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Trust Guideline for the Management of Heparin Induced Thrombocytopenia in Adults

For Use in:	Clinical areas which use any form of heparin
By:	Clinical staff caring for patients receiving heparin
For:	Patients receiving any form of prophylactic or therapeutic heparin
Division responsible for document:	Medical
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Compliance links: *(is there any NICE related to guidance)*	None
If Yes - does the strategy/policy deviate from the recommendations of NICE? If so why?	

This guideline has been approved by the Trust's Clinical Guidelines Assessment Panel as an aid to the diagnosis and management of relevant patients and clinical circumstances. Not every patient or situation fits neatly into a standard guideline scenario and the guideline must be interpreted and applied in practice in the light of prevailing clinical circumstances, the diagnostic and treatment options available and the professional judgement, knowledge and expertise of relevant clinicians. It is advised that the rationale for any departure from relevant guidance should be documented in the patient's case notes.

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Version and Document Control:

Version Number	Date of Update	Change Description	Author
5.1	08/04/2022	Reviewed, minor changes only	Hamish Lyall

This is a Controlled Document

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Quick reference guideline

HIT suspected
(Patient receiving heparin, new onset thrombocytopenia +/-new thrombotic event)

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Discuss with haematologist and perform 4Ts score

	Points 0,1 or 2 for each category; max score =8		
	2	1	0
thrombocytopenia	>50% fall or nadir 20-100 x10^9/l	30-50% fall OR nadir 10-19x10^9/l	fall <30% OR nadir <10 x10^9/l
timing of fall or other sequelae	clear onset between d 5-10; or less than 1d if heparin in last 100d)	consistent with immunisation but not clear eg missing counts or onset of thrombocytopenia after d10	platelet fall too early (no recent heparin exposure)
thrombosis or other sequelae	new thrombosis; skin necrosis; post heparin bolus acute reaction	progressive or recurrent thrombosis; erythematous skin lesions; suspected but not proven thrombosis	none
other cause for thrombocytopenia	no other cause evident	possible other cause evident	definite other cause present

Low probability (score 0-3)

No change in management required. Continue heparin if still clinically indicated

*Calculate eGFR using creatinine clearance calculator alculators/Renal/

Intermediate / high probability (score 4-8)

- Stop heparin
- Send sample for HIT antibody screen
- Commence alternative anticoagulant (see below)

- eGFR* ≥30ml/min – **fondaparinux (**treatment dose**)**
- eGFR* < 30ml/min or high bleeding risk - **argatroban infusion**
- eGFR* < 30ml/min and severe liver disease (argatroban contraindicated) – discuss options with haematologist

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Commence oral anticoagulant once platelet count normal and patient clinically stable

Objective/s

Heparin induced thrombocytopenia (HIT) is a rare, transient pro-thrombotic disorder initiated by heparin. It can be fatal if not recognised and treated.

Rationale for the Recommendations

This guideline summarises local implementation of national guidelines from the British Committee for Standards in Haematology entitled 'Guidelines on the diagnosis and management of heparin induced thrombocytopenia 2nd edition' www.bcshguidelines.com

Background

HIT is caused by the development of an IgG antibody which binds to complexes of platelet factor 4 (PF4) and heparin. These HIT-IgG/PF4/heparin complexes bind to platelet surfaces and cause aggregation and thrombosis. Venous thrombosis or arterial thrombosis can occur.

Types of HIT

- isolated HIT – thrombocytopenia but without obvious thrombosis; at high risk of clot formation
- HITT - HIT with thrombosis

When to suspect HIT(T)

- Development of new arterial or venous thrombosis or extension of existing thrombosis whilst on heparin
- Severe erythematous/necrotic skin reaction at heparin injection site
- Acute systemic/anaphylactoid symptoms shortly after administration of heparin
- Unexplained thrombocytopenia whilst receiving heparin
    - Platelet count typically begins to fall 5-10 days after starting heparin. Rarely the onset of HIT can be day 10-15. The platelet count usually falls by at least 50% with a median nadir of 55 x 10^9/l. Severe thrombocytopenia is unusual.
    - If heparin exposure in previous 100 days thrombocytopenia may occur before day 5

Laboratory tests

- Tests should only be performed after calculating the 4Ts score (see page 2) and should not be done if the score is ≤3
- Tests for HIT antibodies can be requested on webICE (search 'heparin induced thrombocytopenia'). Samples are sent to an external laboratory for testing.

General points

- All types of heparin must be stopped once a diagnosis of HIT(T) is suspected (4Ts score >3) and an alternative anticoagulant used. See appendix 1 for dosing guidance
- LMWH cannot be substituted for UFH because of cross-reactivity of HIT antibodies
- **Therapeutic** anticoagulation is required for both HITT and isolated HIT as the risk of thrombosis is very high

- Prophylactic platelet transfusions are relatively contraindicated as the risk of bleeding is low and platelets may contribute to thrombosis. If major bleeding discuss with haematologist

Management of urgent invasive procedures in patients with HIT

- Whenever possible surgery should be avoided in the setting of acute HIT because of the high risk of thrombosis and clinical need for uninterrupted anticoagulation
- If surgery cannot be deferred discuss with haematology
  - argatroban has a short half life (50mins). Stop 3-4 hours before major operations with high bleeding risk and 1-2 hours before minor operations; monitor aPTT before/during the intervention.
  - fondaparinux has a longer half life (17 hours) and no reversal agent. Interventional procedure may need to be performed whilst anticoagulated or deferred for >24 hours

Management of bleeding on argatroban and fondaparinux

- In life-threatening bleeding with argatroban discontinue infusion and check aPTT/other coag tests after 4 hours.
- In life threatening bleeding with fondaparinux management is supportive until drug excreted

Transition to oral anticoagulation

- <u>Switching from argatroban or fondaparinux to Direct Oral Anticoagulant (DOAC)</u>

- Argatroban: Stop infusion and start DOAC with 2 hours of discontinuation
- Fondaparinux: Give DOAC 24 hours after last dose of fondaparinux

  Dosing:
  Rivaroxaban 15mg bd for 3 weeks then 20mg daily
  Apixaban 10mg bd for 7 days then 5mg bd (in cases of HIT without thrombosis can start with 5mg bd)
  Dabigatran: Must have had argatroban or fondaparinux for at least 5 days then start dabigatran 150 mg bd.

<u>Switching from argatroban to vitamin K antagonist (e.g. warfarin)</u>

- Do not give warfarin until the platelet count > 150 x 10^9/L (Risk of warfarin induced skin necrosis and gangrene if commenced too early)
- Start warfarin at 3 - 5mg/day. Avoid large loading doses.
- Monitor INR daily
- Argatroban interferes with the INR assay. This must be accounted for when assessing warfarin effect whilst on argatroban infusion. See below:
  - When INR is ≥ 4.0 for 2 days stop argatroban infusion and check INR after 4 hours.
  - If INR > 2 no further argatroban required

- If INR <2 restart argatroban infusion. Reassess daily

- Switching from fondaparinux to vitamin K antagonist
  - Start warfarin 3-5mg daily (avoid large loading doses)
  - Check INR daily - fondaparinux does not interfere with INR
  - Fondaparinux can be discontinued when INR > 2 for 2 consecutive days

Anticoagulation in patients with a history of HIT

- Avoid all forms of heparin and use an alternative anticoagulant. If severe renal failure discuss options with haematologist.

Record keeping and alerts

- The diagnosis should be explained to the patient
- The diagnosis of HIT should be clearly recorded as a serious allergy in the patient's notes and EPMA

Clinical Audit Standards derived from guideline

Not defined.

Summary of development and consultation process undertaken before registration and dissemination

During the development process this guideline has been reviewed by the thrombosis and thromboprophylaxis committee.

Distribution list/ dissemination method

via the Trust Intranet

References/ source documents

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4. American College Chest Physicians: Antithrombotic therapy and prevention of thrombosis 9th edition (2012)
5. Lori-Ann Linkins et al. Systematic review of fondaparinux for heparin-induced thrombocytopenia: when there are no randomised control trials. *Res Pract Thromb Haemostat*. 2018;00:1-6
6. Coagulation assays and anticoagulant monitoring. American Society Hematology education book 2012 D.Funk
7. Wirral University Teaching Hospitals NHS Trust Argatroban protocol
8. Warketin et al. Direct oral anticoagulants for treatment of HIT: update of Hamilton experience and literature review. *Blood* Aug 31 2017 130: 1104-1113

9. Cuker et al. American Society for Hematology 2018 guidelines for the management of venous thromboembolism: heparin induced thrombocytopenia. (and associated pocket guide)

Appendix 1 Alternative anticoagulants available at NNUHFT

Fondaparinux

- Fondaparinux is a synthetic pentasaccharide. It is not specifically licensed for the treatment of HIT but is an acceptable alternative anticoagulant
- It is given by once daily by subcutaneous injection as per schedule below
- Fondaparinux is renally excreted and is therefore not recommended in persons with severe renal impairment (eGFR <30ml/min).
- Fondaparinux has a long half life (17 hours)
- There is no reversal agent for fondaparinux
- Dose of fondaparinux
    - 5mg daily if <50kg
    - 7.5mg daily if 50-100kg
    - 10mg daily if 100kg

Argatroban

- All prescriptions should use the NNUHFT argatroban prescription chart (available via Trust Docs or Click for Clots intranet site (under forms))
- Argatroban is a direct thrombin inhibitor licensed for the treatment of HIT
- Administered by continuous IV infusion
- Short half-life (approx. 50 minutes)
- Not renally excreted
- Not significantly removed by membranes used in haemodialysis or CVVH.
- If renal replacement required and patient is already established on argatroban infusion no change in dosing required.
- If haemodialysis or CVVH is commenced simultaneously with argatroban a bolus dose will be required (to prevent filter occlusion). See prescription chart for details.
- Monitoring is required for all patients using the standard laboratory APTT assay

Direct oral anticoagulants (DOAC's) e.g. apixaban, dabigatran, edoxaban, rivaroxaban

- Do not cross react with HIT antibodies
- Case series suggest these drugs can be effective in both initial treatment of HIT and when switching from parenteral therapy, however evidence is limited
- Apixaban or rivaroxaban will usually be preferable due to not requiring initial parenteral therapy
- Clinical situations where these drugs could be considered
    - As initial therapy in cases without thrombosis, as an alternative to fondaparinux for initial treatment of HIT with non-severe thrombosis, or switching from parenteral therapy

- AND:
  - Clinically stable
  - Acceptable renal function
  - No significant drug interactions
  - Not requiring interventional procedures

Bivalirudin

- Guidelines recommend bivalirudin as the alternative anticoagulant of choice in patients undergoing PCI with HIT. This drug is on formulary at NNUHFT.