Medicines Optimisation of Direct-Acting Oral Anticoagulants (DOACs) for Atrial Fibrillation (AF) Programme

Rationale for Programme

- Cheshire and Merseyside healthcare partnerships are reviewing all patients currently receiving a Direct Oral Anticoagulant (DOAC) or non-vitamin K antagonist oral anticoagulant (NOAC) for stroke prevention in AF. This project is supported by the Northwest Cardiac Strategic Clinical Network and Cardiovascular Board.
- All patients on a DOAC for AF should have a medicine optimisation review to ensure their existing DOAC is appropriate according to recent bloods and weight. All patients prescribed any oral anticoagulant (OAC) should discuss the options with a healthcare professional at least once a year NICE QS93[1]. Adherence and compliance should be assessed regularly to support patients to take medication appropriately and safely. Stroke and bleeding risk will change over time and must be recalculated at least annually. Blood monitoring including Haemoglobin (Hb), liver and renal function should be monitored at least annually, and more regularly in people with renal dysfunction, over the age of 75 years or those who are frail (see separate document - SOP, appendix 1, table 1).
- Currently, all DOACs (edoxaban, dabigatran, rivaroxaban and apixaban) are recommended as options for anticoagulation in the NICE AF Guidelines (NG196) considering individual patient bleeding risks and co-morbidities [2].
- NHS England (NHSE) recently published Commissioning Guidance for DOACs [3] which recommends that clinicians should use edoxaban, where clinically appropriate, consistent with the latest guidance from NICE [2]. This approach has also been endorsed by the UK's leading stroke charity, Stroke Association.
- There are no head-to-head comparative trials that demonstrates that one DOAC is significantly better than another and treatment should be based on individual patient factors and bleeding risk.
- Patients newly diagnosed with AF who require anticoagulation should be initiated on edoxaban unless there is a clinical reason to use warfarin or another DOAC.

What is non-valvular atrial fibrillation (AF)?

- The most recent European Society Cardiology guidance on AF (2020[4]) suggests replacing the historic term 'non-valvular' AF with reference to the specific underlying conditions.
- The term "valvular AF" refers to patients with mitral stenosis (moderate or severe) or mechanical heart valves and such patients should be considered only for warfarin therapy for stroke prevention.
- The term "non-valvular AF" therefore encompasses cases of AF in the absence of the above. For the purposes of this review, all patients with AF will be reviewed.
- Biological valve replacements, or other valvular heart conditions, such as mitral regurgitation, aortic stenosis and aortic regurgitation, do not tend to result in conditions of low flow in the left atrium, and therefore are not thought to further increase the risk of thromboembolism brought by AF. This group of patients, when it comes to choice of oral anticoagulation, can also be included under the term non-valvular AF and the choice of oral anticoagulant (OAC) could include either warfarin or a DOAC.
- Edoxaban can be used 3 months after implantation of a bioprosthetic heart valve within the license.
- Apixaban, rivaroxaban and dabigatran do not recommend their use with any prosthetic valve in the SPC.

Individual patient considerations - *Which patients should not be prescribed a DOAC?*

- Creatinine Clearance (CrCl) <15ml/min in patients for edoxaban, rivaroxaban and apixaban are contraindicated and not appropriate – refer to the GP to review if anticoagulation appropriate and warfarin should be used if required.
- Patients with CrCl <30mls/min are contraindicated with dabigatran. It is advisable that if CrCl falls below 50mls/min then an alternative DOAC be considered other than dabigatran.
- Metallic heart valves – warfarin is recommended for these patients.
- Recent diagnosis of DVT/PE (in past 6 months) - rivaroxaban or apixaban remains the first choice for these patients depending on local policy. Edoxaban and dabigatran require at least 5 days of parenteral anticoagulation prior to initiation
- DOACs are contraindicated for those who are pregnant or breast feeding.
- A non-significant trend towards decreasing efficacy with increasing creatinine clearance was observed for edoxaban compared to well-managed warfarin and the SPC advises that it should be used with caution. However, all DOACs have some degree of renal clearance and all three Factor X inhibitors show the same trend to decreasing efficacy with increasing creatinine clearance.
- See the SPC for each DOAC for a full list of contraindications.

Can edoxaban be used in patients with extremes of weight?

- Patients with a BMI > 40 kg/m^2 or weight >120kg have traditionally been considered for warfarin as first line due to limited evidence for efficacy in this patient population.
- Newer evidence indicates that in patients with nonvalvular AF, DOACs compared to warfarin were associated with better safety and effectiveness across all BMI categories, including underweight and morbidly obese patients [5,6].
- The efficacy and safety of edoxaban in overweight patients with BMI 30 to >40kg/m^2 were assessed in a sub analysis of the ENGAGE AF-TIMI 48 study which suggests that obese patients (BMI ≥ 30 kg/m^2) receiving edoxaban are at lower risk of stroke/systemic embolic events (SEE) and show better survival rates but are at increased risk of bleeding as compared to patients with normal BMI (18.5-25 kg/m^2). The net clinical outcome of edoxaban 60 mg once-daily as compared to warfarin did not change significantly according to BMI [7]

Individual patient considerations – When is there a clinical indication to be initiated on apixaban or stay on existing apixaban treatment?

- It may be appropriate to initiate apixaban rather than an alternative DOAC in certain clinical situations. The same applies when reviewing patients on existing DOAC therapy. This will depend on the individual patient circumstances and background
- Decision aid flow charts have been developed with advice from regional experts to ensure the appropriate DOAC is prescribed taking into account individual patient characteristics when initiating a de novo DOAC and when reviewing existing DOAC therapy
- There are no head-to-head comparative trials between the four DOACs, however apixaban and dabigatran 110mg BD have not shown a significant increase in gastrointestinal bleeds unlike other DOACs [8]
- Patients who have mild reflux or indigestion or who are on other medication that may increase the risk of GI bleed (e.g. aspirin, SSRI, bisphosphonate) can be initiated on edoxaban with a proton pump inhibitor (PPI)
- Patients on a PPI may be initiated on edoxaban rather than apixaban unless they have ongoing symptoms

- Patients who should be initiated or maintained on apixaban include:

    - Patients at high risk of GI bleeding including those with current or recent gastrointestinal ulceration (within previous 6-8 weeks)
    - Patients who have been changed from an alternative DOAC before due to intolerance/treatment failure
    - Patients taking apixaban for another indication or for off-licence use started under a specialist

Will we need to change again if the price of other DOACs reduces?

- The proposed DOAC medicine optimisation review has been developed to ensure a consistent approach is taken to support the regular review of DOAC prescribing. The required frequency of the DOAC monitoring should be based on guidance and individual patient circumstances (see separate document - SOP appendix I, table 1).
- The national price for edoxaban has been agreed with NHS England and expected to remain until the patent expires.
- Should DOAC prices change or become generically available, further changes could be considered at the next planned medicine optimisation review. Patients would not be required to have an earlier review.
- Dabigatran is due to go off-patent first, however, using the flowchart the most appropriate DOAC should have been selected and is unlikely to need to be changed.
- A further switch will only be considered if clinical evidence emerges that a specific DOAC is more effective and/or safer for patients.

How to use the Decision Aid to review apixaban

- If any of the criteria in box 1 are met, then patients should remain on apixaban.
- If patients do not need to remain on apixaban, check the individual patient characteristics that flow from box 2 to determine the most appropriate DOAC to change the patient to.
- If more than one characteristic/co-morbidity is relevant, determine the appropriate DOAC that is recommended in all applicable boxes and use clinical judgement and patient preference (e.g. frequency of dose, blister packs etc.).

Is the preferred/recommended DOACs for specific patient cohorts evidence based?

- The recommendations are based on advice in the CHEST Guidelines on Antithrombotic therapy for AF [5]
- Real-world evidence in AF patients have found that DOACs were more effective than warfarin at reducing stroke risk and lowered the risk of all-cause mortality, cerebral haemorrhage, and severe bleeding in AF patients compared to warfarin.
- Newer meta-analysis has shown that edoxaban has similar bleeding outcomes as apixaban (with the exception of gastric bleeding) [9,10]
- NICE TA 355 [12] summarised that all the DOACs appeared to have comparable efficacy for the composite primary and bleeding outcomes.
- Lead clinicians from cardiology, stroke, Primary Care and haematology are all supportive of this guidance on the basis of current available evidence.
- This has been endorsed by the Cheshire and Mersey Cardiovascular Board and a regional statement supports this position.

Should HAS-BLED or ORBIT be used to assess bleeding risk in AF patients?

- The appropriate use of bleeding risk assessment is to focus on modifiable bleeding risk factors for mitigation, and to flag up high bleeding risk patients for early review and follow up.
- NICE AF Guidelines NG196[2] recommends using the ORBIT tool to assess bleeding risk for patients with AF. This is currently not available in EMIS.
- HAS-BLED was the tool previously used to assess bleeding risk in AF patients and this is still available on EMIS and a score will be pulled into the EMIS template for DOAC reviews. NICE states other bleeding risk tools can be used if embedded in EMIS until ORBIT is established.
- Solely using ORBIT to assess the bleeding risk may categorise a great proportion of patients into the very low risk category and it does not take into consideration modifiable risk factors [13]. Also, HAS-BLED is supported by prospective trial evidence, with appropriate use associated with less major bleeding and an increase in oral anticoagulation uptake [14]. Therefore the following should be assessed and support offered if appropriate:

    - Uncontrolled hypertension (see NICE's guideline on hypertension in adults)
    - Concurrent medication, including antiplatelets, selective serotonin reuptake inhibitors (SSRIs) and non-steroidal anti-inflammatory drugs (NSAIDs)
    - Harmful alcohol consumption (see NICE's guideline on alcohol-use disorders: diagnosis, assessment and management of harmful drinking and alcohol dependence)
    - Reversible causes of anaemia

Undertaking individual patient reviews ***- Do I need to use the Cockcroft-Gault equation to estimate renal function or can I use eGFR?***

- All DOACs may require a dose adjustment based on renal impairment.
- Renal function should be calculated using the Cockcroft and Gault equation using **actual body weight** as per the trials and licensed information.
- **Creatinine clearance must be used for calculating renal function** using the Cockcroft and Gault equation (see below). eGFR is **not** a suitable alternative:

$$\text{CrCl (ml/min)} = \frac{(140 - \text{age}) \times \text{wt (kg)} \times 1.04 \text{ (female) or } 1.23 \text{ (male)}}{\text{serum creatinine (micromol/l)}}$$

- The actual body weight must be used to calculate CrCl.

NB The clinical system mainly used in primary care (EMIS) has an inbuilt Cockcroft-Gault based renal function calculator which can be used to dose DOACs. EMIS now recognise if the patient is prescribed a DOAC and will use actual body weight to calculate CrCl for these patients. The exception are patients taking Dabigatran who are also obese, in this case the calculator uses ideal body weight. In these cases you should record the creatinine clearance for actual body weight in the consultation. The pharmaceutical industry was contacted, and they confirmed that it was actual body weight used in the clinical trials for AF with all DOACs.

Please check your local clinical system.

- Another option is to use the MD+ CALC Creatinine Clearance calculator (it can be downloaded as an app to an apple or android device). Always use the most up to date values and check the default units are correct when entering weight, serum creatinine and

height. It would be good practice for the clinician reviewing the patient to document what method was used.

Undertaking individual patient reviews – Considerations with concurrent antiplatelet therapy [15, 16]

- Before initiating a DOAC, or when reviewing patients on existing DOAC treatment, concurrent antiplatelet should be reviewed
- In general, triple therapy (dual antiplatelet therapy plus anticoagulation) is not recommended for most patients due to an increased risk of bleeding. If triple therapy is needed, a short duration (e.g., no more than 30 days) is recommended
- When combined with an anticoagulant, clopidogrel is the recommended antiplatelet agent for most patients. If aspirin is used, it should be limited to 75 mg daily dosing. Triple therapy should only be given on the advice of a Cardiologist
- For PCI with stable ischemic heart disease or acute coronary syndrome, use of OAC plus a $P2Y_{12}$ inhibitor for no more than 12 months is recommended, followed by oral anticoagulation alone
- Patients with cerebrovascular disease without carotid stenting, oral anticoagulation monotherapy is recommended
- Patients with carotid stenting or peripheral artery disease, a short course of anticoagulation plus $P2Y_{12}$ inhibitor may be recommended, followed by oral anticoagulation alone as advised by a Vascular consultant
- A proton pump inhibitor (PPI) is recommended for patients on concurrent OAC and antiplatelet treatment

Undertaking individual patient reviews – Considerations when CrCl >95mls/min

- The Cheshire and Mersey regional viewpoint is that edoxaban can be used if CrCl>95mls/min
- There was a trend towards decreasing efficacy with increasing CrCl observed for edoxaban compared to well-managed warfarin. The data from the trials was non-significant and in small patient numbers. There were no statistically significant differences for any of the endpoints in the study (ref ENGAGE)
- The EHRA [16] states that decreased efficacy of edoxaban 60 mg OD compared with warfarin was observed in patients with a CrCl of >95 mL/min. Interestingly, as a result of these findings, further post hoc analyses revealed a similar effect also for Rivaroxaban and Apixaban." The references for this are no longer available on the FDA site but a similar table for apixaban was presented in a conference abstract earlier last year [17].
- Although there was an apparent decrease in relative efficacy to prevent arterial thromboembolism in the upper range of CrCl, the safety and net clinical benefit of edoxaban compared with warfarin are consistent across the range of renal function.[18]

Undertaking individual patient reviews - *What happens if a patient has more than one indication to be on a DOAC?*

- There are several reasons why a patient might be taking a DOAC either for a fixed period of time or for the long-term.
- All DOACs are licenced and approved by NICE for stroke prevention in NV-AF and treatment of a DVT/PE. Some DOACs are also used for thromboprophylaxis following joint replacement. This medicine optimisation review project is focussing on patients receiving a DOAC for stroke prevention in AF. If a patient is on a long-term DOAC for another indication it is advisable to confirm the dose and treatment length is appropriate.
- Rivaroxaban and apixaban remains the first choice agent depending on local formulary for the treatment of DVT and PE. The use of edoxaban and dabigatran to treat DVT/PE requires initial treatment with heparin for 5 days and is not necessarily a suitable first choice for this indication.
- Patients on a DOAC for a DVT/PE more than 6 months prior should be reviewed to ensure the DOAC and dose is still appropriate and adjust accordingly.
- Patients on a DOAC for an off-license indication as recommended by a specialist should not be changed to edoxaban without discussing with the specialist.

Undertaking individual patient reviews - *If clinically appropriate how do I change a patient to an alternative DOAC?*

- If patients meet the criteria for changing, discuss the change and issue/arrange issue of a prescription for the new DOAC with verbal and written explanation of how to change.
- Advise to use up the supply of existing DOAC before changing to the new DOAC.
- Advise to change to the new DOAC when the next dose of the existing DOAC would be due i.e. if changing from apixaban 2.5mg BD, take the last dose of apixaban then start the new DOAC 12 hours later when the next dose of apixaban was due.
- The new DOAC should then be taken every 24 hours (edoxaban and rivaroxaban) or every 12 hours (dabigatran).

Undertaking individual patient reviews - *What drugs interact with DOACs and what should I do about them?*

- As with other anticoagulants, the risk of bleeding is increased if DOACs are used in combination with one or more antiplatelet drugs. This combination may be clinically appropriate in certain circumstances, but this should only be prescribed on the advice of a specialist and a clear treatment plan describing the intended duration of treatment.
- As with all anticoagulants the possibility may exist that patients are at increased risk of bleeding in case of concomitant use with SSRIs or SNRIs due to their reported effect on platelets.
- Chronic use of NSAIDs with DOACs is not recommended due an increased clinically relevant risk of bleeding.
- All DOACs should be checked for clinically relevant interactions and adjusted accordingly – see SPC of individual DOACs and appendix 4, table 7 from the SOP.

Undertaking individual patient reviews - *Can DOACs go into a patient compliance device or be crushed?*

- There are no known issues with using edoxaban, apixaban and rivaroxaban in a compliance device.
- Dabigatran capsules must be stored within the manufacturer's original packaging (aluminum foil strips/bottles) to prevent physical instability. It is therefore not suitable for dispensing in compliance aids.

Undertaking individual patient reviews - *Is there an antidote to DOACs?*

- There are reversal agents available for both thrombin inhibitors and Xa inhibitors which could be considered if rapid reversal is required.
- Andexanet alpha is a reversal agent for factor Xa inhibitors and is licensed for apixaban and rivaroxaban.
- Andexanet alpha may be used off-license for patients on edoxaban as it is also a factor Xa inhibitor although this must be documented in the notes and the patient informed.
- Off-license use with edoxaban has been agreed across the region and is recommended by the North West Cardiology Strategic Clinical Network.
- Andexanet alpha is only approved for certain clinical situations e.g. gastrointestinal bleeds.
- Idarucizumab is an available reversal agent for dabigatran, a thrombin inhibitor. This should be reserved for serious bleeds and recommended according to local guidelines.

Ongoing review of patients prescribed DOACs - *What happens if renal function changes?*

- If renal function decreases significantly then the DOAC dose may need to be reviewed.
- DOACs are not recommended if the CrCl is <15ml/min for edoxaban, apixaban and rivaroxaban or CrCl <30mls/min for dabigatran. These patients should receive warfarin if there is a clinical indication for long-term anticoagulation.
- If CrCl <50mls/min avoid dabigatran unless specifically indicated.
- Alternatively, if a reduced dose of a DOAC has been started during an acute impairment of renal function, then the dose will need to be reviewed if renal function subsequently improves.
- These optimisation reviews should facilitate a regular review to ensure patients who have a change in renal function are managed appropriately.

Ongoing review of patients prescribed DOACs [4]- *How often do I need to check weight, renal function, haemoglobin (Hb) and liver function tests (LFTs)?*

- At initiation of treatment or when changing to an alternative DOAC, the renal function should have been confirmed within the last 3 months.
- Thereafter, renal function, Hb and LFTs should be monitored as per the table below:

Monitoring for DOACs	
Interval	**Patient Cohort**
Yearly	Patients other than those specified below
6 - monthly	≥75 years (especially if on dabigatran) or frail
X - monthly	If renal function CrCl ≤60 mL/min: recheck interval = CrCl/10 (giving the X monthly value)
If needed	Any intercurrent condition that may impact renal or hepatic function

- At initiation of treatment or when changing to an alternative DOAC, the weight should have been recorded within the previous 3 months. If there has been recent acute illness or there is evidence of a suspicion of weight loss/gain, a more recent weight should be obtained.
- Once a patient has been reviewed and confirmed to be on the appropriate dose of DOAC, weight should be checked and reviewed annually or more frequently if intercurrent illness is causing weight fluctuations.

References

1. NICE QS93. Atrial Fibrillation Quality Standard QS93. July 2015. https://www.nice.org.uk/guidance/qs93
2. NICE AF Guidelines NG196 2021 https://www.nice.org.uk/guidance/ng196
3. NHSE Operational note: National Procurement for DOACs version 1. Dec 2021
4. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS). European Heart Journal (2020) 42, 373498 doi:10.1093/eurheartj/ehaa612
5. Barakat AF, Jain S, Masri A, Alkukhun L, Senussi M, Sezer A, Wang Y, Thoma F, Bhonsale A, Saba S, Mulukutla S. Outcomes of Direct Oral Anticoagulants in Atrial Fibrillation Patients Across Different Body Mass Index Categories. JAC Clin Electrophysiol. 2021 May;7(5):649-658.
6. Lee SR, Choi EK, Jung JH, Park SH, Han KD, Oh S, Lip GYH. Body Mass Index and Clinical Outcomes in Asian Patients With Atrial Fibrillation Receiving Oral Anticoagulation. Stroke. 2021 Jan;52(2):521-530. doi: 10.1161/STROKEAHA.120.030356. Epub 2021 Jan 11. PMID: 33423512
7. Boriani G *et al*. Edoxaban versus Warfarin in Patients with Atrial Fibrillation at the Extremes of Body Weight: An Analysis from the ENGAGE AF-TIMI 48 Trial. Thromb Haemost 2021; 121:140-149
8. Ruff CT, Giugliano RP, Braunwald E, et al. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials. Lancet. 2014;383(9921):955-962.
9. Lip GYH *et al.* Antithrombotic Therapy for Atrial Fibrillation CHEST Guideline and Expert Panel Report. Chest. 2018 Nov;154(5):1121-1201. doi: 10.1016/j.chest.2018.07.040.
10. **Chao TF**, Joung B, Takahashi Y, Lim TW, Choi EK, Chan YH, Guo Y, Sriratanasathavorn C, Oh S, Okumura K, **Lip GYH.** 2021 Focused Update Consensus Guidelines of the Asia Pacific Heart Rhythm Society on Stroke Prevention in Atrial Fibrillation: Executive Summary..Thromb Haemost. 2022 Jan;122(1):20-47. doi: 10.1055/s-0041-1739411. Epub 2021 Nov 13.
11. Lee SR, Choi EK, Kwon S, Han KD, Jung JH, Cha MJ, Oh S, Lip GYH. Effectiveness and Safety of Contemporary Oral Anticoagulants Among Asians With Nonvalvular Atrial Fibrillation. Stroke. 2019 Aug;50(8):2245-2249.
12. NICE TA355. Edoxaban for preventing stroke and systemic embolism in people with non-valvular atrial fibrillation. Sept 2015 https://www.nice.org.uk/guidance/ta355
13. Proietti M, Romiti GF, Vitolo M, Potpara TS, Boriani G, **Lip GYH.** Comparison of HAS-BLED and **ORBIT** Bleeding Risk Scores in AF Patients treated with NOACs: A Report from the ESC-EHRA EORP-AF General Long-Term Registry. Eur Heart J Qual Care Clin Outcomes. 2021 Sep 23:qcab069. doi: 10.1093/ehjqcco/qcab069.
14. **Guo Y**, Lane DA, Chen Y, **Lip GYH**; mAF-App II Trial investigators. Regular Bleeding Risk Assessment Associated with Reduction in Bleeding Outcomes: The mAFA-II Randomized Trial. **Am J Med**. 2020 Oct;133(10):1195-1202.e2. doi: 10.1016/j.amjmed.2020.03.019.
15. NICE GG185 Acute Coronary Syndromes published 18th Nov 2020
16. 2021 European Heart Rhythm Association. Practical Guide on the Use of Non-Vitamin K Antagonist Oral Anticoagulants in Patients with Atrial Fibrillation. Europace (2021) 23, 1612–1676 doi:10.1093/europace/euab065
17. Ziad Hijazi, Stefan H. H Hohnloser, Ulrika Andersson et al. Abstract 12404: Efficacy and Safety of Apixaban Compared With Warfarin in Patients With Atrial Fibrillation and Normal Renal Function over Time: Insights From the ARISTOTLE Trial. Originally published 6 Nov 2015 Circulation. 2015;132:A12404 https://doi.org/10.1161/circ.132.suppl_3.12404
18. Erin A. Bohula, et al. Renal Function on Outcomes With Edoxaban in the ENGAGE AF-TIMI 48 Trial. *Circulation.* 2016;134:24-36. DOI: 10.1161/CIRCULATIONAHA.116.022361

Written on behalf of the Cheshire and Merseyside healthcare partnerships (HCP), Cheshire and Merseyside Medicines Optimisation Steering Group, Cheshire and Merseyside Cardiac Strategic Clinical Network and Cheshire and Merseyside Cardiovascular Board. With thanks to:

Jo Bateman	Deputy Clinical Services Manager/Lead Cardiology Pharmacist, Countess of Chester Hospital NHS Foundation Trust. Chair of Cardiac and Stroke Pharmacist Forum, North-West Coast clinical networks
Prof Gregory Lip	Price-Evans Chair of Cardiovascular Medicine, at the University of Liverpool, UK – and Director of the Liverpool Centre for Cardiovascular Science at the University of Liverpool and Liverpool Heart & Chest Hospital.
Dr Joe Mills	Consultant Cardiologist, Liverpool Heart and Chest NHS Trust. UK National CVD Prevention Co-Ordinator (affiliated role between the British Cardiovascular Society and the European Society of cardiology). Cardiac Lead for the North-West Coast clinical networks
Susanne Lynch	Head of Medicines Management NHS South Sefton CCG and NHS Southport and Formby CCG, Chair Medicines Optimisation Committee, HCP
Janet Fay	Lead Pharmacist, South Sefton CCG and Southport and Formby CCG
Dr Tina Dutt	Consultant Haematologist, Roald Dahl Haemostasis and Thrombosis Centre, Associate Medical Director – Patient Experience, Liverpool University Hospitals NHS Foundation Trust, NIHR CRN NWC SRG Lead for Haematology, NHSE Blood Disorders CRG
Dr Nikhil Sharma	Clinical Lead for Stroke – Cheshire and Mersey Integrated Stroke Delivery Network
Prof Deirdre Lane	Professor of Cardiovascular Health, Liverpool Centre for Cardiovascular Sciences, University of Liverpool and Liverpool Heart and Chest Hospital, Liverpool, UK
Dr John Paul Bishop	GP Partner Lawton House Surgery, Clinical Director Congleton and Holmes Chapel PCN. Clinical Lead Thriving, Surviving & Prevention Programme Cheshire CCG. Primary Care Clinical Lead Cheshire & Mersey Cardiac Network
Dr Sue Kemsley	GP partner Swanlow Medical Centre, Winsford, Cheshire. Primary care clinical lead for Cheshire and Mersey Strategic Cardiac Network. Primary Care Clinical Lipid Lead for Innovation Agency
Dr Stephen McGoldrick	Consultant Gastroenterologist, Countess of Chester Hospital

Acknowledgement to Tayside NHS Trust
Version 1 December 2021
Version 2 Sept 2022
Review date Sept 2025 or sooner if new information becomes available