Briefing Paper for Surrey Heartlands Integrated Care System (ICS) Area Prescribing Committee (APC)

Integrated Care Partnerships (ICPs) (Surrey Downs, Guildford & Waverley, North West Surrey, East Surrey (as part of the CRESH system) & associated partner organisations.

NICE NATIONAL GUIDANCE: Local implementation

NICE National Guidance	Venous Thromboembolic Diseases: diagnosis, management and thrombophilia testing (NG158)		
Available at	https://www.nice.org.uk/guidance/ng158		
Date of issue	26 March, 2020	**Implementation deadline**	None – National Guidance aims to improve quality of management of a group of patients and can be implemented over a period of time.

Summary of Guidance

This Guideline (NICE NG158) updates and replaces NICE guideline CG144. It aims to support diagnosis and treatment of deep vein thrombosis (DVT) or pulmonary embolism (PE). It also covers testing for conditions that can make a DVT or PE more likely.

Key medication-related changes to recommendations since the last Guidance was published:

- Offer either apixaban or rivaroxaban to people with proximal DVT or PE, or if neither is suitable offer:
  - low molecular weight heparin (LMWH) for at least 5 days followed by dabigatran or edoxaban ***or***
  - LMWH concurrently with a vitamin K antagonist (VKA) for at least 5 days, or until the INR is at least 2.0 in 2 consecutive readings, followed by a VKA on its own.
- The duration of treatment should be 3 months. If the VTE was unprovoked, longterm prophylaxis should be prescribed.
- Offer people with active cancer and proximal DVT or PE anticoagulation treatment for 3 to 6 months with a direct-acting oral anticoagulant or, if this is unsuitable, consider LMWH alone or LMWH concurrently with a VKA for at least 5 days or until the INR is at least 2.0 in 2 consecutive readings, followed by a VKA on its own.

A VTE working Group was formed to consider these recommendations. The Group consisted of Pharmacy representatives from each of the local hospital trusts and the 4 ICPs in Surrey Heartlands CCG.

Summary of recommendations to APC from the VTE Working Group

1. All 4 DOAC drugs should be added to the Surrey PAD and Trust Formularies as NICE has approved them all for this indication. They should be BLUE drugs for this indication – diagnosis requires specialist input and urgent initiation of treatment. Apixaban and rivaroxaban should be assigned BLUE preferred status for initiation in most patients because they do not require initial treatment with 5 days of LMWH. Edoxaban and dabigatran should be reserved for those few patients who are **not** clinically suitable for apixaban or rivaroxaban eg those with excellent renal function where dabigatran is the best choice.

ACTION: agree traffic light status to be assigned to the Surrey PAD and RSCH/GW Joint Formulary.

2. A treatment pathway has been developed which summarises the standard patient journey and the setting in which the different stages of treatment will generally occur (Appendix A). During the consultation period for this paper it was suggested that it would be simpler to adopt the NICE treatment pathway rather than formatting our own. This has been included in Appendix A for comparison.
   ACTION: The Committee is asked to agree which pathway should be adopted.

3. Discharge communication to Primary Care must be improved and must include a summary of monitoring results from during the admission and to be carried out in Primary care. There must also be a clear treatment plan for the duration and choice of DOAC, to be used going forward. Any ongoing monitoring by Secondary care must be clearly planned and communicated with the patient's GP
   ACTIONS:
   - Agree transfer of prescribing template – for integration into the EPMS at each Trust (see Appendix B). MOGs to ensure this template is adapted and implemented appropriately at each Trust.
   - In 6 months, check whether the procedure for transfer of care is being followed by the Trusts and whether it is effective.

4. The patient must receive medication as follows:
   a. Diagnosis in Outpatients or A&E: the first month of treatment for VTE from the secondary care provider
   b. Diagnosis during an Inpatient admission: a minimum of the first month from Secondary Care with at least 14 days medication on discharge

   This means that all patients will have received any initial loading doses and be on the maintenance phase of their anti-coagulation treatment prior to the GP taking over prescription.
   ACTIONS: Agree durations of supply from Secondary Care

5. The VTE group felt strongly that it was important not to swap patients from one DOAC to another when entering the long-term prophylaxis phase of treatment. From a risk management perspective, this is where treatments often go wrong and the consequence of inadvertently taking 2 DOACs, or none, would be potentially life-threatening.
   ACTION: Agree that swapping DOAC when entering long-term prophylaxis is not supported and add this to the PAD narrative.

6. The previous guidance recommended that all patients have full MRI scanning to check for cancer while the new guidance recommends imaging only if there is a clinical concern that cancer is present. Due to this change, there must be a discussion between the diagnosing clinician and patient about VTE being an early symptom of cancer in some patients. They must give advice on other warning symptoms of cancer and who to contact if the patient has any concerns. If there is significant concern that the patient may have cancer, then they must be urgently referred for further investigation.
   ACTION: Secondary care centres to ensure that their protocols are updated to reflect the above changes.

7. The following issues were identified during feedback for this document:
   a. **Management of cancer patients** - both those on active treatment and those who are living with a previous diagnosis of cancer in the Community. Those on active treatment should receive all their medication from their Specialist Centre. The questions to be considered are communication between the

patient's GP and the Specialist Centre and whether those who are not on active treatment should be managed in the community after receiving the first month of treatment from Secondary Care.

b. **Community diagnosis of DVT**. There is a pathway (not currently being used – initiates rivaroxaban) in North-West Surrey and one in East Surrey (rarely used – initiates LMWH). These pathways should be reviewed at APC in the light of NG158 and this pathway. A system-wide decision is needed on this way to diagnose and manage VTE. Decisions are needed to ensure that diagnosis and all aspects of management are in line with the NICE guidance: not just the medication. The principle that all citizens should have equal access to the same standard of evidence-based care must be applied. It is proposed that this should be raised at the Surrey Clinical Priorities Committee or the Urgent and Integrated Care Team at the CCG.

c. **Further refinement of treatment choice** to prefer one agent only. Further work will be needed to look more closely at the local differences in cost effectiveness, in collaboration with the Specialist Clinicians and other interested parties.

ACTIONS: Add to APC workplan to be discussed at a future meeting.

8. **Subsequent additions to the paper:**
DOACs are not suitable for major blood clots as there were not significant number of patients with this in the trials. It is the responsibility of centres treating VTE to have this clearly indicated in their internal pathways.
ACTION: Secondary Care to ensure that this information is included in their VTE policies/pathways.

Disease and potential patient group	
Brief description of disease	Venous thromboembolism (VTE) is a condition in which a blood clot (a thrombus) forms in a vein, most commonly in the deep veins of the legs or pelvis. This is known as deep vein thrombosis, or DVT. The thrombus can dislodge and travel in the blood, particularly to the pulmonary arteries. This is known as pulmonary embolism, or PE. The term VTE includes both DVT and PE. VTE is an important cause of death and its prevention and management is a priority for the NHS. Non-fatal VTE is also important because it can cause serious longer-term conditions such as post-thrombotic syndrome and chronic thromboembolic pulmonary hypertension.[2]
Potential patient numbers per 100,000	UK estimated incidence rate of 1-2 per 100,000 population per annum. VTE is a significant cause of mortality and disability in England with thousands of deaths directly attributed to it each year. One in twenty people will have VTE during their lifetime and more than half of those events are associated with prior hospitalisation. At least two thirds of cases of hospital-associated thrombosis are preventable through VTE risk assessment and the administration of appropriate thromboprophylaxis, however currently VTE is one of the most common forms of hospital mortality.[3]

SUMMARY

NICE recommendations

In terms of anticoagulation, the main sections of interest are recommendations 1.3 and 1.4 which are shown in full below:

1.3 Anticoagulation treatment for suspected or confirmed DVT or PE

NICE has also produced a visual summary of the recommendations on anticoagulation treatment for DVT or PE.

1.3.1 When offering anticoagulation treatment, follow the recommendations on shared decision making and supporting adherence in the NICE guidelines on medicines optimisation, medicines adherence and patient experience in adult NHS services. **[2020]**

Interim therapeutic anticoagulation for suspected DVT or PE

1.3.2 Follow the recommendations on when to offer interim therapeutic anticoagulation for suspected proximal DVT or PE in the section on diagnosis and initial management. **[2020]**

1.3.3 If possible, choose an interim anticoagulant that can be continued if DVT or PE is confirmed (see the section on anticoagulation treatment for confirmed DVT or PE). **[2020]**

In March 2020, direct-acting anticoagulants and some low molecular weight heparins (LMWHs) were off label for the treatment of suspected DVT or PE. See NICE's information on prescribing medicines.

1.3.4 When using interim therapeutic anticoagulation for suspected proximal DVT or PE:

- carry out baseline blood tests including full blood count, renal and hepatic function, prothrombin time (PT) and activated partial thromboplastin time (APTT)
- do not wait for the results of baseline blood tests before starting anticoagulation treatment review, and if necessary act on, the results of baseline blood tests within 24 hours of starting interim therapeutic anticoagulation. **[2020]**

Anticoagulation treatment for confirmed DVT or PE

1.3.5 Offer anticoagulation treatment for at least 3 months to people with confirmed proximal DVT or PE. For recommendations on treatment after 3 months see the section on long-term anticoagulation for secondary prevention. **[2020]**

1.3.6 If not already done, carry out baseline blood tests, as outlined in recommendation 1.3.4, when starting anticoagulation treatment. **[2020]**

1.3.7 When offering anticoagulation treatment, take into account comorbidities, contraindications and the person's preferences.

1.3.8 Offer either apixaban or rivaroxaban to people with confirmed proximal DVT or PE (but see recommendations 1.3.11 to 1.3.20 for people with any of the clinical features listed in recommendation 1.3.7). If neither apixaban nor rivaroxaban is suitable offer:

- LMWH for at least 5 days followed by dabigatran or edoxaban **or**
- LMWH concurrently with a vitamin K antagonist (VKA) for at least 5 days, or until the INR is at least 2.0 in 2 consecutive readings, followed by a VKA on its own. **[2020]**

1.3.9 Do not routinely offer unfractionated heparin (UFH) with a VKA to treat confirmed proximal DVT or PE unless the person has renal impairment or established renal failure (see recommendations 1.3.13 and 1.3.14) or an increased risk of bleeding. **[2020]**

1.3.10 Do not routinely offer self-management or self-monitoring of INR to people who have had DVT or PE and are having treatment with a VKA. **[2012]**

Anticoagulation treatment for DVT or PE in people at extremes of body weight

1.3.11 Consider anticoagulation treatment with regular monitoring of therapeutic levels for people with confirmed proximal DVT or PE who weigh less than 50 kg or more than 120 kg, to ensure effective anticoagulation.

Note the cautions and requirements for dose adjustment and monitoring in the medicine's summary of product characteristics (SPC), and follow locally agreed protocols or advice from a specialist or multidisciplinary team. **[2020]**

Anticoagulation treatment for PE with haemodynamic instability

1.3.12 For people with confirmed PE and haemodynamic instability, offer continuous UFH infusion and consider thrombolytic therapy (see the section on thrombolytic therapy). **[2020]**

Anticoagulation treatment for DVT or PE with renal impairment or established renal failure

In March 2020, some LMWHs were off label for the treatment of DVT or PE in people with severe renal impairment (estimated creatinine clearance 15 ml/min to 30 ml/min) or established renal failure (estimated creatinine clearance less than 15 ml/min). See NICE's information on prescribing medicines.

1.3.13 Offer people with confirmed proximal DVT or PE and renal impairment (estimated creatinine clearance between 15 ml/min and 50 ml/min) one of:

- apixaban
- rivaroxaban
- LMWH for at least 5 days followed by:
  - edoxaban **or**
  - dabigatran if estimated creatinine clearance is 30 ml/min or above
- LMWH or UFH, given concurrently with a VKA for at least 5 days or until the INR is at least 2.0 in 2 consecutive readings, followed by a VKA on its own.

Note the cautions and requirements for dose adjustment and monitoring in the medicine's SPC, and follow locally agreed protocols or advice from a specialist or multidisciplinary team. **[2020]**

1.3.14 Offer people with confirmed proximal DVT or PE and established renal failure (estimated creatinine clearance less than 15 ml/min) one of:

- LMWH
- UFH
- LMWH or UFH concurrently with a VKA for at least 5 days or until the INR is at least 2.0 in 2 consecutive readings, followed by a VKA on its own.

Note the cautions and requirements for dose adjustment and monitoring in the medicine's SPC, and follow locally agreed protocols or advice from a specialist or multidisciplinary team. **[2020]**

Anticoagulation treatment for DVT or PE with active cancer

In March 2020, most anticoagulants were off label for the treatment of DVT or PE in people with active cancer. See NICE's information on prescribing medicines.

1.3.15 Offer people with active cancer and confirmed proximal DVT or PE anticoagulation treatment for 3 to 6 months. Review at 3 to 6 months according to clinical need. For recommendations on treatment after 3 to 6 months see the section on long-term anticoagulation for secondary prevention. **[2020]**

1.3.16 When choosing anticoagulation treatment for people with active cancer and confirmed proximal DVT or PE, take into account the tumour site, interactions with other drugs including those used to treat cancer, and the person's bleeding risk. **[2020]**

1.3.17 Consider a direct-acting oral anticoagulant (DOAC) for people with active cancer and confirmed proximal DVT or PE. **[2020]**

1.3.18 If a DOAC is unsuitable consider LMWH alone or LMWH concurrently with a VKA for at least 5 days, or until the INR is at least 2.0 in 2 consecutive readings, followed by a VKA on its own. **[2020]**

1.3.19 For people with confirmed DVT or PE and cancer that is in remission, follow the recommendations in the section on anticoagulation treatment for confirmed DVT or PE. **[2020]**

Anticoagulation treatment for DVT or PE with antiphospholipid syndrome

1.3.20 Offer people with confirmed proximal DVT or PE and an established diagnosis of antiphospholipid syndrome LMWH concurrently with a VKA for at least 5 days, or until the INR is at least 2.0 in 2 consecutive readings, followed by a VKA on its own. **[2020]**

Treatment failure

1.3.21 If anticoagulation treatment fails:

- check adherence to anticoagulation treatment
- address other sources of hypercoagulability
- increase the dose of anticoagulant or change to an anticoagulant with a different mode of action. **[2020]**

NICE technology appraisal guidance on anticoagulation treatment for confirmed DVT or PE

For NICE technology appraisal guidance see:

- Apixaban for the treatment and secondary prevention of deep vein thrombosis and/or pulmonary embolism
- Dabigatran etexilate for the treatment and secondary prevention of deep vein thrombosis and/or pulmonary embolism
- Edoxaban for treating and for preventing deep vein thrombosis and pulmonary embolism
- Rivaroxaban for treating pulmonary embolism and preventing recurrent venous thromboembolism
- Rivaroxaban for the treatment of deep vein thrombosis and prevention of recurrent deep vein thrombosis and pulmonary embolism.

1.4 Long-term anticoagulation for secondary prevention

1.4.1 Assess and discuss the benefits and risks of continuing, stopping or changing the anticoagulant with people who have had anticoagulation treatment for 3 months (3 to

6 months for people with active cancer) after a proximal DVT or PE. Follow the recommendations on shared decision making and supporting adherence in the NICE guidelines on medicines optimisation, medicines adherence and patient experience in adult NHS services. **[2020]**

1.4.2 Consider stopping anticoagulation treatment 3 months (3 to 6 months for people with active cancer) after a provoked DVT or PE if the provoking factor is no longer present and the clinical course has been uncomplicated. If anticoagulation treatment is stopped, give advice about the risk of recurrence and provide:

- written information on symptoms and signs to look out for
- direct contact details of a healthcare professional or team with expertise in thrombosis who can discuss any new symptoms or signs, or other concerns
- information about out-of-hours services they can contact when their healthcare team is not available. **[2020]**

1.4.3 Consider continuing anticoagulation beyond 3 months (6 months for people with active cancer) after an unprovoked DVT or PE. Base the decision on the balance between the person's risk of venous thromboembolism (VTE) recurrence and their risk of bleeding. Discuss the risks and benefits of long-term anticoagulation with the person, and take their preferences into account. **[2020]**

1.4.4 Explain to people with unprovoked DVT or PE and a low bleeding risk that the benefits of continuing anticoagulation treatment are likely to outweigh the risks. **[2020]**

1.4.5 Do not rely solely on predictive risk tools to assess the need for long-term anticoagulation treatment. **[2020]**

1.4.6 Consider using the HAS-BLED score for major bleeding risk to assess the risk of major bleeding in people having anticoagulation treatment for unprovoked proximal DVT or PE. Discuss stopping anticoagulation if the HAS-BLED score is 4 or more and cannot be modified. **[2020]**

1.4.7 Take into account the person's preferences and their clinical situation when selecting an anticoagulant for long-term treatment. **[2020]**

1.4.8 For people who do not have renal impairment, active cancer, established antiphospholipid syndrome or extreme body weight (less than 50 kg or more than 120 kg):

- offer continued treatment with the current anticoagulant if it is well tolerated **or**
- if the current treatment is not well tolerated, or the clinical situation or person's preferences have changed, consider switching to apixaban if the current treatment is a direct-acting anticoagulant other than apixaban. **[2020]**

1.4.9 For people with renal impairment, active cancer, established antiphospholipid syndrome or extreme body weight (less than 50 kg or more than 120 kg), consider carrying on with the current treatment if it is well tolerated. **[2020]**

1.4.10 If anticoagulation treatment fails follow the recommendation on treatment failure. **[2020]**

1.4.11 For people who decline continued anticoagulation treatment, consider aspirin 75 mg or 150 mg daily.

In March 2020, the use of aspirin for secondary prevention of DVT or PE was off label. See NICE's information on prescribing medicines. **[2020]**

1.4.12 Review general health, risk of VTE recurrence, bleeding risk and treatment preferences at least once a year for people taking long-term anticoagulation treatment or aspirin. **[2020]**

Cost implications*

Annual drug cost per patient:

Drug	Dose	Cost of first 3 months (13 weeks) of treatment (£)	Annual Cost of Preventative treatment (£)❁
Apixaban	**Initiation:** apixaban 10mg twice daily for 1 week then **Maintenance:** apixaban 5mg twice daily **Prevention of recurrent VTE** (long term): apixaban 2.5mg twice daily.	186.20	693.50
Rivaroxaban	**Initiation:** Rivaroxaban 15mg twice daily after food for 3 weeks **Maintenance:** rivaroxaban 20mg daily after food **Prevention of recurrent VTE** (long term): Rivaroxaban 10mg or 20mg daily after food	235.20	766.50
Edoxaban	**Prevention of recurrent VTE** (longterm): edoxaban 60mg daily		638.75

❁Prices taken from the Drug tariff online, March 2021. NHS Electronic Drug Tariff (nhsbsa.nhs.uk). Locally there is a price agreement for edoxaban (confidential – detail on application).

Has dose escalation been considered as part of the NICE costing template? n/a

Costing information/100,000 population and per CCG:
The estimated financial impact of implementing this guideline for England in the next 5 years is a saving of around £0.8 million in 2020/21, rising to a saving of around £4.1 million per year from 2024/25 onwards. The resource impact from 2024/25 onwards consists of savings of around £2.1 million to prescribing budgets because of changes in the anticoagulant therapy treatment pathway, and around £2 million noncash releasing savings for providers because of reductions in imaging screening.

NG158 included a resource impact template to help with assessing the overall cost implication of implementing the full guidance at a local level (see appendix C for this template with Surrey Heartlands data selected). The bottom-line estimate of savings in Surrey Heartlands is £61,568. – about half of which will apply to the prescribing budget. The other 50% will be realised from reduced imaging requirements to assess patients for a diagnosis of cancer.

On more detailed analysis, the drug related cost savings will mostly relate to reductions in secondary care – using more DOACs than LMWH to treat VTE in cancer patients (leading to a 33% cost saving for that cohort).

It is projected that the proportion of patients who have had a VTE but are not known to have cancer receiving apixaban/rivaroxaban will rise from 40% (currently) to 70%. This increase will come equally from reductions to low molecular weight heparin (LMWH) leading to either dabigatran or edoxaban, or warfarin and has been calculated to be cost neutral. However, the Hospitals will still use LMWH for those patients will extensive clots who require admission until they have been stabilised so this picture will not be completely accurate.

It is projected that changing to use of apixaban/rivaroxaban for the majority of patients and moving away from current prescribing of LMWH/warfarin and LMWH/dabigatran or edoxaban will be overall cost neutral.

The distribution of savings will be complex and will relate to reduction in use of LMWH and reduced monitoring of INR for patients on warfarin. Consideration will have to be given to the provision of warfarin monitoring service and how it could be scaled back in proportion to reduced need.

Availability of PAS and details (if appropriate): None

Availability of homecare service (if appropriate): Not necessary

**NICE funding requirements are based on Quality Adjusted Life Years (QALY) threshold. If there is evidence that the incremental cost rises above this threshold in the future, the APC may reconsider the commissioning status.*

Alternative treatments and cost per patient (per year / per month as appropriate)

Other NICE recommended products:
n/a

Options not reviewed by NICE but used in standard practice:
n/a

Impact to patients

Patients must understand the decision to initiate a DOAC to treat their VTE and the planned duration of therapy.

They must understand the importance of complying with the treatment and the monitoring which will be necessary. If they were previously on warfarin, they must not interpret the reduction in monitoring as meaning that side effects or interactions with other medicines are not risks with this treatment.

They must be clear about whether the monitoring will be in primary or secondary care and whom to contact if they have any queries or concerns about either a further clot or bleeding. The patients must understand that the main side effect associated with this therapy is related to bleeding and that the risk of this is less than the risk associated with another clot.

Impact to primary care prescribers

Improved communication from Secondary Care to focus on clear understanding of the planned duration of therapy and whether or not the patient will reviewed by the Haematology team within the Trust (see Appendix B for a template letter which may be used or incorporated in the Discharge Communication from the Trust).

May be more patients on long-term DOAC for prevention of recurrence of VTE than would have been on warfarin for this indication. This is still a relatively small cohort, compared with those on DOACs for prevention of stroke in atrial fibrillation (the incidence of which is 7.2% in over 65 year olds).

No supply issues have historically with any of these medicines. All 4 DOACs are on Surrey PAD and the RSFT/GW Joint Formulary, so it will be straightforward to change to an alternative, if there is a supply problem in the future.

Impact to secondary care

Ensure trust VTE pathway is in line with NG158 – this needs to take account of the different channels for presentation i.e. via A&E, Outpatients or in an inpatient.

DOACs are not suitable for major blood clots as there were not significant number of patients with this in the trials. It is the responsibility of centres treating VTE to have this clearly indicated in their internal pathways.

Communicate intention for duration and monitoring of anti-coagulant therapy clearly to the GP – including whether care is to be transferred to the GP or the date of future follow up in secondary care. (see Appendix B for a template showing the information which must be communicated – may be incorporated into existing discharge information from the Trust).

Impact to CCGs

MOGs to work out how they will communicate out to all relevant teams, emergency care, respiratory, anticoagulant service, pharmacy etc. They must ensure that the transfer of care documents will be adopted in the Trust systems etc.

There is a Pathway for Community d-dimer testing for DVT which is currently implemented in North West Surrey and East Surrey. These protocols will need to be clinically reviewed in light of this NICE Guidance (NG158) and the costing reviewed. This should be done as a separate piece of work and brought to the APC for approval.

Implementation

The VTE working group decided to go with the NICE recommended treatment choice of either apixaban or rivaroxaban, to be decided by the initiating Trust. All of the local Trusts currently use one of these 2 drugs as their preferred option, so implementation of this part of the guidance is straightforward.

The Formulary must clearly define the preferred DOAC for each indication. The picture is complex currently with different DOACs selected for the management of different indications.

Anti-coagulation for the treatment of VTE is currently only initiated in the community in Surrey where the Pathway for Community D-dimer Testing has been implemented. This pathway must be reviewed as part of the implementation of NG158. The following changes are needed:

- The current D-dimer test which is used is qualitative. NG158 states that quantitative testing must be used
- The protocol must be reviewed to ensure that it is in line with NG158
- Communication with the patient and their GP must be reviewed to ensure that it is in line with the NICE Guidance

There must be improved communication from the Trust to the GP in terms of follow-up planned and duration of anti-coagulation. This should take the form of a letter from the Trust Haematology Team (example included in Appendix A from South West London, 2018).

Other changes in the guidance must be worked through by individual Trusts, to ensure that their practice is in line with the updated guidance or that they have discussed and agreed their policy in light of the information in the NICE guidance. Where the NICE recommendation has not been followed, there should be clearly documented reasoning outlining the reasons for that decision. These decisions should be discussed at, and recorded by, the Trust DTCs.

Recommendation to APC

PbRe: No
Recommended traffic light status:

Surrey PAD: All DOACs listed as green for initiation to treat VTE.

Local Trust formularies are as follows (as on 31st March, 2021):

Drug	Ashford and St Peter's Hosptial Formulary	Epsom Hospital Formulary	Guildford and Waverley Joint Formulary	Surrey and Sussex Healthcare Formulary
Apixaban	Not listed for VTE	Listed as a treatment option in VTE but no Traffic light	Blue preferred	Green – not listed for VTE
Dabigatran	Not listed for VTE	Listed as a treatment option in VTE but no Traffic light	Blue preferred for patients at high risk of bleeding	Green – not listed for VTE
Edoxaban	Not listed for VTE	Listed as a treatment option in VTE but for hospital use only	Blue non-preferred	Green (first line AF) but listed for VTE indication
Rivaroxaban	Not listed for VTE. However this is the preferred choice in a VTE pathway which will go to their next DTC meeting.	Listed as a treatment option in VTE but no Traffic light	Red Non-preferred	Green – listed for VTE indication

Blue would generally be the most appropriate category for these drugs in VTE. Most patients will be discharged to the community following treatment initiation in secondary care, with only a few requiring follow-up review by the Haematology team.

The first month (initiation phase) of treatment must be suppled from Secondary care following diagnosis after which care can be transferred to the GP with clear information as to what the ongoing monitoring and review from Secondary care will include (see Appendix B for Transfer of care letter). Note: we differ here from SWL and SEL. They decided to supply the full 3 month treatment course from secondary care and only transfer care and prescribing for those patients who will remain on long-term anti-coagulation.

As a minimum, the first month of treatment must be supplied by Secondary Care, and a minimum of 14 days of medication should be sent home with the patient on discharge. This allows the initiation pack to be supplied for rivaroxaban and means the GP will know they need to supply the continuation dose for this product.

There is a d-dimer screening service in the community in North West Surrey (LCS programme) and in East Surrey both of which need to be reviewed to ensure compliance with NG158 too. The Clinicians operating this community service will be regarded as Specialists in terms of carrying out the test and initiating treatment where appropriate. All patients with a positive test are referred into Secondary care as part of the Pathway. Thus,

the drugs would remain Blue on the Formulary.

Additional comments:
DOACs are currently on the Guildford and Waverley Formulary as Green for Atrial Fibrillation and Red for prophylaxis following hip/knee replacement. Edoxaban is the preferred treatment locally for Atrial fibrillation due to a favourable local price agreement. The choice of preferred DOAC for othropaedic prophylaxis has been decided by individual trusts.

In this document we are recommending either apixaban or rivaroxaban for VTE treatment and prophylaxis. This is in line with the existing decisions at all the local Acute Trusts. The VTE Working Group agreed that there were considerable safety concerns around changing anti-coagulant choice more than necessary. For this reason it was decided to:

- **Not** consider edoxaban or dabigatran for initial management of VTE as they both involve using a low molecular weight heparin for 5 days at the start of the treatment. There will be exceptions where it is clinically preferrable to use one of these drugs, in which case they should be initiated eg patients at high risk of bleeding or those with excellent renal function for whom dabigatran would be the best choice of treatment. These decisions will be clinical and based on discussion between the Consultant and the individual patient.
- **Not** consider switching from apixaban or rivaroxaban to edoxaban at the end of the 3 month treatment phase

The decision to recommend either apixaban or rivaroxaban is also in line with that of South West London, which borders Surrey Heartlands. This will aid patient flow; particularly for East Surrey and Surrey Downs which often refer patients into South West London. Indeed, the SWL pathway, which was agreed in December, 2020 has, with permission, been used as the basis for our own pathway (see appendix A).

In Appendix A the visual summary from NG158 which relates to anticoagulation has also been included for comparison. The APC is invited to compare the 2 pathways and choose which it feels is preferrable for use in Surrey Heartlands.

This has resulted in a complex picture for DOAC selection locally. For example, there is currently a different DOAC of choice for each of the 3 indications at the Royal Surrey Foundation Trust.

In future, it would be ideal to work towards one DOAC being preferred for all of the indications. For expedience, however, it has been decided to continue with the current status quo for now.

New NICE Guidance on Atrial Fibrillation is currently being developed but there is no publication date for that document. An updated AF pathway was published on 1st March, 2021 – which reflects the information from previously published guidance.

References:

1 NG158. Venous Thromboembolic diseases: diagnosis, management and thrombophilia testing. Nice Guidance. Published 26 March, 2020. https://www.nice.org.uk/guidance/ng158

2 Venous thromboembolism in adults: diagnosis and management Published 2013. Quality Standard 29. Last updated Jan, 2021.https://www.nice.org.uk/guidance/qs29

3 All-party parliamentary thrombosis group. Annual review March, 2020.

4	Evidence review D: Evidence review for pharmacological treatment in people with suspected or confirmed deep vein thrombosis and/or pulmonary embolism. For NG158. March 2020 https://www.nice.org.uk/guidance/ng158/evidence/d-pharmacological-treatment-pdf-8710588337

Prepared by:

Lynne Hargreaves, Medicines Optimisation Pharmacist, Guildford and Waverley ICP on behalf of the VTE working group.

Declaration of Interest:

Attended 2 webinars in June, 2020 which discussed DOACs in VTE. They were hosted by Morph Consultancy and sponsored by Daichi Sankyo (who manufacture edoxaban)

Date: 18/02/21

Reviewed by:

Members of the VTE working group:

	MACKAY, Rachel (NHS Surrey Heartlands CCG) AL-SHWAIKH, Reham (NHS SURREY HEARTLANDS CCG) STANFORD, Lis (NHS SURREY HEARTLANDS CCG) SMITH, Nikki (NHS SURREY HEARTLANDS CCG) CONWAY, Grainne (SURREY AND SUSSEX HEALTHCARE NHS TRUST) GURNEY, Laura (ASHFORD AND ST PETER'S HOSPITALS NHS FOUNDATION TRUST) HOUGH, Dawn (ROYAL SURREY COUNTY HOSPITAL NHS FOUNDATION TRUST) CANDIA, Felice (ASHFORD AND ST PETER'S HOSPITALS NHS FOUNDATION TRUST) NASMIN, Shahnaz (EPSOM AND ST HELIER UNIVERSITY HOSPITALS NHS TRUST) CLARK, Liz (NHS SURREY HEARTLANDS CCG) HARGREAVES, Lynne (NHS SURREY HEARTLANDS CCG) SOARES, Alexandra (NHS SURREY HEARTLANDS CCG)

Declaration of Interest:

Nothing to declare confirmed by Reham Al-Shwaikh, Lis Stanford and Nikki Smith at time of submission.

Date: 20/05/21

Update of contacts. August 2021

Alexandra Soares is on Maternity Leave and has been replaced by Helen Marlow

Grainne Conway has moved to a different Trust and has been replaced by Ammara Zamir.

Appendix A

Pathway for the Treatment of VTE in Surrey Heartlands CCG

NHS Surrey Heartlands Clinical Commissioning Group

1) Confirmed VTE Diagnosis- Pulmonary Embolism (PE) and Deep Vein Thrombosis (DVT):
URGENT REFERRAL to thrombosis (and, if PE, Respiratory) team(s) *follow local pathways.*

SECONDARY CARE

2) Baseline Checks (within 24 hours of starting anticoagulation)**:**
Renal function: using actual body weight, serum creatinine and creatinine clearance (CrCl) in Cockcroft and Gault calculation (MD+Calc)
Full blood count (FBC): Haemoglobin (Hb), platelet count**,** clotting profile (PT, APTT, INR) and **Liver function (LFTs)**: AST/ALT, Bilirubin
BMI: If >40kg/m^2 or specific patient groups (*see table below*), refer to AC clinic for warfarin and/or low molecular weight heparin (LMWH)
Bodyweights <50kg and >120kg: refer to AC or haematology clinic for monitoring. Initiate LMWH followed by warfarin
Communicate these results to primary care via discharge letter/outpatient clinic letter (*link: VTE patient pathway for DOACs*)
Consider contra-indications, co-morbidities and patient preference when choosing an anticoagulant (*see specific patient groups table below*)

Specific Patient Groups	Recommendations	Specific Patient Groups	Recommendations
Renal impairment CrCl < 30ml/min	Specialist advice required: reduced DOAC dose or alternative options	**Active or underlying cancer**	Seek specialist advice, anticoagulate for at least 6 months*
Renal impairment CrCl <15ml/min	Specialist advice required: DOACs contra-indicated, use warfarin/heparin	**Lactose intolerance**	Edoxaban (plus loading with LMWH) as rivaroxaban and apixaban contain lactose
Known antiphospholipid syndrome (APLS)	DOACs contra-indicated, use warfarin	**Prosthetic heart valves**	Warfarin
Pregnancy/breastfeeding	LMWH preferred and specialist advice required	**Interacting medications will be considered at initiation of DOAC**	Specialist advice as indicated (https://bnf.nice.org.uk/interaction/rivaroxaban-2.html)

3) If a DOAC is suitable **prescribe Apixaban or Rivaroxaban for 1 month** (for a provoked DVT/PE):
Initiation: Apixaban 10mg twice daily for 1 week, **or** Rivaroxaban 15mg twice daily after food for 3 weeks, or then
Maintenance: Apixaban 5mg twice daily, **or** Rivaroxaban 20mg daily after food (caution in CrCl<30ml/min- *see table above*).
Prevention of recurrent VTE (long term): Apixaban 2.5mg twice daily, **or** Rivaroxaban 10mg or 20mg daily after food.

Approval Date: Review Date:
Not to be used for commercial marketing purposes. Strictly for use within the NHS. NOTE that all DOACs are available in line with NICE TAs
Surrey Heartlands Area Prescribing Committee. A partnership between NHS organisations in Surrey Heartlands Clinical Commissioning Group (the ICPs of East Surrey, Guildford and Waverley, Northwest Surrey and Surrey Heath) and Ashford an
Peter's and the Royal Surrey NHS Acute Foundation Trusts. This guidance was originally developed by Southwest London Medicines' Optimisation Group (2020) and has been adapted with their permission.
This guidance was originally developed by Southwest London Medicines' Optimisation Group (2020) and has been adapted with their permission.

4) For DOACs: Initiation and first one month supplied by secondary care

If treatment beyond 3 months is required (eg provoking factor cannot be removed/corrected, recurrent DVT/PE, or significant on-going VTE risk) prescribing and monitoring is transferred to the patient's GP. Patients with active cancer should receive at least 6 months of anticoagulation from their Specialist Oncologist or Haematologist.

Correspondence with Primary Care must contain the information in the Template Discharge Letter. It must also include Trust –specific details of which team the patient is under and when that team will review them in clinic.

PRIMARY CARE

5) Review (for patients on long term DOAC therapy) by primary care with secondary care support as indicated:

On receipt of correspondence from secondary care, the healthcare provider should make contact with the patient to agree the process for prescribing and monitoring.

Each year review: ongoing need for anticoagulation based on assessment of thrombotic risk and bleeding risk including any planned surgery, pregnancy or long-haul travel: always discuss stopping therapy with the thrombosis team.

Monitor patient for signs of bleeding and/or anaemia and, if severe bleeding occurs, stop therapy (may be a temporary halt to anticoagulation whilst investigated).

FBC: if platelets <100 ($x10^9$/L), if Hb <100g/L or change from baseline >20g/L, investigate for cause and consider referral to/review by specialist based on initial investigations

Monitor renal function according to the frequency dictated by baseline CrCl and adjust DOAC dose accordingly (*calculate CrCl using MD+Calc or as in 2 above*)

LFTs: If ALT/AST > 2xULN or total bilirubin >1.5xULN- review therapy.

Medicines optimisation: Check adherence to therapy, adverse effects and review of concomitant medicines. **Review** general health, bleeding risk and treatment preferences: refer to the thrombosis team if treatment requires a review. *NICE guidance (2020) recommends aspirin 75mg daily as an option: preventing VTE recurrence if longterm Anticoagulant is declined.*

References: *accessed 02/07/20*

1) Venous thromboembolic diseases: diagnosis, management and thrombophilia testing; NICE guideline [NG158] Published date: 26 March 2020 https://www.nice.org.uk/guidance/NG158
2) Summary of Product Characteristics for rivaroxaban: https://www.medicines.org.uk/emc/product/2793/smpc
3) British National Formulary: https://bnf.nice.org.uk/drug/rivaroxaban.html
4) MHRA advice: Rivaroxaban should be taken with food (July 2019); https://www.gov.uk/drug-safety-update/rivaroxaban-xarelto-reminder-that-15-mg-and-20-mg-tablets-should-be-taken-with-food
5) MHRA: Direct-acting oral anticoagulants (DOACs): reminder of bleeding risk, including availability of reversal agents (June 2020) https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/896274/June-2020-DSU-PDF.pdf
6) NICE guidance: Rivaroxaban for the treatment of deep-vein thrombosis and prevention of recurrent deep-vein thrombosis and pulmonary embolism (July 2012) https://www.nice.org.uk/guidance/ta261
7) NICE guidance: Rivaroxaban for treating pulmonary embolism and preventing recurrent venous thromboembolism (June 2013) https://www.nice.org.uk/guidance/ta287

DVT or PE: anticoagulation

PE with haemodynamic instability

Offer continuous UFH infusion and consider thrombolytic therapy

Body weight

If body weight <50 kg or >120 kg consider anticoagulant with monitoring of therapeutic levels.

Note cautions and requirements for dose adjustments and monitoring in SPCs. Follow local protocols, or specialist or MDT advice

INR monitoring

Do not routinely offer self-management or self-monitoring of INR

Prescribing in renal impairment and active cancer

Some LMWHs are off label in renal impairment, and most anticoagulants are off label in active cancer.

Follow GMC guidance on prescribing unlicensed medicines

Treatment failure

If anticoagulation treatment fails:

- check adherence
- address other sources of hypercoagulability
- increase the dose or change to an anticoagulant with a different mode of action

- Measure baseline full blood count, renal and hepatic function, PT and APTT but start anticoagulation before results available. Review and if necessary act on results within 24 hours
- Offer anticoagulation for at least 3 months. Take into account contraindications, comorbidities and the person's preferences
- After 3 months (3 to 6 months for active cancer) assess and discuss the benefits and risks of continuing, stopping or changing the anticoagulant with the person. See long-term anticoagulation for secondary prevention in the guideline

No renal impairment, active cancer, antiphospholipid syndrome or haemodynamic instability	Renal impairment (CrCl estimated using the Cockcroft and Gault formula; see the BNF)	Active cancer (receiving antimitotic treatment, diagnosed in past 6 months, recurrent, metastatic or inoperable)	Antiphospholipid syndrome (triple positive, established diagnosis)
Offer apixaban or rivaroxaban If neither suitable, offer one of: • LMWH for at least 5 days followed by dabigatran or edoxaban • LMWH and a VKA for at least 5 days, or until INR at least 2.0 on 2 consecutive readings, then a VKA alone	CrCl 15 to 50 ml/min, offer one of: • apixaban • rivaroxaban • LMWH for at least 5 days then – edoxaban **or** – dabigatran if CrCl ≥ 30 ml/min • LMWH or UFH and a VKA for at least 5 days, or until INR at least 2.0 on 2 consecutive readings, then a VKA alone CrCl < 15 ml/min, offer one of: • LMWH • UFH • LMWH or UFH and a VKA for at least 5 days, or until INR at least 2.0 on 2 consecutive readings, then a VKA alone Note cautions and requirements for dose adjustments and monitoring in SPCs. Follow local protocols, or specialist or MDT advice	Consider a DOAC If a DOAC is not suitable, consider one of: • LMWH • LMWH and a VKA for at least 5 days or until INR at least 2.0 on 2 consecutive readings, then a VKA alone Offer anticoagulation for 3 to 6 months Take into account tumour site, drug interactions including cancer drugs, and bleeding risk	Offer LMWH and a VKA for at least 5 days or until INR at least 2.0 on 2 consecutive readings, then a VKA alone

© NICE 2020. All rights reserved. Subject to Notice of rights.

Appendix B
Template: Information which must be included

Transfer of Prescribing Responsibility

Direct Oral anticoagulants (DOACs) for the acute treatment

and secondary prevention of venous thromboembolism (VTE)

This template includes the minimum detail necessary to allow the patient's Primary care Team to take back responsibility for the prescription and monitoring of DOAC prescribed following confirmed diagnosis of VTE. The Trust can choose to either incorporate this information into their standard 'Transfer of Care' Letter or to have it as a separate Template on their system.

Patient Details: Name, Address, DOB, Hospital Number and NHS number

GP Practice details: Name, Address, Telephone Number, nhs.net e-mail

Consultant details: Name, Organisation, Clinic name, Address, Telephone Number, nhs.net email

Date:

Dear Dr ,

This patient has been initiated on a DOAC for:

- ☐ treatment of DVT which was provoked / unprovoked (delete as appropriate)
- ☐ treatment of PE which was provoked / unprovoked (delete as appropriate)
- ☐ secondary prevention of VTE

DOAC (see formulary choices)	**Date initiated**	**Dose on transfer**	**Intended Duration of treatment**	**Date of next Consultant Review (if applicable)**
			☐ 3 months ☐ 6 months (Patient with active cancer) ☐ 3 months followed by long-term prophylaxis	

I have now supplied the first one month of therapy for this patient and am writing to transfer the prescribing responsibility for this patient's on-going anticoagulation.

This transfer of care document should be reviewed in conjunction with the Guidance: Anticoagulant choice for VTE treatment (Feb 2021)

All patients receiving DOAC therapy for VTE for the duration of over one year: Primary Care Team to review at least annually, in line with local guidelines.

Include date and detail of any further review which is planned in secondary care (to include any concerns or monitoring advice re the risk of cancer).

Most recent results

Test	**Result**	**Date of test**	**Please repeat in (months):**
Serum Creatinine (mMol/L)			
Creatinine clearance (CrCl) (mL/min)			
Haemoglobin (g/dL)			
ALT / AST (units/L) (delete as appropriate)			

eGFR should **not** be used to guide dosing decisions.
CrCl must be estimated using the Cockcroft-Gault equation calculator and the patient's **actual** body weight.

Anti-platelet Therapy:

Is the patient on anti-platelet therapy: Yes / No	
Anti-platelets in use:	Indication:
Is the antiplatelet to be withheld whilst on anticoagulation: Yes / No	
Comments (incl plan for antiplatelet therapy)	

Other relevant information:

- ☐ I confirm that I have prescribed in line with the current Local VTE Guidance
- ☐ I confirm that the patient has been made aware of the benefits and risks of DOAC therapy, including risks of both major and minor bleeding, and that they know how to seek medical help should bleeding occur.
- ☐ I confirm that an anticoagulation card and/or medic-alert bracelet have been provided
- ☐ I confirm that the patient has consented to treatment
- ☐ For female patients of child-bearing age: I have explained the risks of falling pregnant whilst on this treatment and recommended appropriate contraceptive measures are taken

Signed: **Name of Clinician:** **Date:**

Approval Date: Review Date:

Not to be used for commercial marketing purposes. Strictly for use within the NHS. NOTE that all DOACs are available in line with NICE TAs

Surrey Heartlands Area Prescribing Committee. A partnership between NHS organisations in Surrey Heartlands Clinical Commissioning Group (the ICPs of East Surrey, Guildford and Waverley, Northwest Surrey and Surrey Heath) and Ashford and St Peter's and the Royal Surrey NHS Acute Foundation Trusts. This guidance was originally developed by Southwest London Medicines' Optimisation Group (2020) and has been adapted with their permission.

Appendix C: Costing template
Venous thromboembolic diseases: diagnosis, management and thrombophilia testing

NICE National Institute for Health and Care Excellence

Resource impact template	Resource impact for selected population using standard NICE assumptions		
	Surrey Heartlands Health and Care Partnership		
	Unit cost (£) / proportion	Units	Total cost (£)
Adult population		661,772	
People with a venous thromboembolism (VTE) each year		993	
People with an unprovoked VTE who may be suspected of having cancer		467	
People with VTE and active cancer requiring anticoagulation therapy		199	
People with VTE who are not known to have cancer who require anticoagulation therapy		794	
Rec 1.3.8 treatment for people with VTE who are not known to have cancer			
People with VTE who are not known to have cancer who are treated with apixaban	550.76	159	87,475
People with VTE who are not known to have cancer who are treated with rivaroxaban	546.98	159	86,873
People with VTE who are not known to have cancer who are treated with LMWH followed by either dabigatran or edoxaban	518.32	278	144,065
People with VTE who are not known to have cancer who are treated with LMWH with VKA, followed by VKA on its own	82.42	199	16,363
VAT on above at 20% for treatment in secondary care - 10 days for LMWH with VKA and 4 weeks for the remainder			4,988
Total Rec 1.3.8			**339,765**
Rec 1.3.15, 1.3.17 and 1.3.18 treatment for people with VTE and cancer			

People with VTE and active cancer who are treated with apixaban	360.05	15	5,361
People with VTE and active cancer who are treated with rivaroxaban	366.30	15	5,454
People with VTE and active cancer who are treated with low molecular weight heparin (LMWH) and vitamin K antagonist (VKA)	69.84	10	693
People with VTE and active cancer who are treated with LMWH on its own	1,223.00	159	194,244
VAT on above at 20% for treatment in secondary care - full year			41,150
Total Rec 1.3.15, 1.3.17 and 1.3.18			**246,902**
Rec 1.8.1 and 1.8.2 imaging screening in people with unprovoked VTE			
People who have further imaging to assess for cancer following history taking and examination	229.00	313	71,583
People who only have their medical history taken and have a physical examination	125.00	154	19,245
Total Rec 1.8.1 and 1,8,2			**90,828**
Estimated costs of current practice			**677,495**
Future practice			
Rec 1.3.8 treatment for people with VTE who are not known to have cancer			
People with VTE who are not known to have cancer who are treated with apixaban	550.76	278	153,081
People with VTE who are not known to have cancer who are treated with rivaroxaban	546.98	278	152,029
People with VTE who are not known to have cancer who are treated with LMWH followed by either dabigatran or edoxaban	518.32	159	82,323
People with VTE who are not known to have cancer who are treated with LMWH with VKA, followed by VKA on its own	82.42	79	6,545
VAT on above at 20% for treatment in secondary care - 10 days for LMWH with VKA and 4 weeks for the remainder			5,996
Total Rec 1.3.8			**399,974**

Rec 1.3.15, 1.3.17 and 1.3.18 treatment for people with VTE and cancer			
People with VTE who are not known to have cancer who are treated with rivaroxaban	360.05	60	21,444
People with VTE who are not known to have cancer who are treated with LMWH followed by either dabigatran or edoxaban	366.30	60	21,817
People with VTE who are not known to have cancer who are treated with LMWH with VKA, followed by VKA on its own	69.84	10	693
People with VTE and active cancer who are treated with apixaban	1,223.00	69	84,982
VAT on above at 20% for treatmen in secondary care - full year			25,787
Total Rec 1.3.15, 1.3.17 and 1.3.18			**154,723**
Rec 1.8.1 and 1.8.2 imaging screening in people with unprovoked VTE			
People who have further imaging to assess for cancer following history taking and examination	229.00	28	6,410
People who only have their medical history taken and have a physical examination	125.00	439	54,820
Total Rec 1.8.1 and 1,8,2			**61,230**
Estimated costs of future practice			**615,927**
Non-cash releasing saving (provider - secondary care)			**-29,598**
Cash saving (provider - primary/secondary care)			**-31,970**
Resource impact (cash and non-cash)			**-61,568**