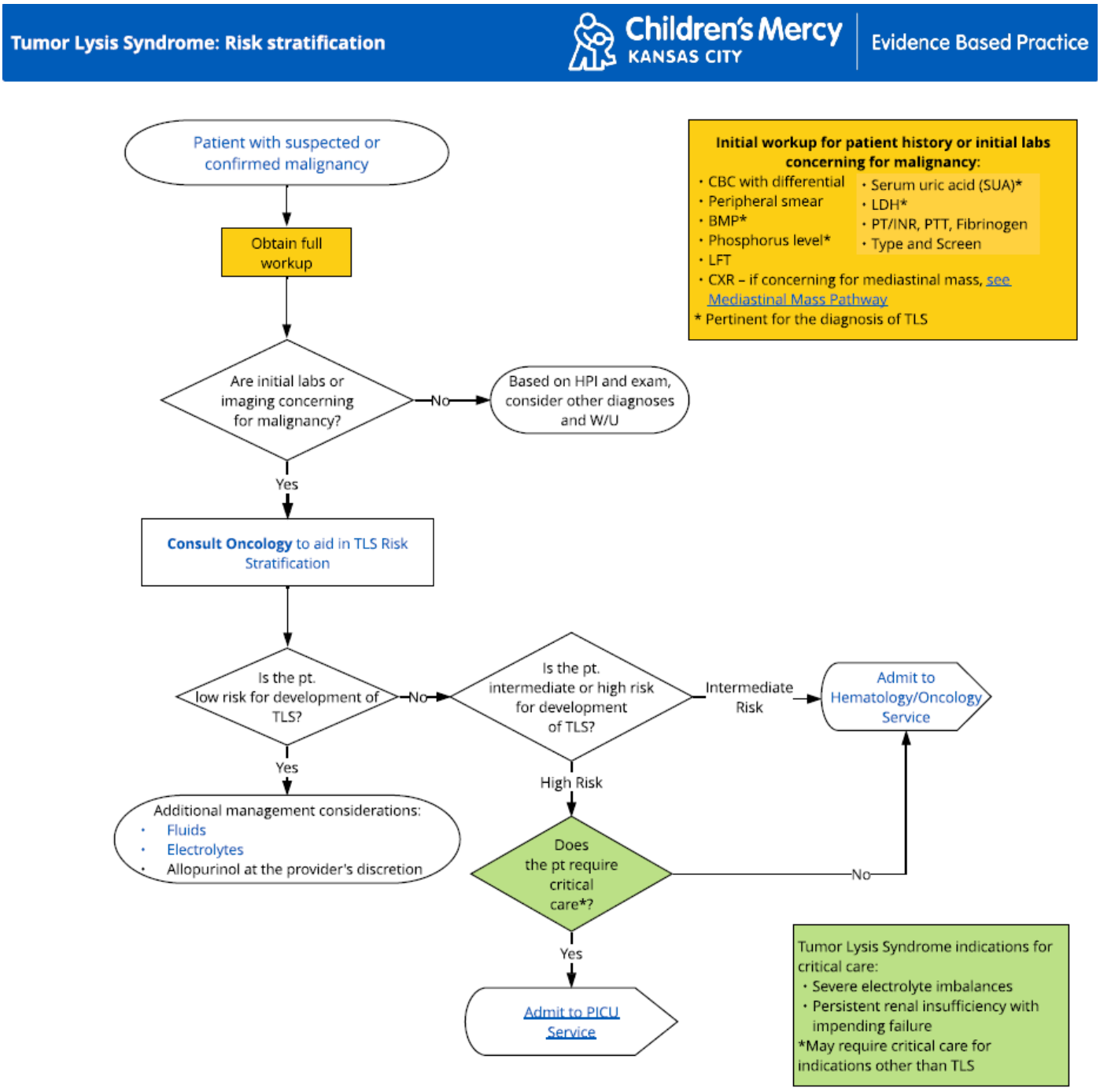
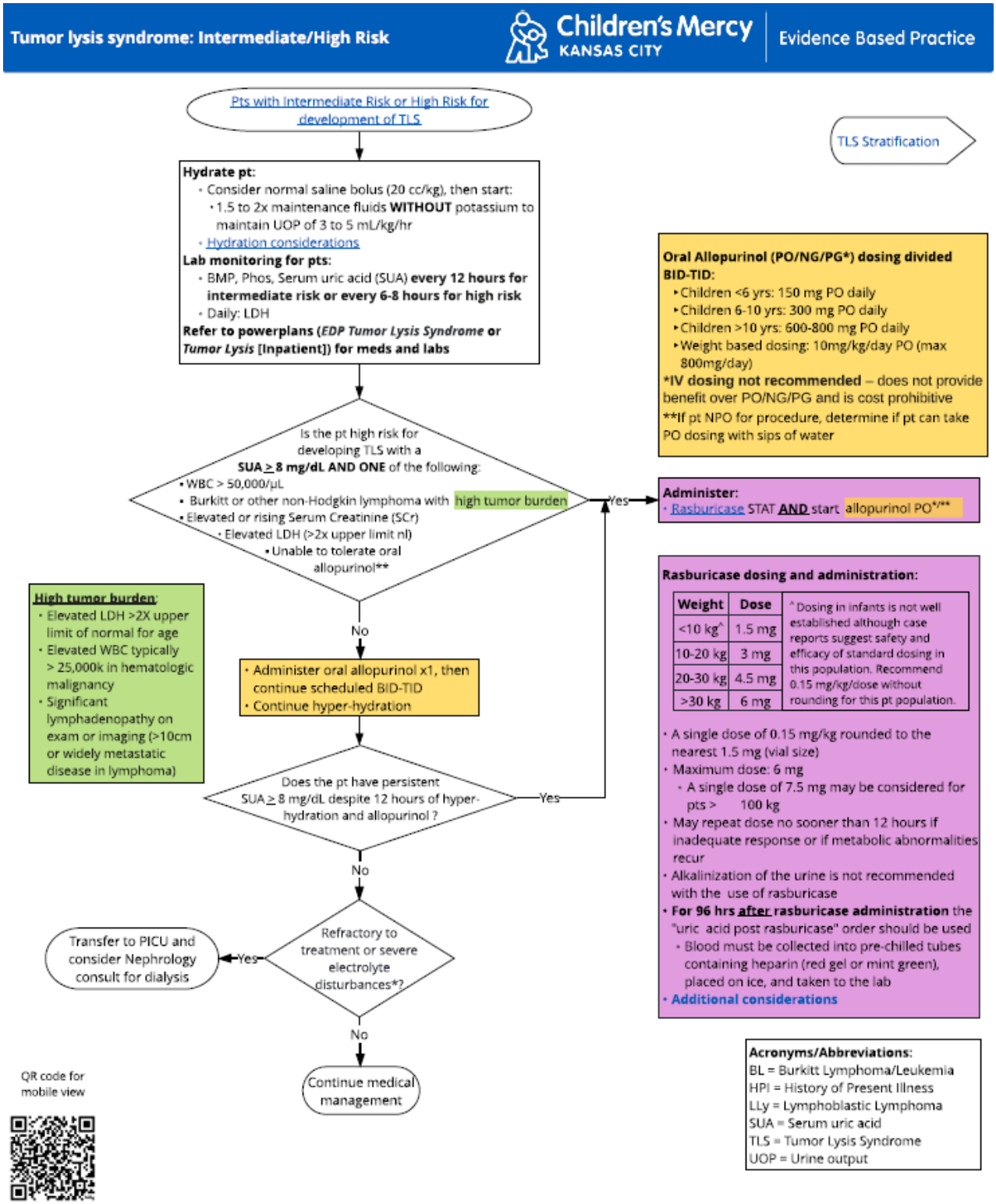
Tumor Lysis Syndrome (TLS)
Clinical Pathway Synopsis



These clinical pathways do not establish a standard of care to be followed in every case. It is recognized that each case is different, and those individuals involved in providing health care are expected to use their judgment in determining what is in the best interests of the patient based on the circumstances existing at the time. It is impossible to anticipate all possible situations that may exist and to prepare a clinical pathway for each. Accordingly, these clinical pathways should guide care with the understanding that departures from them may be required at times.



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Objective of Clinical Pathway

The objective of this clinical pathway 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

Inclusion Criteria

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

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 Clinical Pathway Committee. See Tables 1-3 for AGREE II.

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.

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.

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

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.

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

Additional Questions Posed by the Clinical Pathway Committee

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 pathways.
- Prompt administration of allopurinol following rasburicase to avoid re-accumulation of uric acid.
- Appropriate usage of post-rasburicase laboratory order.
- Others

Recommendations Specific for Children's Mercy

Children's Mercy adopted the majority of 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).

Updates from Previous Versions of the Clinical Pathway

- *No Change*

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 CLINICAL PATHWAY development
- Standardized order set for Emergency Department and Inpatient stay

Order Sets

- EDP Tumor Lysis
- Inpt: Tumor Lysis Pathway

Pathway Preparation

This Pathway was prepared by the Evidence Based Practice Department in collaboration with subject matter experts at Children's Mercy Kansas City. If a conflict of interest is identified, the conflict will be disclosed next to the committee member's name.

Implementation & Follow-Up

Once approved, the pathway was 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 pathway is scheduled for revision in 2028.

Clinical Pathway Representation.

This clinical pathway was originally created with representation from Hematology, Oncology, and Blood and Marrow Transplantation, Critical Care, and Emergency Medicine.

Committee Members Revision 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

EBP Committee Members

- Todd Glenski, MD, MSHA, FASA | Anesthesiology and Evidence Based Practice
- Jarrod Dusin, PhD, RD, CPHQ | Evidence Based Practice

Pathway Development Funding

The development of this pathway 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 pathway was reviewed and approved by the EBP Department and the pathway committee after committee members garnered feedback from their respective divisions/departments. It was then approved by the Medical Executive Committee.

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 pathway 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.
8/2025	Version 2: No updates

Disclaimer

When evidence is lacking or inconclusive, options in care are provided in the supporting documents and the power plan(s) that accompany the clinical pathway. These clinical pathways do not establish a standard of care to be followed in every case. It is recognized that each case is different, and those individuals involved in providing health care are expected to use their judgment to determine what is in the best interests of the patient based on the circumstances existing at the time. It is impossible to anticipate all possible situations that may exist and to prepare clinical pathways for each. Accordingly, these clinical pathways should guide care with the understanding that departures from them may be required at times.

P**lanned Review Date:**

8/2028

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.