NHS South West Yorkshire Partnership NHS Foundation Trust

NHS Barnsley Hospital NHS Foundation Trust

NHS South Yorkshire Integrated Care Board

Shared Care Guideline
for
Tinzaparin (Innohep®) for the Treatment and Prophylaxis of Venous Thromboembolism

This shared care guideline (SCG) has been written to enable the continuation of care by primary care clinicians of patients initiated on tinzaparin by Barnsley Hospital NHS Foundation Trust (BHNFT), where this is appropriate and, in the patients' best interests. Primary care will only be requested to take over prescribing of tinzaparin within its licensed indication unless specifically detailed otherwise below.

Introduction

Low Molecular Weight Heparins (LMWH's) such as tinzaparin are now widely used for a number of licensed and unlicensed indications including the prevention and treatment of venous (and sometimes arterial) thromboses in selected patient groups. The availability of LMWH's which are administered by subcutaneous injection only once or twice daily means that patients can often self-administer their anticoagulant.

This guideline is only for use in NON-PREGNANT patients whose CrCL is 20mLs/min or above. Patients with severe renal impairment require additional monitoring and will be managed by the acute trust until further guidance can be written and approved.

Barnsley Hospital now use tinzaparin (Innohep®) for the treatment and prophylaxis of all VTE associated indications.

Indication/Licensing information

- Prophylaxis of venous thromboembolism in adult patients undergoing surgery, particularly orthopaedic, general or oncological surgery.
- Prophylaxis of venous thromboembolism in non-surgical adult patients immobilised due to acute medical illness including: acute heart failure, acute respiratory failure, severe infections, active cancer, as well as exacerbation of rheumatic diseases.
- Prevention of clotting in extracorporeal circuits during haemodialysis and haemofiltration in adults.
- Treatment of venous thrombosis and thromboembolic disease including deep vein thrombosis and pulmonary embolus in adults.
- Extended treatment of venous thromboembolism and prevention of recurrences in adult patients with active cancer.
- Not licensed for, but used in bridging anticoagulant treatment in patients undergoing procedures (not expected to impact on Shared Care).

Pharmacology

Tinzaparin sodium is an antithrombotic agent. It potentiates the inhibition of several activated coagulation factors, especially Factor Xa, its activity being mediated via antithrombin III.

Dosage and administration

Indication	Dose	Duration of Treatment
Treatment of venous thromboembolism in the following patient groups: ▪ Injectable drug users ▪ Patients in whom it has not been possible to stabilise oral anticoagulation	• Under 40kg: 175units/kg ONCE a day • 40-49kg: 8,000 units ONCE a day • 50-59kg: 10,000 units ONCE a day • 60-69kg: 12,000 units ONCE a day • 70-84kg: 14,000 units ONCE a day • 85-94kg: 16,000 units ONCE a day • 95-109kg: 18,000 units ONCE a day • 110-119kg: 20,000 units ONCE a day	First event: 3 – 6 months as instructed Recurrent idiopathic event: long term For ongoing risk factors such as cancer or if

▪ **NOT pregnancy**	• 120-129kg: 22,000 units ONCE a day • 130-139kg: 24,000 units ONCE a day • 140-154kg: 26,000 units ONCE a day • Over 154kg: 175units/kg ONCE a day	inability to stabilise on long term oral anticoagulation: consider continuing long term while risk factors are prevalent.
Prevention of venous thromboembolism in orthopaedic patients (hip fracture, hip arthroplasty, or high risk patients immobilised in lower limb cast)	• Under 31kg: 50 units/kg ONCE a day • 31-49kg: 2,500 units ONCE a day • 50-99kg: 4,500 units ONCE a day • 100-149kg: 3,500 units TWICE a day • Over 149kg: 4,500units TWICE a day	Hip fracture = 28 days For lower limb cast = until cast removed / mobility regained (which is usually around 6/52)
Prophylaxis of thromboses associated with central venous lines or other medical reasons	• Under 31kg: 50 units/kg ONCE a day • 31-49kg: 2,500 units ONCE a day • 50-99kg: 4,500 units ONCE a day • 100-149kg: 3,500 units TWICE a day • Over 149kg: 4,500units TWICE a day	For the duration that the central line is in-situ (or the duration of the risk)
Extended *treatment and prophylaxis* of DVT or PE in patients with **solid tumors**.	• Under 32kg: 175units/kg ONCE a day • 32-37kg: 6,000 units ONCE a day • 38-42kg: 7,000 units ONCE a day • 43-48kg: 8,000 units ONCE a day • 49-54kg: 9,000 units ONCE a day • 55-59kg: 10,000 units ONCE a day • 60-65kg: 11,000 units ONCE a day • 66-71kg: 12,000 units ONCE a day • 72-77kg: 13,000 units ONCE a day • 78-82kg: 14,000 units ONCE a day • 83-88kg: 15,000 units ONCE a day • 89-94kg: 16,000 units ONCE a day • 95-99kg: 17,000 units ONCE a day • 100-105kg: 18,000 units ONCE a day • Over 105kg: 175units/kg ONCE a day	6 months - treatment beyond 6 months should be evaluated. Plt. count <50,000mm^3 discontinue tinzaparin until platelets recover to >50,000mm^3

NB some of the doses use for patients with higher body weight within this document are outside of the license for tinzaparin (Innohep®) due to concerns around evidence of treatment failure at licensed doses in high body weight patients. Further evidence of safety and efficacy of the higher (off-license) doses have been assessed by the Lead Pharmacist and Consultant Haematologist in compiling this document.

All patients will be supplied with 28 days of tinzaparin treatment upon initiation or discharge from BHNFT.

Preparations available:
Innohep® is available as single-dose syringes in the following strengths/doses:

- *10,000 units/mL* as 2,500units/0.25mL; 3,500units/0.35mL; 4,500units/0.45mL
- *20,000 units/mL* as 8,000units/0.4mL; 10,000units/0.5mL; 12,000units/0.6mL; 14,000units/0.7mL; 16,000units/0.8mL; 18,000units/0.9mL

Responsibilities of the specialist clinician initiating treatment

Summary

- To assess the suitability of the patient for treatment and initiate tinzaparin in appropriate patients. (including confirming the patient has no contra-indications to treatment and considering the relevance of any cautions, including interactions).
- To discuss the benefits and side effects of treatment with the patient/carer and the need for long term monitoring if applicable. Obtain informed consent in line with national guidance. This is particularly important for unlicensed products. To discuss the patient's responsibilities (see relevant section) in relation to the shared care agreement.
- To perform baseline tests and if appropriate routine tests until the patient is stable (see details of baseline and routine tests which should be carried out by the specialist in the monitoring section below).
- To monitor platelet counts for the emergence of Heparin Induced Thrombocytopenia (HIT) within the first 14 days of treatment. If HIT is identified it is the responsibility of the initiating specialist to inform primary care clinicians and adjust treatment as necessary.
- To prescribe for the first 28 days of treatment
- To ask the GP whether they are willing to participate in shared care.
- To provide the GP with a summary of information relating to the individual patient to support the GP in undertaking shared care (see shared care request form in Appendix A which includes a link to the shared care guideline).
- To advise the GP of any dosage adjustments required, monitoring required, when to refer back, and when and how to stop treatment (if appropriate).
- To advise the GP when the patient will next be reviewed by the specialist but if ongoing specialist co-ordination of the patient's care is not required, an individual care plan should be agreed on a case-by-case basis
- To monitor the patient for adverse events and report to the GP and where appropriate Commission on Human Medicines/MHRA (Yellow Card scheme).
- To provide the GP with contact details in case of queries.
- To provide patient / carer with contact details for support and help if required; both in and out of hours.

Baseline Tests
Include platelet counts, full blood count and U&E's for patients at risk of hyperkalaemia (e.g. patients with diabetes mellitus, or taking potassium supplements or potassium sparing diuretics).

Routine Tests
Routine monitoring of serum potassium levels may be required for patients at risk of hyperkalaemia. These should be done on a monthly basis.

Disease monitoring
The frequency of review of the patient will depend on the indication and likelihood of continuing treatment on a long-term basis. The review period must be specified on the shared care referral

Responsibilities of the primary care clinician

Acceptance of Responsibility by the Primary Care Clinician
It is optional for the primary care clinician to participate in taking on responsibility for shared care for the patient. Primary care clinicians will take on shared care only if they are willing and able.

Summary

- To reply to the request for shared care as soon as possible.
- To prescribe and adjust the dose as recommended by the specialist **- where appropriate, tinzaparin should be prescribed in full pack sizes (multiples of 10 pre-filled syringes). This is to ensure the supply is received in an original manufacturer's pack (the packs are colour coded according to strength/dose of the pre-filled syringes) with the original patient information leaflet for patient safety.**
- To ensure there are no interactions with any other medications initiated in primary care.
- To continue monitoring as agreed with secondary care in the monitoring section below.
- To inform the specialist if the patient discontinues treatment for any reason.

- To seek the advice of the specialist if any concerns with the patient's therapy. For example:
  - Patient or general practitioner is **not** comfortable to continue with the existing regime due to either change in condition or drug side effects.
  - Advice in respect of concordance.
  - Special situations, (e.g. Pregnancy).
- Discontinue the drug as directed by the specialist if required.
- To conduct an annual medication review or more frequently if required.
- To identify adverse events if the patient presents with any signs and liaise with the hospital specialist where necessary. To report adverse events to the specialist and where appropriate the Commission on Human Medicines/MHRA (Yellow Card scheme).

Responsibilities of Patients or Carers

Summary

- To be fully involved in, and in agreement with, the decision to move to shared care.
- To attend hospital and primary care clinic appointments and to bring monitoring information e.g. booklet (if required). Failure to attend will potentially result in the medication being stopped.
- Present rapidly to the primary care prescriber or specialist should the clinical condition significantly worsen.
- Report any suspected adverse effects to their specialist or primary care prescriber whilst taking tinzaparin
- To read the product information given to them.
- To take tinzaparin as prescribed.
- Inform the specialist, primary care prescriber or community pharmacist dispensing their prescriptions of any other medication being taken – including over-the-counter medication.

Clinical Particulars

The details of side-effects, cautions, contraindications and interactions are not a complete list and the current BNF (https://www.medicinescomplete.com/#/) and the SPC (https://www.medicines.org.uk/emc/) remain authoritative.

BNF therapeutic class	2.8.1 Parenteral Anticoagulants
Cautions and Contraindications	• History of Heparin Induced Thrombocytopenia • Significant hepatic impairment • Active gastric or duodenal ulceration or oesophageal varices • Haemophilia and other inherited bleeding disorders / major bleeding disorders • Thrombocytopenia with platelets <50 x 10^9/l • Recent cerebral haemorrhage • Severe hypertension • Recent neurosurgery or eye surgery • Acute bacterial endocarditis • Hypersensitivity to tinzaparin
Pregnancy and breast feeding	**Pregnancy** Not known to be harmful, low molecular weight heparins do not cross the placenta. **Breastfeeding** The passage of tinzaparin into human breast milk is expected to be very low. The oral absorption of any trace amount of tinzaparin sodium in the breast milk to the infant is very unlikely. Tinzaparin can be used during breastfeeding.
Adverse Drug Reactions	• Heparin induced thrombocytopenia – HIT usually presents between 5 and 14 days after starting therapy. This should be considered if platelet count falls below normal range, or to less than 50% of baseline platelet count. BHNFT will undertake monitoring for HIT during first 2 weeks of therapy, if indicated. **If patient develops signs and symptoms of thrombocytopenia, skin reaction or**

	new thrombosis within 14 days of starting therapy, HIT should be considered. Refer as an emergency to Medical SDEC for assessment and treatment. • Hyperkalaemia: Heparin inhibits aldosterone secretion and may cause hyperkalaemia (patients with diabetes, chronic renal failure, acidosis, raised potassium or taking potassium-sparing drugs most susceptible). Risk increases with duration of therapy. • Haemorrhage • Thrombocytopenia (monitoring for HIT required by secondary care as above) • Injection site reactions (consider change to alternative LMWH) • Osteoporosis (following long term use) • Skin necrosis and hypersensitivity reactions • Anaemia • Angioedema • Priapism • Stevens-Johnson syndrome • Thrombocytosis
Monitoring	When the appropriate monitoring for HIT and hyperkalaemia have been performed (and results are satisfactory) the responsibility for re-prescribing the drug and further monitoring for hyperkalaemia (if appropriate in higher risk patients) will pass to the patient's practice. The practice will be informed of this transfer of prescribing responsibilities and the patient provided with a further 2 weeks' supply of drug by the hospital pharmacy. Monitoring of tinzaparin for heparin-induced thrombocytopenia (HIT) is not required in some patient groups (e.g. pregnant patients receiving LMWH for prophylaxis, not covered in this guideline), whereas others usually require only limited monitoring for the first 2 weeks of treatment. This will be carried out by BHNFT. Occasional patients require ongoing monitoring for hyperkalaemia. Patients at high risk of developing hyperkalaemia and renal impairment include those with pre-existing renal impairment, patients taking medications such as ACE inhibitors, angiotensin receptor blockers and aldosterone antagonists, and patients taking medication which may alter renal blood flow.
Interactions	Systemic salicylates, non-steroidal anti-inflammatory drugs (NSAIDs), clopidogrel, dipyridamole (increased risk of bleeding), ACE inhibitors (increased risk of hyperkalaemia), dextran, ticlopidine, systemic glucocorticoids, thrombolytics, anticoagulants. <u>This is not a comprehensive list. Please see current BNF for complete information.</u>
Additional information	Not applicable.
Re-Referral guidelines	Patients who are being treated on the advice of the secondary care team, but are no longer being seen in that setting, may still need review should problems arise. The appropriate level of care and/or advice should be available from the secondary care team in a timely manner without requiring a new referral. Include 'route of return' should their condition change (such as a return of symptoms, or a development of adverse effects).
Ordering information	Not applicable.

Communication and contact details

Specialist to primary care clinician
The specialist will inform the primary care clinician when they have initiated tinzaparin. When the patient is near completing the satisfactory initiation period, the specialist will write to the primary care clinician to request they take over prescribing and where possible give an indication as to the expected length of treatment. The specialist will also send a shared care request form to support the primary care clinician in undertaking shared care. (Appendix A)

Primary Care Clinician to specialist
If the primary care clinician has concerns over the prescribing of tinzaparin, they will contact the specialist as soon as possible.

Contact names and details

Contact Details	**Telephone number**	**Email**
Consultant Haematologists: Dr D. Chan-Lam Dr R Rashid	01226 730000	dchanlam@nhs.net rumana.rashid@nhs.net
Medicines Information:	01226 432857	gilliansmith2@nhs.net or medicine.information1@nhs.net
Anticoagulant Lead Pharmacists: Umar Patel	01226 431460	umar.patel@nhs.net

Equality and diversity
Tinzaparin is a LMWH that is porcine-derived, so it may not be suitable for some patient populations.

References
1. Summary of Product Characteristics (SPC) for tinzaparin (Innohep®) accessed via https://www.medicines.org.uk/emc/product/3632/smpc
2. BNF accessed via https://www.medicinescomplete.com/#/content/bnf/_380849985?hspl=Tinzaparin%20sodium

https://www.england.nhs.uk/wp-content/uploads/2018/03/responsibility-prescribing-between-primary-secondary-care-v2.pdf

Development Process
This guidance has been produced by Tsz Hin Wong (Senior Pharmacist – Interface) following an AMBER classification status of tinzaparin by the Barnsley Area Prescribing Committee. This guideline has been subject to consultation and endorsement by Dr D. Chan-Lam (Consultant Haematologist, BHNFT) and Mr J Bannister (Associate Medical Director and Chair of the Venous Thromboembolism Committee, BHNFT) and was ratified by the Area Prescribing Committee on 13th March 2024.

Appendix A – Shared Care request form (Amber) for tinzaparin

- Specialist to complete when requesting primary care clinician to enter a shared care arrangement.
- Primary care clinician to return signed copy of form. [Insert details of how to return the form e.g. to a safe haven e-mail address, postal address if the form should be returned by post]
- Both parties should retain a signed copy of the form in the patient's record.

From (**Specialist**): _____ **To** (**Primary care clinician**): _____

As per the agreed Barnsley shared care guideline for tinzaparin, this patient is now suitable for prescribing to move to primary care.

The patient fulfils the criteria for shared care and I am therefore requesting your agreement to participate in shared care. I have carried out baseline tests and initial monitoring as detailed in the shared care guideline.

Patient details

Name: _____ NHS Number: _____

Address: _____ DOB: _____

Diagnosed condition: _____

Amber Drug details

Drug name: Tinzaparin Dose and frequency: _____ units _____
by subcutaneous injection

Date of initiation: _____

Length of treatment: 3 months / 6 months/ 12 months / long term / other (please specify)
(circle as appropriate)

U&E monitoring requirements:(tick as appropriate):

☐ High risk - high risk of hyperkalaemia or renal impairment – monitor monthly

☐ Low risk – only needs to be done periodically as deemed necessary by clinical condition

The patient has been provided with sufficient medication to last until: _____

The patient will be reviewed by the consultant on: _____

The patient should be reviewed by the primary care clinician by: _____

Monitoring

The following monitoring should be undertaken by the primary care clinician. Refer to the monitoring section of the shared care guideline.

Parameter		BHNFT Reference Range	Result	Date test done
FBC	Platelets	150 – 400 x 10^9 /L		
	RBC	4.33 – 5.6 x 10^{12} /L		
	Hb	13.2 – 16.9 g/dL (males) 11.9 – 14.9 g/dL (females)		
U&E's	Sodium	133 – 146 mmol/L		
	Potassium	3.5 – 5.3 mmol/L		
	Creatinine	51 – 96 micromol/L		
	Urea	2.5 – 7.8 mmol/L		

The following monitoring should be undertaken by the GP:

Parameter	Date next test due	Frequency
U&E's		Monthly if high risk, as required if low risk (see above)
FBC		Periodically as deemed necessary by clinical condition

Communication

Consultant
Telephone number: _____ Fax number:_____

Email address: _____

Specialist Nurse
Telephone number: _____ Fax number: _____

Email address: _____

Confirmation of acceptance of shared care

Specialist (Doctor/Nurse) name: _____

Specialist (Doctor/Nurse) signature: _____ Date: _____

I, ……., can confirm I :

☐ accept the request to participate in shared care for the patient named above and will complete the monitoring as set out in the shared care guideline for this medicine/condition.

☐ reject the request to participate in shared care for the patient named above. The reason for this being …….

Signature of primary care clinician: _____Date:_____

To save resources you have been sent appendix A of the shared care document. The full document (Shared Care Guideline for Tinzaparin for the Treatment and Prophylaxis of Venous Thromboembolism *date approved March 2024)* can be accessed on the Barnsley BEST website at the following link: http://best.barnsleyccg.nhs.uk/clinical-support/medicines/shared-care-guidelines/
Or via the Barnsley Area Formulary www.barnsleyformulary.nhs.uk