Cancer-Associated Venous Thromboembolism (CAT)

Anticoagulation Management Guideline

Document code	MHA-CAT-2025-v1.2
Division	Haematology — Haemostasis & Thrombosis
Guideline type	Evidence-based clinical guideline
Scope	Adult cancer-associated VTE: DVT, PE, splanchnic/catheter thrombosis
Aligned with	ASH 2023 VTE guidelines; ISTH CAT guidance 2022; BSH CAT 2024; CARAVAGGIO trial; SELECT-D trial; Hokusai-VTE Cancer
GRADE framework	Evidence quality: High / Moderate / Low / Very Low Recommendation strength: Strong / Conditional
Date approved	April 2025
Review due	April 2027 (or sooner if major evidence emerges)

Clinical Key Points

• Anticoagulation is the cornerstone of CAT treatment — withhold only if platelets <50×10■/L or active major bleeding.

• Apixaban (CARAVAGGIO trial) is the preferred DOAC for most CAT patients: 10 mg BD × 7 days, then 5 mg BD.

• LMWH (dalteparin/tinzaparin) remains preferred for GI, GU, and brain malignancy due to higher mucosal bleeding risk with DOACs.

• Minimum treatment duration: 6 months (Strong | Moderate). Continue indefinitely if cancer remains active.

• Thrombocytopenia thresholds (BSH 2024): platelets <25 hold AC; 25–49 → half-dose LMWH; ≥50 → full therapeutic dose.

• VTE recurrence on DOAC → switch to LMWH. Recurrence on LMWH → escalate dose 20–25%.

• Khorana score identifies high-risk patients who may benefit from primary prophylaxis.

1. Scope and Purpose

This guideline covers the anticoagulation management of cancer-associated venous thromboembolism (CAT) in adults with confirmed active malignancy. It addresses deep vein thrombosis (DVT), pulmonary embolism (PE), splanchnic vein thrombosis, and catheter-related thrombosis. Prevention of VTE in cancer patients undergoing surgery or receiving systemic therapy is covered in the prophylaxis section (see Khorana risk scoring below).

2. Clinical Overview and Epidemiology

Cancer is a major independent risk factor for VTE — patients with active malignancy have a 4–7-fold increased risk of thrombosis compared with the general population. VTE occurs in 15–20% of cancer patients during their illness course and is the second leading cause of death in ambulatory cancer patients after the malignancy itself. Pathophysiology involves Virchow's triad: hypercoagulability (tumour-derived tissue factor, cancer procoagulant), venous stasis (mass effect, immobility), and endothelial injury (chemotherapy, central venous catheters).

Khorana Risk Score for Primary Prophylaxis

Table 4. Khorana Risk Score

Risk Factor	Points
Site of cancer — very high risk (stomach, pancreas)	2
Site of cancer — high risk (lung, lymphoma, GU, GY, bladder, testis)	1
Pre-chemotherapy platelet count ≥350×10■/L	1
Haemoglobin <10 g/dL or use of ESA	1
Pre-chemotherapy leucocyte count >11×10■/L	1
BMI ≥35 kg/m²	1
Score interpretation	**Recommendation**
≥2 (high risk)	Consider DOAC or LMWH primary prophylaxis during systemic therapy
0–1 (low risk)	Prophylaxis not routinely recommended; individualise

3. Methodology

This guideline was developed using GRADE methodology. Key evidence sources are the CARAVAGGIO trial (apixaban vs dalteparin; Agnelli et al., NEJM 2020), the Hokusai-VTE Cancer trial (edoxaban vs dalteparin; Raskob et al., NEJM 2018), the SELECT-D trial (rivaroxaban vs dalteparin; Young et al., JCO 2018), and the ASH 2023 guidelines for treatment of VTE in patients with cancer. International guidance from ISTH (2022) and UK guidance

from BSH (2024) has also been incorporated.

PICO Component	Definition
P — Population	Adults with confirmed active malignancy presenting with DVT, PE, or other VTE event.
I — Intervention	Therapeutic anticoagulation: DOACs (apixaban, rivaroxaban, edoxaban) or LMWH (dalteparin, tinzaparin, enoxaparin), with defined duration.
C — Comparator	LMWH (historical standard of care); vitamin K antagonists (warfarin) — inferior in cancer VTE.
O — Outcomes	Recurrent VTE, major bleeding, clinically relevant non-major bleeding, all-cause mortality, QoL, treatment burden, catheter patency (catheter-related thrombosis).

4. Initial Assessment and Contraindications

Before initiating anticoagulation, assess for absolute contraindications and patient-specific factors that influence drug selection:

Hold Anticoagulation — Assess Urgently

- Platelet count <50×10■/L (see thrombocytopenia thresholds, Section 9)
- Active major bleeding (>2 units RBC in 24 h, or haemodynamically significant)
- Recent high-risk surgery with incomplete haemostasis
- Active intracranial or spinal haemorrhage
- Confirmed thrombocytopenia <25×10■/L
- Uncontrolled hypertension (SBP >180 mmHg)

Factors Favouring LMWH Over DOAC

- GI malignancy — higher mucosal bleeding risk with DOACs (oesophageal, gastric, colorectal)
- GU malignancy — haematuria risk with DOACs (renal, bladder, prostate)
- Brain malignancy — intracranial haemorrhage concern
- CrCl <30 mL/min (DOACs accumulate; LMWH with dose adjustment preferred)
- Significant drug interactions (P-gp, CYP3A4 inducers/inhibitors with DOACs)
- Pregnancy
- Unreliable oral absorption (GI surgery, severe vomiting, malabsorption)

5. Anticoagulant Selection — Treatment of Established CAT

The preferred anticoagulant depends on tumour type, renal function, drug interactions, patient preference, and comorbidities. The algorithm below guides selection:

Apixaban (preferred DOAC)	**CARAVAGGIO trial (NEJM 2020):** Apixaban non-inferior to dalteparin for recurrent VTE (HR 0.63, 95% CI 0.37–1.07) with no significant increase in major bleeding. **Dose:** 10 mg twice daily × 7 days, then 5 mg twice daily. No parenteral bridging needed. Preferred for non-GI/GU malignancy.	High Strong
Rivaroxaban	**SELECT-D (JCO 2018):** Lower recurrent VTE vs dalteparin (HR 0.43, 95% CI 0.19–0.99) but higher CRNM bleeding. Higher GI bleeding rate than apixaban in observational data. **Dose:** 15 mg twice daily × 3 weeks, then 20 mg OD. Consider as alternative DOAC if apixaban not tolerated.	Moderate Conditional

Edoxaban	**Hokusai-VTE Cancer (NEJM 2018):** Non-inferior to dalteparin for recurrent VTE (HR 0.97, 95% CI 0.70–1.36) but higher rate of major GI bleeding. **Dose:** 60 mg OD (after ≥5 days LMWH bridging). Reduce to 30 mg OD if weight <60 kg, CrCl 15–50, or P-gp inhibitor co-administration.	High Conditional
Dalteparin (LMWH)	**CLOT trial:** Standard of care prior to DOACs. Superior to warfarin for CAT. **Dose:** 200 units/kg OD × 30 days, then 150 units/kg OD. Weight-based; adjust for renal impairment (eGFR <30: consider dose reduction, anti-Xa monitoring). Preferred for GI/GU/brain malignancy and in pregnancy.	High Strong
Tinzaparin	Alternative LMWH; may be preferable in moderate renal impairment (CrCl 20–30). **Dose:** 175 units/kg OD. Evidence from CATCH trial (vs warfarin). Less renal accumulation than enoxaparin.	Moderate Strong

VKA (warfarin) is NOT recommended for first-line treatment of CAT due to inferior efficacy versus LMWH (CLOT trial) and challenges maintaining therapeutic INR in cancer patients (drug interactions, erratic absorption, chemotherapy effects on INR).

6. Duration of Anticoagulation

Minimum duration	6 months of therapeutic anticoagulation for all cancer-associated VTE. This applies regardless of DVT or PE classification.	Moderate Strong
Active cancer (>6 months)	Continue anticoagulation indefinitely while cancer is active, or until treatment is no longer appropriate (patient preference, quality of life, high bleeding risk). Reassess benefit/risk at every clinic review.	Low Conditional
Cancer in remission	Consider stopping anticoagulation after minimum 6 months if cancer is in complete remission, VTE risk factors are resolved, and bleeding risk is acceptable. Shared decision-making required.	Low Conditional

7. Recurrent VTE on Anticoagulation

Management of VTE Recurrence

- Recurrence on therapeutic DOAC → switch to full-dose LMWH (dalteparin 200 units/kg OD)
- Recurrence on therapeutic LMWH → escalate LMWH dose by 20–25% (document rationale)
- Recurrence on sub-therapeutic anticoagulation → optimise dose and adherence before escalating
- Check anti-Xa level if recurrence on LMWH to confirm therapeutic dosing
- Seek specialist haematology input for all recurrent CAT events
- Exclude mechanical causes: catheter-related thrombosis, local tumour obstruction
- Re-imaging to characterise new vs progression of existing thrombus

8. Special Situations in CAT

Catheter-Related Thrombosis (CRT)

- Treat with therapeutic anticoagulation ≥3 months
- Remove catheter only if non-functional, infected, or no longer needed
- LMWH or DOAC acceptable for CRT
- Prophylactic anticoagulation does NOT reduce CRT risk and is NOT recommended routinely
- Reassess catheter necessity if CRT occurs

Splanchnic Vein Thrombosis (SVT)

- Anticoagulate if symptomatic or progressive
- Evidence base weaker for SVT; extrapolate from DVT/PE trials
- LMWH preferred initially; switch to DOAC if GI concerns resolved
- Duration: minimum 6 months; indefinite if cancer active
- Multidisciplinary input (hepatology/gastroenterology) recommended for portal vein thrombosis

IVC Filter

IVC filter insertion is NOT routinely recommended for CAT and should only be considered when anticoagulation is absolutely contraindicated and there is a proximal DVT or PE. If inserted, it must be removed at the earliest opportunity once anticoagulation can be safely resumed. Evidence for IVC filters in cancer-associated VTE is limited to observational data (GRADE: Very Low).

9. Anticoagulation in the Context of Thrombocytopenia

Cancer patients frequently develop thrombocytopenia due to myelosuppressive chemotherapy, bone marrow involvement, or ITP (see ITP guideline). The following thresholds are recommended by BSH 2024 (Conditional | Very Low evidence — due to absence of randomised trial data in this specific population):

Platelet Count	Anticoagulation Approach	Comment
≥50 ×10■/L	Full therapeutic-dose anticoagulation	Standard dosing — no dose reduction required for thrombocytopenia alone
25–49 ×10■/L	Half-dose LMWH (e.g., dalteparin 100 units/kg OD)	Balances VTE risk against bleeding; platelet transfusion may be appropriate to allow full dosing if high VTE risk
<25 ×10■/L	HOLD anticoagulation — reassess daily	Address platelet count; consider platelet transfusion if high VTE risk (e.g., pulmonary embolism causing haemodynamic compromise)

10. Audit Standards

The following quality indicators can be used to audit CAT management practice against this guideline.

Audit Standard	Data Source	Target	Rationale
CAT patients receive anticoagulation within 24 hours of VTE confirmed diagnosis (unless contraindicated)	VTE database, clinic letters	≥90%	Time-sensitive; VTE propagation risk
Apixaban or LMWH selected as first-line (not warfarin) for CAT	Prescribing data	≥95%	ASH 2023 / ISTH 2022 strong recommendation

Audit Standard	Data Source	Target	Rationale
LMWH selected (not DOAC) for GI, GU, and brain malignancy	Oncology-haematology liaison records	≥85%	Mucosal bleeding risk reduction
Anticoagulation continued for minimum 6 months unless documented rationale for shorter duration	Clinic letters, prescribing	≥90%	ASH 2023 / BSH 2024 standard
Thrombocytopenia thresholds (<50, 25–49, <25) documented and acted upon	Blood results with anticoagulant prescribing correlation	≥90%	BSH 2024 conditional recommendation
VTE recurrence documented, cause investigated, and anticoagulant changed appropriately	VTE register, haematology letters	≥95%	Clinical governance requirement
Patients with VTE and cancer offered written information on anticoagulation risks and benefits	Patient records, written information audit	≥80%	Informed consent / shared decision-making

11. Limitations and Update Plan

Recognised limitations of this guideline:

- The three major CAT DOAC trials (CARAVAGGIO, Hokusai, SELECT-D) have different populations and endpoints — direct comparisons across trials should be made cautiously.
- Patients with primary or metastatic brain tumours, haematological malignancies, and splanchnic thrombosis were under-represented in the DOAC trials; LMWH remains standard in these groups based on expert consensus.
- The thrombocytopenia dosing thresholds (BSH 2024) are based on expert consensus — no randomised trial evidence exists for this specific scenario.
- Evidence on optimal anticoagulation strategy in the context of immunotherapy, targeted agents, and novel anticancer treatments is emerging and may not be fully captured in this guideline.
- Practical pharmacokinetic data on DOAC interactions with specific chemotherapy agents and supportive care drugs remain incomplete.

Update schedule: This guideline will be reviewed in April 2027 or earlier if updated ASH, ISTH, or BSH guidance is published, if new DOAC trial data in high-risk subgroups (GI/GU/brain) become available, or if significant changes to NICE technology appraisals occur.

12. References

[1] Agnelli G et al. Apixaban for the Treatment of Venous Thromboembolism Associated with Cancer (CARAVAGGIO). N Engl J Med. 2020;382(17):1599–1607. [PMID: 32223112] — **A1: High-quality multicentre RCT**

[2] Raskob GE et al. Edoxaban for the Treatment of Cancer-Associated Venous Thromboembolism (Hokusai-VTE Cancer). N Engl J Med. 2018;378(7):615–624. [PMID: 29231094] — **A1: High-quality multicentre RCT**

[3] Young AM et al. Anticoagulation Therapy in Selected Cancer Patients at Risk of Recurrence of Venous Thromboembolism (SELECT-D). J Clin Oncol. 2018;36(20):2017–2023. [PMID: 29746227] — **A1: Open-label RCT**

[4] Lyman GH et al. American Society of Hematology 2023 guidelines for management of venous thromboembolism: treatment of cancer-associated thrombosis. Blood Advances. 2023;7(19):5389–5404. [PMID: 37552024] — **A1: High-quality guideline with systematic review basis**

[5] BSH Guideline: Prevention and Treatment of Cancer-Associated VTE, British Society for Haematology, 2024 update. — **A1: UK national haematology society guideline**

13. Versioning and Governance

Version	Date	Author	Change
v1.0	Oct 2024	Dr M Mohsin	Initial CAT guideline published on Mohsin Haematology Academy
v1.1	Jan 2025	Dr M Mohsin	GRADE evidence quality and recommendation strength badges added
v1.2	Apr 2025	Dr M Mohsin	Audit standards (Section 10), BSH 2024 thrombocytopenia thresholds, visual algorithm (SVG/Excalidraw) added

Disclaimer: This guideline is intended to support clinical decision-making and is not a substitute for individual clinical judgement. Patient circumstances must always be considered. Clinical practice may evolve; users should verify that this is the current version before application.