# Joint Formulary Committee (JFC): Minutes

**Minutes from the meeting held on 18th January 2024**

| | | Present | Apologies |
|---|---|---|---|
| **Members** | | | |
| Prof A Hingorani | NCL JFC Chair | ✓ | |
| Dr B Subel (Chair) | NCL JFC Vice Chair | ✓ | |
| Ms L Coughlan | NCL ICB, Deputy Chief Clinical Officer & ICS Chief Pharmacist | ✓ | |
| Ms W Spicer | RFL, Chief Pharmacist | ✓ | |
| Dr P Jasani | RFL, DTC Chair | | ✓ |
| Dr K Boleti | RFL, DTC Chair | | ✓ |
| Dr A Scourfield | UCLH, DTC Chair | | ✓ |
| Mr J Harchowal | UCLH, Chief Pharmacist | ✓ | |
| Dr R Urquhart | UCLH, Divisional Clinical Director | | ✓ |
| Dr K Tasopoulos | NMUH, DTC Chair | | ✓ |
| Ms A Stein | NMUH, Interim Chief Pharmacist | | ✓ |
| Dr M Kelsey | WH, DTC Chair | ✓ | |
| Mr S Richardson | WH, Chief Pharmacist | ✓ | |
| Dr S Ishaq | WH, Consultant Anaesthetist | | ✓ |
| Dr A Worth | GOSH, DTC Chair | | ✓ |
| Ms J Ballinger | GOSH, Chief Pharmacist | | ✓ |
| Mr V Raman | RNOH, DTC Chair | ✓ | |
| Mr A Shah | RNOH, Chief Pharmacist | ✓ | |
| Prof A Tufail | MEH, DTC Chair | | ✓ |
| Ms N Phul | MEH, Chief Pharmacist | | ✓ |
| Ms K Delargy | BEH, Chief Pharmacist | | ✓ |
| Ms L Reeves | C&I, Chief Pharmacist | | ✓ |
| Dr L Waters | CNWL, Consultant Physician in HIV | ✓ | |
| Ms R Clark | NCL ICB, Head of Medicines Management (Camden) | | ✓ |
| Mr P Gouldstone | NCL ICB, Head of Medicines Management (Enfield) | ✓ | |
| Ms E Mortty | NCL ICB, Interim Head of Medicines Management (Haringey) | | ✓ |
| Ms M Singh | NCL ICB, Head of Medicines Management (Barnet) | ✓ | |
| Mr A Dutt | NCL ICB, Head of Medicines Management (Islington) | | ✓ |
| Dr D Roberts | NCL ICB, Clinical Director (Islington) | ✓ | |
| **Attendees** | | | |
| Ms S Sanghvi | IPMO Programme Team, JFC Principal Pharmacist | ✓ | |
| Ms S Amin | IPMO Programme Team, Lead Pharmacist | ✓ | |
| Ms S Maru | IPMO Programme Team, JFC Support Pharmacist | ✓ | |
| Ms P Varu | IPMO Programme Team, JFC Support Pharmacist | ✓ | |
| Ms M Butt | IPMO Programme Team, Director | ✓ | |
| Mr G Grewal | RFL, Deputy Chief Pharmacist | ✓ | |
| Ms I Samuel | RFL, Formulary Pharmacist | ✓ | |
| Mr H Shahbakhti | RFL, Formulary Pharmacist | ✓ | |
| Mr A Barron | UCLH, Principal Pharmacist | ✓ | |
| Mr S O'Callaghan | UCLH, Formulary Pharmacist | | ✓ |
| Ms H Thoong | GOSH, Formulary Pharmacist | ✓ | |
| Mr D Sergian | MEH, Formulary Pharmacist | ✓ | |
| Mr G Purohit | RNOH, Formulary Pharmacist | ✓ | |

| | | | |
|---|---|---|---|
| Ms S Ahmed | WH, Formulary Pharmacist | | ✓ |
| Ms N Patel | NMUH, Formulary Pharmacist | | ✓ |
| Ms M Thacker | GOSH, Deputy Chief Pharmacist | ✓ | |
| Ms J Bloom | MEH, Associate Chief Pharmacist | ✓ | |
| Ms H Weaver | NHSE, Specialised Commissioning Pharmacist (Observer) | ✓ | |
| Ms A Fakoya | NCL ICB, Contracts & Commissioning Pharmacist | ✓ | |
| Ms EY Cheung | Deputy Head of Medicines Management, NCL ICB (Camden) | ✓ | |
| Mr A Daneshmend | Clinical Pharmacology Registrar, UCLH | ✓ | |
| Ms E Adeyeye | Clinical Pharmacology Consultant, UCLH | ✓ | |
| Ms M Formica | Respiratory Pharmacist, WH | ✓ | |
| Ms K Malhotra | Orthopaedic Consultant, RNOH | ✓ | |
| Mr T Azamgarhi | Antimicrobial Pharmacist, RNOH | ✓ | |
| Mr S Warren | Antimicrobial Consultant, RNOH | ✓ | |
| Ms A Tynan | Principal Pharmacist, Medicine, RFL | ✓ | |
| Ms N Kanani | Principal Hepatology Pharmacist, RFL | ✓ | |

## 2. Meeting attendees

Prof Hingorani welcomed members, observers, and applicants to the meeting (see above). The Committee thanked Ms Poonam Varu for her hard work supporting the Committee over the past year and wished her well in her new role.

## 3. Members' declaration of interests

The Declarations of Interests register for Committee members was included for information. No further interests were declared at the meeting.

## 4. Minutes of the last meeting

Minutes and abbreviated minutes of the November 2023 meeting were ratified. The minutes from the August 2023 meeting require a correction. Item 8.1 regarding the use of mitotane with EDP incorrectly states 'P' is paclitaxel but this will be corrected as 'P' is cisplatin.

## 5. Matters arising

## 5.1 Unlicensed varenicline for smoking cessation

The Committee considered a request from RFL, UCLH and WH to approve the use of unlicensed varenicline (Apotex®) on the NCL Joint Formulary. Thistle Pharma can import Apotex® (a parallel import from North America). Licensed varenicline (previously known as Champix®) was withdrawn from the UK market in October 2021 due to concerns around unsafe levels of nitrosamine. The Committee noted that there has been a positive NICE TA123 for varenicline monotherapy in smoking cessation and a JFC approval in May 2020 for the use of varenicline monotherapy or varenicline in combination with NRT, however no alternative varenicline preparation has been available. The dosing of unlicensed varenicline is the same as Champix®, however the Committee noted that starter packs are not available for Apotex® and that supply of Apotex® may currently be limited to approximately 10-15% of the peak volume of Champix®.

In terms of quality assurance, Thistle Pharma have provided a patient leaflet, product information and nitrosamine compliance statement. Additionally, all batch details have been risk assessed by the MHRA as part of their consent to import into the UK. As the product is unlicensed, each Trust would additionally apply their own local risk assessment process. JFC support confirmed with Trust QA Leads at interested NCL Trusts that there are no anticipated barriers from a quality perspective in procuring Apotex®.

Due to the limited supply and unlicensed nature of Apotex®, prescribing would be restricted to secondary care and an NCL prescribing consensus from clinicians was proposed as outlined below.

- Respiratory clinician to initiate (or approve initiation of) varenicline in line with NICE TA/JFC approved criteria with minimum 4-week supply
- 2 weeks after initiation, review via telephone for compliance and tolerance by clinical team or tobacco dependency team. Supply further 8 weeks of treatment, if evidence of tolerance and adherence.
- Review 4 weeks later (preferably in person) for abstinence check.
- 3-month review (in person) once initial 12-week course is complete to determine if further 12 week course is required.

- 6-month review for patients who receive a second 12-week course (i.e. maximum of 2 12-week courses per patient.

In terms of cost, the stated price point is similar to Champix® however additional costs for shipping and handling and assembly of, "starter packs" may be applicable. Overall, no significant budget impact is anticipated due to previous approval of varenicline within drug budgets and limited supply. The Committee agreed it was appropriate for prescribing and monitoring to be restricted to secondary care but noted that this would impact on clinician time and outpatient appointment requirements.

The Committee conditionally approved the use of Apotex® but noted the limited supply and highlighted a preference for NCL clinicians to provide criteria for rational clinical prioritisation if possible. If unable to provide these criteria, the Committee would support "first-come first-serve" as a last resort. It was noted that each Trust would need to reserve a full course (at least 12 weeks supply) if a patient commences treatment and consider suitable options for providing initiation doses e.g., starter packs.

The Committee also requested that an NCL patient sheet for consent is developed outlining that the product is unlicensed and providing information on nitrosamine impurities safety considerations. Additionally, the GP would need to be informed of varenicline initiation. A recommendation was made to add Apotex® to the NCL Red List as prescribing will be restricted to secondary care.

**Decision**: Conditionally approved - pending clarification on clinical prioritisation criteria, supply of initial course (i.e whether starter packs are required) and the development of NCL patient information sheet/consent form.
**Prescribing**: Secondary care only, restricted to initiation by (or following discussion with) respiratory clinicians
**Tariff status**: N/A - unlicensed
**Funding**: Trust
**Fact sheet or shared care required**: N/A
**Other information**: Add to the NCL Red List

**Post-meeting note:** Clarification on the outstanding queries were received from the clinical team as follows:

i. No appropriate clinical prioritisation criteria could be identified by the team beyond the current license and NICE recommendations, however, noting the limited supply, they agree that initiation of varenicline should be restricted to respiratory clinicians only and any clinician outside of respiratory will need to discuss with a respiratory physician prior to initiation (to determine appropriateness and plan for follow-up). The clinical team will inform the GP when starting a new medicine.
ii. The initiation course will be packed down in Trust dispensaries. The company have offered to supply packaging for free to pack down into.
iii. Trusts will need to reserve a full course if a patient commences treatment. Implementation of this will need to be agreed at each Trust.
iv. Development of a PIL/consent form is underway and will be brought to a future JFC meeting for sign-off.

These suggestions were approved via JFC Chair's action and it was noted that JFC approval of the PIL/consent form is the only outstanding action.

## 6. NHSE Updates

### 6.1. Future NICE Appraisals

The Committee noted a new monthly NHSE Specialised Commissioning circular highlighting upcoming NICE appraisals and implementation requirements and agreed to include this on future JFC agendas for information.

### 6.2. Anastrazole licensing

Deferred.

### 6.3. DOACs Update

The updated NHSE commissioning recommendations for DOACs for the management of atrial fibrillation was highlighted to the Committee. Generic apixaban is now considered the best-value DOAC (since the removal of the patent). The Committee was informed that the previous Edoxaban Working Group will reconvene to review the NHSE recommendations and update the NCL position statement accordingly, noting that generic apixaban is now first-line for new AF patients. The updated position statement will be brought to JFC for approval. The Committee noted the considerable resource and effort dedicated to delivering the initial set of DOAC commissioning recommendations, which have now been reversed, and that concerns regarding the initial recommendations had been formally escalated by JFC to NICE and NHSE in 2022. Ms Coughlan agreed to feedback these concerns to NHSE.

## 7. Review of action tracker

Action tracker included for information. Closed actions have been updated on the tracker.

## 8. JFC outstanding items & work plan

These items were included for information only. Any questions should be directed to Ms Sanghvi.

## 9. Local DTC recommendations/minutes

| DTC site | Month | Drug | Indication | JFC outcome |
|---|---|---|---|---|
| UMC | November 2023 | High-intensity rivaroxaban | Antiphospholipid syndrome – post-RISAPS continuation | **Decision**: Conditionally approved – UCLH only<br>**Prescribing**: Secondary care only<br>**Tariff status**: In tariff<br>**Funding**: Trust<br>**Fact sheet or shared care required**: N/A<br>**Additional information:** Subject to conditions outlined regarding patient assessment and consent. |
| UCLH | November 2023 | FOC scheme: Tofersen†* | Amyotrophic lateral sclerosis with SOD1 mutations | **Decision**: Conditionally approved – UCLH only<br>**Prescribing**: Secondary care only<br>**Tariff status**: N/A<br>**Funding**: FOC scheme<br>**Fact sheet or shared care required**: N/A<br>**Additional information:** Subject to development of SOP, training schedule, risk assessment PIL and internal funding |
| UCLH | November 2023 | Dengue tetravalent vaccine (live, attenuated; Qdenga® | Prevention of dengue in travellers to endemic areas (Private patients only) | **Decision**: Approved – UCLH only<br>**Prescribing**: Secondary care only<br><br>**Not for addition to the NCL Joint Formulary as applicable to private patients only.** |
| UCLH | December 2023 | Tacrolimus and Azathioprine | Chronic histiocytic intervillositis | **Decision**: Conditionally approved – UCLH only<br>**Prescribing**: Secondary care only<br>**Tariff status**: In tariff<br>**Funding**: Trust<br>**Fact sheet or shared care required**: N/A<br>**Additional information:** Subject to development of PIL and data collection |
| UMC | December 2023 | Anakinra* | Severe refractory cytokine release syndrome (CRS) +/- immune effector cell-associated neurotoxicity syndrome (ICANS) | **Decision**: Approved<br>**Prescribing**: Secondary care only<br>**Tariff status**: Not routinely commissioned<br>**Funding**: Trust<br>**Fact sheet or shared care required**: N/A<br>**Additional information:** N/A |
| UMC | December 2023 | FOC scheme: Aducanumab† | Alzheimer's disease post-EMBARK study | **Decision**: Not approved<br>**Additional information:** N/A |

| | | | | |
|---|---|---|---|---|
| UMC | September 2023 | Intravesical gentamicin (single 24-week course) | Recurrent UTIs due to a gentamicin sensitive uropathogen, in patients who are able to self-catheterise and adhere to treatment, as a last-line option where prophylactic oral antibiotics and other measures had failed. | **Decision**: Approved<br>**Prescribing**: Secondary care only<br>**Tariff status**: In tariff<br>**Funding**: Trust<br>**Fact sheet or shared care required**: N/A<br>**Additional information:** Previously ratified for UCLH only |
| RFL | October 2023 | Atezolizumab (Roche) subcutaneous injection | Multiple malignancies – formulation change | **Decision**: Approved<br>**Prescribing**: Secondary care only<br>**Tariff status**: Not routinely commissioned<br>**Funding**: NHSE<br>**Fact sheet or shared care required**: N/A<br>**Additional information:** N/A |
| RFL | November 2023 | Botulinum toxin type A* | Moderate to severe spasmodic dysphonia | **Decision**: Conditionally approved – RFL only<br>**Prescribing**: Secondary care only<br>**Tariff status**: In tariff<br>**Funding**: Trust<br>**Fact sheet or shared care required**: N/A<br>**Additional information:** N/A |
| RFL | November 2023 | Liposomal bupivacaine injection (Pacira biosiciences) | Post-operative analgesia (Private patients only) | **Decision**: Approved – RFL only<br>**Prescribing**: Secondary care only<br><br>**Not for addition to the NCL Joint Formulary as applicable to private patients only.** |

*Subject to funding consideration; †The relevant commissioner should be notified in line with NCL Free of Charge scheme guidance. Approval is conditional on the provision of a free of charge scheme agreement and funding statement

## 10. New medicine reviews

## 10.1 Tedizolid as a long-term second-line suppressive antibiotic therapy (SAT) agent for multi-drug resistant (MDR) Gram-positive orthopaedic infections

The Committee considered an application for tedizolid tablets, an oxazolidinone, at a dose of 200mg daily, for off-label use as a long-term suppressive antibiotic therapy (SAT) in patients with multi-drug resistant (MDR) Gram-positive orthopaedic infections. The proposed place in therapy is as second-line suppression after oral antibiotics; as an alternative to long-term daily IV antibiotics (which are rarely used in practice because of the risk of line complications and access issues for immobile patients attending tertiary services (e.g. RNOH)) or monthly IV dalbavancin; in patients where a surgical intervention is not an option. Assays for monthly IV dalbavancin are not available in the UK currently which makes it unsuitable for chronic kidney disease (CKD) patients. The applicants do not propose using linezolid, a cheaper drug in the same class, due to previous reports of adverse events with longer-term use and a perception that tedizolid is a safer option. However, linezolid was still included as a comparator within the evidence review to determine the comparative safety profile.

There was no efficacy data to support the use of tedizolid (or linezolid) in this cohort.

The Committee assessed the comparative safety data for tedizolid versus linezolid, noting that some structural differences between tedizolid and linezolid exist but it is unclear from the published literature if these confer any safety advantages.

The Committee first considered comparative evidence for tedizolid vs. linezolid each used within their licensed indications of acute bacterial skin and skin structure infections (ABSSSIs) for 6 and 10 days respectively. This included the pooled safety data of the ESTABLISH-1 and ESTABLISH-2 studies (phase 3, non-inferiority, double-blind, randomised controlled trials) and a network meta-analysis of four phase 3 randomised controlled trials (including the ESTABLISH-1 and -2 studies). Overall, the adverse event profiles were comparable. The network

meta-analysis showed a lower rate of nausea (OR:0.68 (95% CI: 0.49 – 0.94), vomiting (OR: 0.56 (95% CI: 0.24 – 0.96) and abnormal neutrophil counts (OR: 0.36 (95% CI: 0.17 – 0.76) with tedizolid, however all other adverse event incidences showed no statistical difference.

Secondly the Committee reviewed pharmacovigilance retrospective observational analyses from FDA Adverse Event Reporting System (FAERS) data. Lee et al (2017) reported similar rates of thrombocytopenia of 2.4% for tedizolid compared to 2.7% for linezolid over a three-year period. Gatti et al (2021) reported no statistically significant differences between tedizolid and linezolid for several adverse effects including platelet count decrease (ROR: 0.51 (95% CI: 0.24 – 1.08), thrombocytopenia (ROR: 0.98 (95% CI: 0.63 – 1.52), anaemia (ROR: 0.51 (95% CI: 0.26 – 1.00), optic (0.4% vs 0.9%; ROR not available) or peripheral neuropathy (0.63 (95% CI: 0.28 – 1.42) over a 6-year period. The Committee noted that there were several limitations with these pharmacovigilance studies due to the retrospective design, unknown indication and duration of treatment and data bias because adverse event reporting is not mandatory.

Next, the Committee considered the available safety evidence for extended treatment durations of tedizolid. Three non-randomised observational studies by Miller et al (2023; n=39); Senneville et al (2021; n=33) and Ferry et al (n=17) reviewed the safety profile of tedizolid for a treatment duration of 2-6 months in patients with bone and joint infections (BJIs) or prosthetic joint infections (PJIs). While there were no reports of peripheral neuropathy, there was a 25% incidence of myelosuppression in 2 studies, a case of visual disturbances in 2 studies and a 3-6% discontinuation rate across 2 studies. Due to the study design, small sample sizes and insufficient treatment durations, it is difficult to draw conclusions of tedizolid's long-term safety profile from these studies, but myelosuppression and optic neuropathy were notable reported adverse effects. The SPCs for tedizolid and linezolid note thrombocytopenia, anaemia, peripheral and optic neuropathy were associated with treatment durations longer than 28 days with linezolid and longer than 6 days with tedizolid.

The Committee also reviewed two non-comparative retrospective studies by Benavent et al (2021; n=51) and Morisette et al (2022; n=37) reporting on tedizolid safety. Benavent et al (29-day duration study) reported no myelosuppression, peripheral or optic neuropathy, however Morisette et al (188-day study) reported 32% of patients experienced myelosuppression with tedizolid. While there were several limitations of these studies, the results suggest that a longer treatment duration is more likely to result in adverse effects.

Lastly, the Committee reviewed safety evidence for long-term linezolid. Theil et al (2020; n=372) reported a systematic review of 16 non-randomised observational studies in PJI patients treated with linezolid for a mean treatment duration of 58 days. Neuropathy was reported in 0-13% of patients, myelosuppression in 12-79% and discontinuation due to linezolid in 9%. Zhang et al (2015; n=367) reported a meta-analysis of 1 randomised controlled trial (n=239) and 14 non-randomised observational studies in MDR/XDR tuberculosis patients treated with linezolid for a median treatment duration of 12 months. Peripheral neuropathy was reported in 30.9% of patients across the various studies, optic neuropathy in 8% of patients, myelosuppression in 35% of patients and discontinuation due to linezolid in 35% of patients. Limitations in the robustness of study designs e.g. selection bias, variation in linezolid doses, and other confounding factors made it difficult to draw indirect safety comparisons of linezolid with tedizolid from these results.

In terms of cost impact, there was an estimated cohort of 35 patients from RNOH, RFL and UCLH across NCL. The drug cost per annum for this cohort was approximately £1.8 million for tedizolid, £850,000 for linezolid and £700,000 for dalbavancin (not including cumulative costs beyond the first year).

The Committee heard from Dr Warren and Mr Azamgarhi that this is a difficult-to-treat patient cohort with limited treatment options and that patient numbers requiring SAT are expected to rise as implant, graft and revision surgeries increase. Dr Warren confirmed that linezolid would not be used in this cohort for long-term treatment due to safety concerns.

*In camera*, the Committee confirmed that the application was relevant to multiple Trusts, as orthopaedic patients who are non-operative candidates are not referred to RNOH but may still require SAT at other NCL Trusts. The Committee discussed the following concerns when considering if tedizolid is a safer drug than linezolid, both of which are in the same drug class but the latter of which would not be used by the applicants as a treatment option for this patient cohort based on safety concerns:

i) There is a lack of efficacy data available for the use of tedizolid as a long-term SAT in this cohort.

ii) There is no difference reported in the short-term safety profile between linezolid and tedizolid based on the EMA EPAR pooled analysis, Lan et al NMA and pharmacovigilance studies.

iii) Tedizolid and linezolid are both in the same drug class and there is no published evidence to explain differences in safety profile based on the chemical structures or pharmacokinetic profiles of either medicine.

iv) The manufacturing literature recommends that adverse effects with tedizolid are usually reported when used longer than the licensed 6-day duration.

v) The available long-term safety data for tedizolid from non-randomised observational studies reports myelosuppression and optic neuropathy can occur when treating patients for longer than the licensed duration.

vi) Tedizolid has not been used for a sufficiently long period of time to assess its' long-term safety profile reliably.

vii) The 'response-mode' rather than 'hot pursuit' monitoring schedule proposed by the applicants to monitor optic and peripheral neuropathy is insufficient to ensure patient safety.

viii) The treatment cost is substantial.

ix) There remains uncertainty regarding the efficacy and safety of long-term use of tedizolid for the proposed indication. Taking into consideration the applicants' view that this cohort will grow, the Committee considered it important that data is gathered via a research study to establish whether tedizolid (or linezolid) are safe and effective treatment options.

In summary, based on the evidence available and concerns raised above, the Committee could not recommend the use of tedizolid. However, the Committee were supportive of a clinical trial being pursued to provide an evidence base to support this treatment and linking in with the NHSE regional and national antimicrobial leads to pursue a national approach for this cohort.

**Decision:** Not approved

## 10.2 Rivaroxaban for forefoot, soft tissue and bilateral foot surgery

The Committee considered an application for rivaroxaban, a Factor Xa inhibitor, at a dose of 10mg daily for a duration of 14-42 days, for off-label use in patient's weighing 50-120kg, with forefoot, midfoot or bilateral foot surgery with or without immobilisation and deemed to be at higher risk of VTE requiring chemical prophylaxis upon VTE risk assessment, who would otherwise receive low-molecular weight heparins (LMWH).

The Committee heard that the JFC had previously approved the use of rivaroxaban for midfoot and hindfoot surgery in patients requiring plaster immobilisation on the basis of the PRONOMOS trial.

The PRONOMOS trial was a phase 3, randomised, active-comparator controlled, parallel group, double-blind, non-inferiority trial, comparing the efficacy and safety of rivaroxaban and enoxaparin for patients undergoing non-major orthopaedic surgery in the lower limbs, who required at least 2 weeks of thromboprophylaxis (n=3604). Patients were randomised to rivaroxaban 10mg daily or subcutaneous enoxaparin 40mg daily. The primary endpoint (composite of distal or proximal VTE, or VTE–related death during treatment period) was significantly lower with rivaroxaban compared to enoxaparin (0.2% vs 1.1%; RR: 0.25 (95% CI: (0.09 – 0.75), [p<0.001 for non-inferiority and p=0.01 for superiority]). Key limitations of the study were that the study was underpowered due to premature discontinuation of enrolment, 8.4% of patients had incomplete or no assessment of the primary outcome (which necessitated imputations), there was a broad range of lower limb surgeries making it difficult to extrapolate data to the proposed cohort and the small number of events which meant that the trial had limited power to evaluate subgroup effects.

An RNOH audit (n=360) in adults with midfoot or hindfoot surgery who received pharmacological VTE prophylaxis compared two cohorts of rivaroxaban patients with a historical cohort of patients that received tinzaparin. There was a VTE incidence rate of 0.9% and 0.8% in the rivaroxaban cohorts. This was greater than for the tinzaparin cohort (0%) and the audit standard (0.43%). There was a bleeding incidence rate of 0.9% and 1.5% in the rivaroxaban cohorts which was greater than the tinzaparin cohort (0%) but lower than the audit standard of 2%.

The Committee also considered data from a prospective cohort study by Saragas et al (2017; n=142) and retrospective cohort study by Ali et al (2020; n=1004). Both studies indicated rivaroxaban is safe and effective thromboprophylaxis in lower limb immobilisation but were limited by the study design and lack of an appropriate comparator arm.

In terms of safety, there was no significant difference between rivaroxaban and enoxaparin (1.1% vs 1.0%; RR: 1.04 (95% CI: 0.55 – 2.00) for major bleeding or non-major clinically relevant bleeding in the PRONOMOS study.

In terms of budget impact, rivaroxaban is expected to save up to £850 per annum compared to tinzaparin for the small, proposed cohort of 10 patients per annum.

The Committee heard from Dr Malhotra that he is the Chief Investigator of a currently unpublished national prospective observational cohort study across 68 sites in 11,300 foot and ankle surgery patients that reports no difference in VTE incidence rates between rivaroxaban and LMWHs.

*In camera*, the Committee considered the advantage of using rivaroxaban as a less invasive method of administration for patients that would also reduce requirements for community nurse administration. The Committee agreed that in addition to offering increased convenience at a lower cost, the available evidence suggested that rivaroxaban has a similar efficacy and safety profile to LMWHs, albeit in a wider study population than the cohort proposed. However, the Committee sought clarification on how the duration of treatment (proposed range from 14 days to 42 days) would be determined, and whether criteria for this could be incorporated into VTE guidance. Mr Purohit noted that this information would be included within the RNOH guideline update and offered to share this with other Trusts.

In summary, the Committee agreed to add rivaroxaban to the NCL Joint Formulary for thromboprophylaxis following forefoot, midfoot or bilateral foot surgery (with or without immobilisation) for patients deemed high risk following VTE risk assessment.

**Decision**: Approved. RNOH to share clinical criteria for determining appropriate duration of treatment (proposed range from 14 days to 42 days) with other NCL Trusts for incorporation into local guidelines.
**Prescribing**: Secondary care only
**Tariff status**: In tariff
**Funding**: Trust
**Fact sheet or shared care required**: N/A

## 11. Guidelines, Pathways and Position Statements

### 11.1 NCL Cholestatic itch pathway

In March 2022, The JFC approved several medications for the management of cholestatic pruritus. RFL hepatology were asked to create a guideline to support ongoing prescribing in primary care, including monitoring requirements. The guideline was presented to the Committee for approval and any final feedback/comments were requested by Thursday 25th January via email.

## 12. Next meeting

Thursday 15th February 2024

## 13. Any other business

Nil