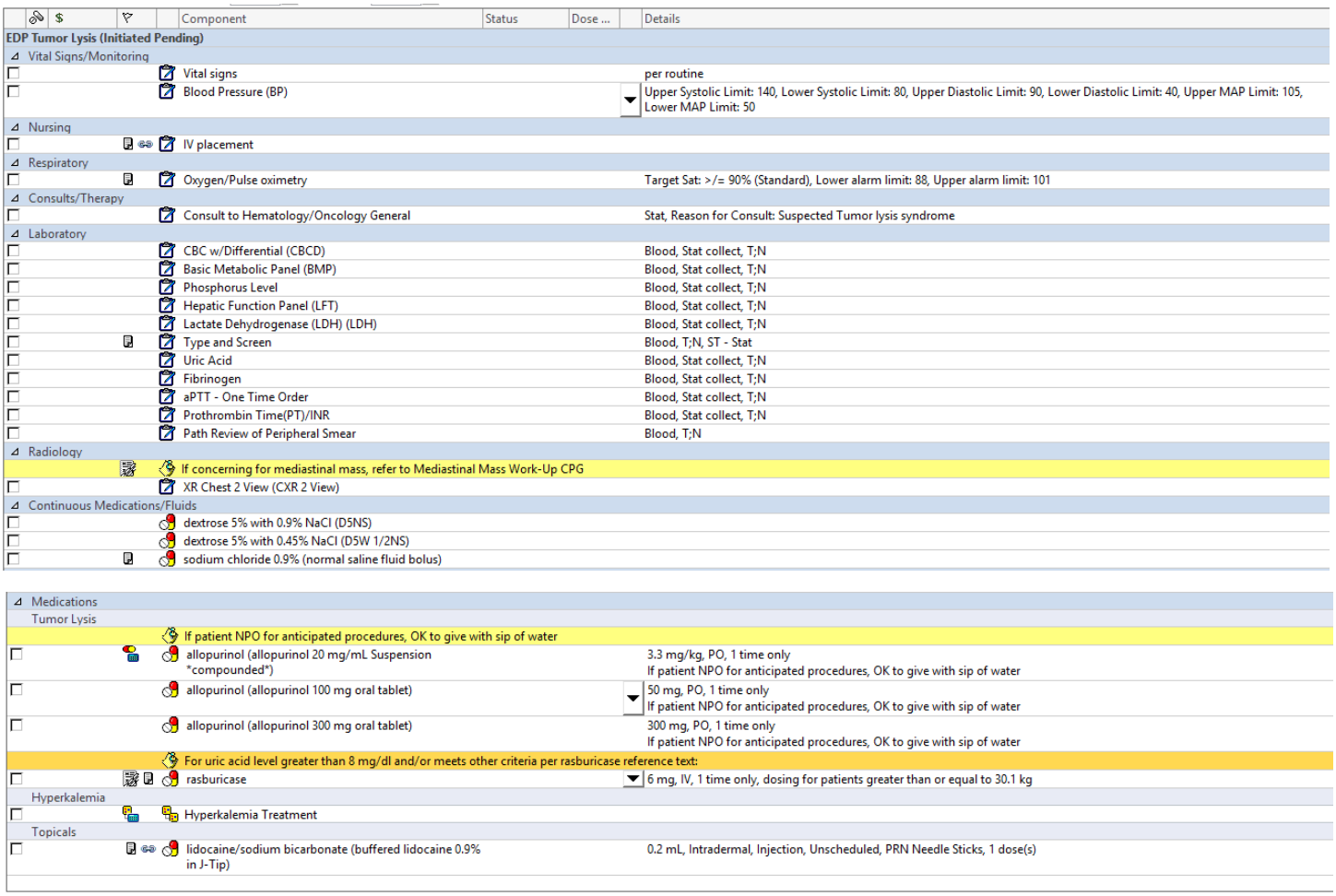
Appendix B: EDP Tumor Lysis



	Component	Status	Dose ...	Details
EDP Tumor Lysis (Initiated Pending)				
Vital Signs/Monitoring				
	Vital signs			per routine
	Blood Pressure (BP)			Upper Systolic Limit: 140, Lower Systolic Limit: 80, Upper Diastolic Limit: 90, Lower Diastolic Limit: 40, Upper MAP Limit: 105, Lower MAP Limit: 50
Nursing				
	IV placement			
Respiratory				
	Oxygen/Pulse oximetry			Target Sat: >/= 90% (Standard), Lower alarm limit: 88, Upper alarm limit: 101
Consults/Therapy				
	Consult to Hematology/Oncology General			Stat, Reason for Consult: Suspected Tumor lysis syndrome
Laboratory				
	CBC w/Differential (CBCD)			Blood, Stat collect, T;N
	Basic Metabolic Panel (BMP)			Blood, Stat collect, T;N
	Phosphorus Level			Blood, Stat collect, T;N
	Hepatic Function Panel (LFT)			Blood, Stat collect, T;N
	Lactate Dehydrogenase (LDH) (LDH)			Blood, Stat collect, T;N
	Type and Screen			Blood, T;N, ST - Stat
	Uric Acid			Blood, Stat collect, T;N
	Fibrinogen			Blood, Stat collect, T;N
	aPTT - One Time Order			Blood, Stat collect, T;N
	Prothrombin Time(PT)/INR			Blood, Stat collect, T;N
	Path Review of Peripheral Smear			Blood, T;N
Radiology				
	If concerning for mediastinal mass, refer to Mediastinal Mass Work-Up CPG			
	XR Chest 2 View (CXR 2 View)			
Continuous Medications/Fluids				
	dextrose 5% with 0.9% NaCl (D5NS)			
	dextrose 5% with 0.45% NaCl (D5W 1/2NS)			
	sodium chloride 0.9% (normal saline fluid bolus)			
Medications				
Tumor Lysis				
	If patient NPO for anticipated procedures, OK to give with sip of water			
	allopurinol (allopurinol 20 mg/mL Suspension *compounded*)			3.3 mg/kg, PO, 1 time only If patient NPO for anticipated procedures, OK to give with sip of water
	allopurinol (allopurinol 100 mg oral tablet)			50 mg, PO, 1 time only If patient NPO for anticipated procedures, OK to give with sip of water
	allopurinol (allopurinol 300 mg oral tablet)			300 mg, PO, 1 time only If patient NPO for anticipated procedures, OK to give with sip of water
	For uric acid level greater than 8 mg/dl and/or meets other criteria per rasburicase reference text:			
	rasburicase			6 mg, IV, 1 time only, dosing for patients greater than or equal to 30.1 kg
Hyperkalemia				
	Hyperkalemia Treatment			
Topicals				
	lidocaine/sodium bicarbonate (buffered lidocaine 0.9% in J-Tip)			0.2 mL, Intradermal, Injection, Unscheduled, PRN Needle Sticks, 1 dose(s)

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Appendix C: AGREE II Assessment for Children's Mercy Hospital's Tumor Lysis CPG

*AGREE II[a] Summary for this Clinical Practice Guideline**

Domain	Percent Agreement
Scope and purpose	92%
Stakeholder involvement	97%
Rigor of development	99%
Clarity and presentation	100%
Applicability	98%
Editorial independence	100%
Reviewer's recommendation for guideline use	Adopt the utilization of this guideline

**Note:* This assessment reflects the views obtained from one external clinician and one internal clinician.

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