UNC SCHOOL OF MEDICINE

THE UNIVERSITY of NORTH CAROLINA at CHAPEL HILL

DEPARTMENT OF PEDIATRICS
DIVISION OF HEMATOLOGY-ONCOLOGY

CAMPUS BOX 7236
CHAPEL HILL, NC 27599-7236

T 919.966.1178
F 919.966.7629

UNC Pediatric Hematology / Oncology Clinical Guidelines

Topic: Peri-Procedure Management of Outpatient Anticoagulants

Date of Last Revision: 22th February 2024

Created by: Lauren Garner, PharmD, BCPPS, CPP; Kynlon Phillips, PharmD, BCOP, BCPS, CPP; Lee Ann Jones, PharmD, MBA, BCPS; Joanna Billings, PharmD; Yasmina Abajas, MD

These guidelines have been developed to aid clinicians in making informed decisions about pediatric hematology and oncology patients. It is not intended to take the place of physician judgement. Recommendations may not be appropriate in all circumstances.

Summary / Recommendation:

Pediatric oncology patients are at an increased risk for thromboembolism. Due to this, pediatric cancer patients may be on therapeutic or prophylactic anticoagulation. In the outpatient setting, the most common anticoagulation agents used in the pediatric population include low molecular weight heparin (LMWH) and rivaroxaban. Common outpatient oncology procedures have been stratified by bleeding risk (table 1).

Recommendations for outpatient anticoagulation management peri-procedure are included below:

- If renal function ≤ 50 mL/min consider consulting your service pharmacist to determine appropriate hold times for anticoagulants
- Moderate risk of bleeding needs 2-3 drug half-lives between the last dose and surgery; aim for mild to moderate residual anticoagulant effect at surgery less than 12% to 25% (refer to table 2)
- High risk of bleeding needs 4-5 drug half-lives between the last dose and surgery; aim for minimal residual anticoagulant effect at surgery less than 3% to 6% (refer to table 2)
- If patient is considered at high risk for periprocedural VTE, consider bridge therapy (refer to table 4).
- If patient is on concomitant anti-platelet therapy, please consult your service pharmacist.

Table 1: Bleeding risk of common *outpatient* oncology procedures in the pediatric population: [5-7]

High Bleeding Risk	Moderate Bleeding Risk	Low Bleeding risk
Lumbar Puncture Intrathecal Chemotherapy Recent surgery of major organ (within 30 days)	Venous port placement	Nasogastric (NG) Tube Placement Ommaya reservoir puncture Non-tunneled CVC placement or removal Tunneled CVC removal PICC placement Bone Marrow Aspiration and Biopsy

Table 2: Half-life elimination time (hours) of outpatient anticoagulants approved in pediatric patients: [3-4]

Agent	Half-Life (hours)
LMWH	4.5 - 7
Rivaroxaban	1.6 - 4.2

Table 3: Anticoagulation hold parameter recommendations:

	LMWH				**DOACS** (dabigatran, rivaroxaban)	
	Treatment		Prophylaxis			
	Take last dose on	Resume after	Take last dose on	Resume after	Take last dose on	Resume after
HIGH RISK PROCEDURES	-24h	-24h	-24h	-24h	-48h	-48h
MODERATE RISK PROCEDURES	-24h	-24h	-24h	-24h	-24h	-24h
LOW RISK PROCEDURES	-24h	-24h	0	0	-24h	-24h

Note: take last dose on days listed as a countdown to the day of procedure which is day 0

Table 4: Risk of periprocedural thromboembolism, adapted from *CHEST* 2022[16]:

RISK CATEGORY	VTE
High > 10%/year risk of ATE or > 10%/month risk of VTE	Recent VTE (< 3 month and especially < 1 month) Severe thrombophilia* Antiphospholipid antibodies Active cancer associated with high VTE risk[#]
Moderate 4-10%/year risk of ATE or 4-10%/month risk of VTE	VTE within past 3-12 month Recurrent VTE Non-severe thrombophilia^ Active cancer or recent history of cancer
Low < 4%/year risk of ATE or < 2%/month risk of VTE	VTE > 12 months ago

ATE: arterial thromboembolism; VTE: venous thromboembolism
*Deficiency of protein C, protein S or antithrombin; homozygous factor V Leiden or prothrombin gene G20210A mutation or double heterozygous for each mutation, multiple thrombophilias.
[#]Pancreatic, myeloproliferative disorders, primary brain cancer, gastric cancer, and esophageal cancer
^Heterozygous factor V Leiden or prothrombin gene G20210A mutation

Background / Data Summary:[1-7]

1) Childhood malignancy and especially acute lymphoblastic leukemia are increasingly associated with thromboembolism. The etiology of pediatric cancer associated thrombosis is multifactorial and may reflect a tumor mass effect, tumor thrombi, alterations of the hemostatic system, treatment-related hazards (e.g. procoagulant changes induced by chemotherapy), presence of central venous lines and comorbidities (e.g. inherited thrombophilia). Given the risk of thromboembolism, pediatric cancer patients are often on therapeutic or prophylactic anticoagulation.
2) Agents used for pediatric thromboembolism treatment and prevention include low molecular weight heparin (LMWH), heparin, and select direct oral anticoagulants (DOACs). The most common agents used in the outpatient setting include LMWH and DOACs. The current DOACs with FDA approval in children for treatment of acute venous thrombosis and for extended secondary prevention include rivaroxaban and dabigatran.
3) Pediatric oncology patients will require procedures throughout the course of their therapy for surgical treatment, disease progression monitoring, IV access and various other reasons. Based on the bleeding risk of each procedure, it is often recommended to hold anticoagulation. Outpatient procedures that most commonly occur in this clinic include lumbar punctures, bone marrow biopsies and nasogastric tube placement.

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