South East London Integrated Medicines Optimisation Committee
Formulary recommendation

Reference	**148**
Intervention:	**Rivaroxaban for post deep vein arterialisation with posterior tibial vein stenting in patients with peripheral arterial disease (off-label use)** (Rivaroxaban is an anticoagulant)
Date of Decision	**November 2023**
Date of Issue:	**December 2023**
Recommendation:	**RED – suitable for prescribing and supply by hospital**
Further Information	· Rivaroxaban is accepted for use as an option in SEL for post deep vein arterialisation (DVA) with posterior tibial vein stenting in patients with peripheral arterial disease (PAD) in adults. This approval only covers use at the tertiary centre for DVA at Guy's and St. Thomas' NHS Foundation Trust. · Revascularisation procedures are the main treatment for critical limb ischaemia in PAD. In this setting the aim of treatment with rivaroxaban is to maintain long term patency of tibial vein stents and minimise possible long-term thrombosis and reintervention following DVA. · Other antithrombotic treatment options for use post revascularisation procedures are: dual antiplatelet therapy (DAPT), single antiplatelet therapy, or warfarin. · The dose of rivaroxaban in this setting is 20mg daily and is continued for up to 12 months, if tolerated. After 12 months, the patient would be transferred to DAPT (ongoing prescribing of DAPT would be undertaken in primary care). · Prescribing of rivaroxaban in this setting will be restricted to and remain under the supervision of the vascular surgery consultant. · The vascular surgery team will provide sufficient notice to primary care clinicians when the first year of rivaroxaban treatment is reaching an end and will advise on prompt DAPT initiation, avoiding any breaks in treatment. · The applicant outlined that there may be certain exceptional circumstances under which patients may require treatment with rivaroxaban 20mg daily beyond 1 year, if: - Foot wounds have not healed after the first year - The patient had thrombotic event(s) of their stent-graft which required lysis - The patient cannot be prescribed DAPT for any reason, e.g. due to a contraindication - The patient is already on rivaroxaban for another medical reason · In the above exceptional circumstances, the initiating vascular surgery specialist may discuss with the primary care clinician on a case-by-case basis the individual patient need for rivaroxaban prescribing to be continued in primary care. Any agreement to do so must include an individual management plan for the patient agreed between the vascular surgery specialist and the primary care clinician, which includes the intended treatment duration and plan for ongoing review. The vascular surgery team will be responsible for providing ongoing follow up and review of patients continuing treatment beyond one year, at agreed intervals, to assess the continued need for rivaroxaban. · Where the primary care clinician does not feel it is clinically appropriate for them to take on prescribing of rivaroxaban, the specialist vascular surgery team will continue prescribing and supply. · Rivaroxaban 20mg daily (full anticoagulant dose) is **not licensed** for use in this indication (off-label use). Informed consent should be gained from the patient before treatment is initiated. · Whilst the Committee was mindful that the evidence base is lacking in this relatively new area of practice, there is expert consensus supporting the use of rivaroxaban. · The applicant will be invited to provide an audit of outcomes (including efficacy and safety) and numbers of patients treated after 2 years.
Shared Care/ Transfer of care required:	N/A

Cost Impact for agreed patient group	· It is estimated that there will be approximately ~ 10 patients per annum eligible for treatment with rivaroxaban in this setting, with the majority from SEL. · The average cost of rivaroxaban 20mg tablets is around £657 per annum per patient. · This would equate to £6,570 (or ~ £338 per 100,000 population) per annum.
Usage Monitoring & Impact Assessment	**Acute Trusts:** · Monitor use and report back to IMOC when required. · Audit use after 2 years and provide a report to the Committee of safety and efficacy outcomes, the numbers of patients treated and the number requiring treatment beyond 12 months (by January 2026)
	SEL Borough Medicines Optimisation teams: · Monitor exception reports from GPs if inappropriate prescribing requests are made to primary care
Evidence reviewed	**References (from evidence review)** 1. Hess NC, et al. A Structured Review of Antithrombotic Therapy in Peripheral Artery Disease With a Focus on Revascularization. A TASC (InterSociety Consensus for the Management of Peripheral Artery Disease) Initiative. Circulation. 2017;135:2534–2555. 2. Clair DG, et al/ PROMISE I: Early feasibility study of the LimFlow System for percutaneous deep vein arterialization in no-option chronic limb-threatening ischemia: 12-month results. J Vasc Surgery 2021; 74: 1626-35 3. Shishehbor MH, et al. Transcatheter Arterialization of Deep Veins in Chronic Limb-Threatening Ischemia. N Engl J Med 2023; 388:1171-1180 4. Rivera-Caravaca, JM, et al. Antithrombotic Therapy in Patients with Peripheral Artery Disease: A Focused Review on Oral Anticoagulation. Int J Mol Sci. 2021 Jul; 22(13): 7113: 5. SmPC: Xarelto 2.5 mg film-coated tablets. Available here [last accessed 06/11/2023] 6. SmPC: Xarelto 20mg film-coated tablets. Available here [last accessed 06/11/2023] 7. NICE Clinical guideline [CG147]: Peripheral arterial disease: diagnosis and management. Published: 08 August 2012 Last updated: 11 December 2020. Available here [last accessed 06/11/2023] 8. Rivaroxaban for preventing atherothrombotic events in people with coronary or peripheral artery disease. Technology appraisal guidance [TA607] Published: 17 October 2019. Available here [last accessed 06/11/2023] 9. NICE. Percutaneous deep venous arterialisation for chronic limb threatening ischaemia Interventional procedures guidance. Published: 18 October 2023. Available here [last accessed 06/11/2023] 10. 2016 AHA/ACC Guideline on the Management of Patients With Lower Extremity Peripheral Artery Disease. Available here [last accessed 06/11/2023] 11. 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS). Available here [last accessed 06/11/2023] 12. Protocol for: Shishehbor MH, Powell RJ, Montero-Baker MF, et al. Transcatheter arterialization of deep veins in chronic limb-threatening ischemia. N Engl J Med 2023;388:1171-80. Available here [last accessed 06/11/2023] 13. Schreve MA. Venous Arterialisation for Salvage of Critically Ischaemic Limbs: A Systematic Review and MetaAnalysis. Eur J Vasc Endovasc Surg (2017) 53, 387e40. Available here [last accessed 06/11/2023] 14. Saan FA, et al. Percutaneous Deep Venous Arterialization: Treatment of Patients with End-Stage Plantar Disease. JSCAI 2022; 1 (6): 100437: 9303%2822%2900435-5/fulltext. Available here [last accessed 06/11/2023] 15. Bonaca MP, et al. Rivaroxaban in Peripheral Artery Disease after Revascularization. N Engl J Med 2020; 382:1994-2004. Available here [last accessed 06/11/2023] 16. Efficacy of oral anticoagulants compared with aspirin after infrainguinal bypass surgery (The Dutch Bypass Oral Anticoagulants or Aspirin Study): a randomised trial. Lancet 2000; 355:346–351.Available here [last accessed 06/11/2023] 17. Johnson WC, et al. Benefits, morbidity, and mortality associated with long-term administration of oral anticoagulant therapy to patients with peripheral arterial bypass procedures: a prospective randomized study. J Vasc Surg 2002; 35:413–421.Available here [last accessed 06/11/2023] 18. Monaco M, et al. Combination therapy with warfarin plus clopidogrel improves outcomes in femoropopliteal bypass surgery patients. J Vasc Surg 2012; 56:96–105. Available here [last accessed 06/11/2023] 19. Anand S, et al. Major Adverse Limb Events and Mortality in Patients With Peripheral Artery Disease: The COMPASS Trial. Journal of the American College of Cardiology 2018; 71: 2306-15. Available here [last accessed 06/11/2023]

NOTES:

a) SEL IMOC recommendations and minutes are available publicly via the website.
b) This SEL IMOC recommendation has been made on the cost effectiveness, patient outcome and safety data available at the time. The recommendation will be subject to review if new data becomes available, costs are higher than expected or new NICE guidelines or technology appraisals are issued.
c) Not to be used for commercial or marketing purposes. Strictly for use within the NHS