North Central London Integrated Care System

NHS
North Central London
Medicines Optimisation Network

Joint Formulary Committee (JFC): Minutes

Minutes from the meeting held on 15th February 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 M Butt	IPMO Programme Team, Director	✓	
Mr G Grewal	RFL, Deputy Chief Pharmacist		✓
Mr K Cahill	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 R Allen	UCLH, Clinical Commissioning 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	✓	
Dr E Payne	Clinical Pharmacology Consultant, UCLH	✓	
Mr A Tailor	Haematology Pharmacist, UCLH	✓	

2. Meeting attendees

Prof Hingorani welcomed members, observers, and applicants to the meeting (see above).

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 January 2024 meeting were ratified.

5. Matters arising

5.1 Dienogest for endometriosis

In October 2023, the Committee agreed to add the use of dienogest for endometriosis to the NCL Joint Formulary for the treatment of endometriosis pending receipt of:

1. Submission of the evidence base pertaining to the shrinkage of endometrial tissue following treatment with dienogest for pre-surgical patients.

   The Committee reviewed data from Gokmen et al (2023; n=76), a prospective observational study, that reported a significant decrease of 22% in the mean endometrioma size at 6-month follow-up in patients aged 17-49 with endometriomas in the per-protocol population (n=64) treated with dienogest 2mg daily. Kohler et al (2009; n=68) reported an open-label, randomized, dose-finding study comparing the efficacy and safety of dienogest 2mg daily with dienogest 4mg daily. Dienogest significantly reduced the mean revised American Fertility Society scores (which factor in endometrioma size) from 11.4 to 3.6 (n=29; $p<0.001$) in the 2mg group and from 9.7 to 3.9 (n=35; $p<0.001$) in the 4mg group.

2. A clearly defined treatment pathway for the proposed place in therapy, including eligibility and stopping criteria.

   The Committee were presented with a treatment pathway developed by the applicant. Comments on the pathway will be reviewed offline and approved via Chair's actions.

Post-meeting note: Comments raised on the pathway were addressed offline and the treatment pathway approved via Chair's actions.

Decision: Approved
Prescribing: Secondary care initiation, primary care continuation
Tariff status: In tariff
Funding: Trust/ICB
Fact sheet or shared care required: N/A

5.2 JFC Evaluations Update

The JFC support team conducted a trial of using PowerPoint presentations for inclusion in the JFC agenda pack instead of a written evaluation. Perceived benefits include reduction in duplication of work across the Word and PowerPoint format, ease of reviewing the evaluations ahead of the JFC meetings for Committee members and enabling applicants to view how their application will be presented ahead of the meeting. The Committee were supportive of continuing to use PowerPoint presentations only instead of written evaluations. A presentation

template and guide on how to complete the presentation will be shared for standardisation and adoption across NCL formulary teams.

6. NHSE Updates

6.1. NHSE Specialised Commissioning NICE Appraisals Update

Nil.

6.2. Anastrazole licensing

The Committee noted a new NHSE circular highlighting that as part of the Medicines Repurposing Programme, anastrazole has secured an MHRA license for a new indication of primary prevention of breast cancer in post-menopausal women. This indication was not applicable to NCL Trust oncology teams, with the potential exception of RFL due to the presence of family genetics clinics. The Committee were informed that the new indication will be formally added to the RFL formulary if applicable to their Trust, following local DTC processes. If prescribing is intended to be transferred to primary care, this will be brought back for review via JFC.

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
MEH	October 2023	Sublingual timolol	For osteo-odonto-kerato-prosthesis (OOKP) to help control intraocular pressure in patients that do not get the desired effect from topical therapy and cannot have their intra-ocular pressure measured accurately.	**Decision**: Approved **Prescribing**: Secondary care only **Tariff status**: In tariff **Funding**: Trust **Fact sheet or shared care required**: N/A **Additional information:** N/A
MEH	June 2020	Mydrane	Rapid dilation prior to cataract surgery, when home dilation has not resulted in adequate mydriasis	**Decision**: Conditionally approved **Prescribing**: Secondary care only **Tariff status**: In tariff **Funding**: Trust **Fact sheet or shared care required**: N/A **Additional information:** Subject to 6-month audit trial to provide information on cost-savings in practice.
WH	September and October 2023	IV Digoxin	Foeticide prior to late surgical termination of pregnancy	**Decision**: Approved – WH only **Prescribing**: Secondary care only **Tariff status**: In tariff **Funding**: Trust **Fact sheet or shared care required**: N/A **Additional information:** N/A
RFL	September 2023	Testavan gel	Male hypogonadism (to assist with the shortage of Testogel and Tostran 2% gel)	**Decision**: Approved **Prescribing**: Primary and secondary care **Tariff status**: In tariff **Funding**: Trust **Fact sheet or shared care required**: N/A **Additional information:** N/A

RFL	December 2023	[FOC Scheme] Pembrolizumab in combination treatment (with trastuzumab, 5-fluorouracil and platinum-based chemotherapy) †	For HER-2 amplified metastatic gastric or GEJ adenocarcinoma	**Decision**: Approved **Prescribing**: Secondary care only **Tariff status**: N/A – FOC Scheme **Funding**: NA – FOC Scheme **Fact sheet or shared care required**: N/A **Additional information:** N/A

*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

9.2 Cyclogest for threatened miscarriage

The Committee heard a request to ratify the use of cyclogest pessaries (400mg BD for up to 16 weeks) for threatened miscarriage. Cyclogest is on the formulary at RFL and NMUH and is routinely used for this indication at UCLH. RFL have developed a local guideline which includes eligibility criteria, a treatment pathway and PIL. The Committee were informed that while cyclogest pessaries are not licensed for threatened miscarriage, it is recommended as an off-label use for this indication in the BNF and NICE guideline (NG 126).

RFL have documented an amber prescribing status in their guideline (initiation of prescribing by a specialist and continuation in primary care). However, they have noted difficulty in transferring prescribing to primary care and therefore tend to provide the complete supply from RFL. Feedback from UCLH, NMUH and primary care on transfer of prescribing is being sought.

The Committee agreed that transfer of prescribing from secondary to primary care should include clear communication of indication, duration of treatment, and stop date. Primary care feedback indicates that currently this information is often not provided by clinics, and the Committee agreed that this should be fed back to clinics to ensure a robust communication mechanism is in place.

In summary, the Committee was supportive of using the RFL guideline to ratify the use of cyclogest pessaries in threatened miscarriage to the NCL Joint Formulary pending resolution of any discrepancies in practice across NCL Trusts by sharing the RFL guidance. Additionally, further primary and secondary input on prescribing status will be obtained for discussion at the Shared Care Group.

Decision: Approved pending resolution of any discrepancies in practice across NCL Trusts
Prescribing: Deferred to Shared Care Group for further discussion
Tariff status: In tariff
Funding: TBC following discussion at NCL SCG
Fact sheet or shared care required: N/A

9.3 Formulary Decisions for Private Patients in Trusts

The Committee discussed how NCL NHS Trusts and Drugs and Therapeutic Committees (DTCs) currently manage medicines governance queries from internal private clinical services, and decisions regarding access to medications that are applicable to private patients only.

In summary, the Committee agreed that the following principles should be applied across the sector for consideration of formulary requests restricted to private patients:

i. The NCL Joint Formulary supports medicines decisions for NHS patients and promotes equitable access to medicines. The NCL Joint Formulary should only include formulary decisions for NHS patients and will not include decisions that are only applicable to private services. Formulary decisions for private patients will be included within NCL JFC minutes for information but not for ratification. Formulary decisions for private patient cohorts may be uploaded by Trusts to the relevant Trust specific section on Netformulary with the following statement 'Assessed as not cost-effective for the NHS, available privately via [*insert name of Trust private service*] only (not for NHS prescribing in primary or secondary care).'
ii. Non-formulary requests for private patients that are reviewed by NHS Trust DTCs should be subject to the same clinical assessment criteria (including efficacy, safety, convenience, and wider healthcare resource implications) but noting that funding and affordability considerations will differ.
iii. Prescribing of non-formulary medicines for private patients must be retained under private services. It is not appropriate for clinicians to request transfer of prescribing to NHS primary care.
iv. NHS Trust DTCs should inform NCL JFC if additional risks or issues are identified in the provision of clinical governance oversight of private services' medicines use.

9.4 Pan-London Ophthalmology Formulary

The London Procurement Partnership (LPP) has developed a Pan-London Ophthalmology Formulary based on the MEH formulary in collaboration with various stakeholders across London. MEH are supportive of the pan-London formulary being adopted in NCL. New ophthalmology formulary reviews from JFC and MEH will be communicated to LPP to ensure ongoing maintenance. The JFC team will work with MEH to implement the pan-London Ophthalmology formulary by updating it on the NCL Netformulary.

10. New medicine reviews

10.1 Eltrombopag for aplastic anaemia (Applicant: Dr E Payne, UCLH; Dr K Stringaris, UCLH; Dr R Hough, UCLH)

The Committee considered an application for eltrombopag tablets, a thrombopoietin receptor agonist, at a dose of 150mg daily, for severe to very severe aplastic anaemia for the following indications:

i. First-line adjunctive therapy in patients who will receive immunosuppressive therapy [IST (anti-thymocyte globulin; ATG + ciclosporin; CSA)] in patients ≥12 years old and <60 years old (off-label indication).
ii. First-line monotherapy or in combination with CSA in new patients who are unsuitable for immunosuppressive therapy (IST) or haematopoietic stem cell therapy (HSCT) in patients aged ≥ 60 years old (off-label indication).
iii. Third-line therapy as a repeated course as an adjunctive therapy with IST (ATG + CSA) in patients who have had an inadequate response to IST with or without eltrombopag at first-line and are unfit for transplant or have no suitable donor in patients ≥2 years old and <60 years old (licensed indication).

The Committee reviewed 2 studies for the first proposed indication.

RACE (Latour et al, 2022; n=197) was a phase 3, open-label, active-controlled, randomized study to compare the efficacy and safety of eltrombopag, ATG and CSA (triple therapy) with ATG and CSA (dual therapy; standard of care) in patients aged over 15 years old with severe or very severe aplastic anaemia not eligible for HSCT. The Committee noted that in the RACE trial, 23% of patients older than 65 years received triple or dual therapy. The primary endpoint, complete response at 3 months, was significantly better with triple therapy compared to dual therapy (22% vs 10%; OR: 3.2 [95% CI: 1.3 – 7.8], p=0.01). The secondary outcome of median time to platelet transfusion independence and red blood cell transfusion independence was lower with triple therapy compared to dual therapy (40 days vs 68 days and 51 days vs 140 days respectively). The median time to best response was shorter for triple therapy compared to dual therapy (3.9 months vs 8.9 months). There was no significant difference noted in overall survival, number of transplants and relapse rates between both arms suggesting eltrombopag supports blood counts but is not disease modifying.

Townsley et al (2017, n=92) reported an open-label, single-arm study in patients ≥2 years old with untreated severe aplastic anaemia administered triple therapy. The complete response at 6 months was 39% and median time to platelet and red blood cell transfusion independence were 32 and 39 days respectively.

For the second proposed indication, there was no efficacy data supporting the use of eltrombopag as first-line monotherapy in new patients unsuitable for IST or HSCT in patients aged ≥ 60 years old.

For the second proposed indication whereby eltrombopag is proposed to be used first-line in combination with CSA in new patients who are unsuitable for IST or HSCT in patients aged ≥ 60 years old, the Committee reviewed 1 study. SOAR (Scheinberg et al (2024; n=54) reported an abstract of an open-label, single-arm phase 2 study in patients aged ≥18 years old with untreated severe aplastic anaemia, administered eltrombopag with CSA. The percentage of patients older than 60 years old was unclear from the abstract. The overall response rate at 6 months was 46% [95% CI: 33-60] with a complete response of 3.7%.

Lastly, the Committee reviewed efficacy data from 4 studies for the third proposed indication. Patel et al (2022; n=280) was a non-randomized, observational study in patients ≥2 years old with severe aplastic anaemia refractory to IST and not suitable for transplant. Patients were administered triple therapy and a historic first-line IST group was used as a comparator. The overall response rate and complete response rate at 6 months for the triple therapy arm was 81% and 44% respectively compared to 67% and 17% in the historic comparator arm. The main limitation of this study was that the study did not compare populations at a similar line in therapy and variations in the populations used in the historic arm made the results not directly comparable. Three non-randomized, observational studies by Olnes et al (2012; n=25), Desmond et al (2014; n=43) and Winkler et al (2019; n=40) reviewed the efficacy of eltrombopag monotherapy (and used with CSA in n=3) in severe aplastic anaemia patients' refractory to IST. The haematological response at 12-24 weeks ranged from 40 -50%.

In terms of safety, the RACE study reported a similar side effect profile between triple and dual therapy in a first-line setting. Triple therapy had a marginally favourable adverse effect profile (≥ grade 3) compared to dual therapy for all safety outcomes except for gastrointestinal disorders (25% vs 8%).

In terms of budget impact, for an estimate of 6 adults per annum on a 6-month course, 2 adults per annum on continuous treatment and 2 paediatrics per annum on a 6-month course, the cost of eltrombopag was significantly high (drug prices redacted for commercial confidentiality). It was noted that there may be potential to off-set these drug costs (using the RACE trial to estimate a reduction in time to platelet and red blood cell transfusion independence). Although not evidence-based, the applicants deem that the use of triple therapy may result in a reduction in inpatient stays and reduction in the need for transplants.

The Committee heard from Dr Payne that a quicker response rate enables better patient outcomes in these cohorts and is the rationale for using sibling transplants (as they are quicker to setup) ahead of unrelated donor transplants in the first-line setting in <40 year olds. In the patient cohort ≥60 years, eltrombopag would always be used first-line in conjunction with CSA unless the patient is unable to tolerate CSA due to their renal function. Dr Payne informed the Committee that the majority of patients would be treated for 6 months in the 1st line setting and once platelet levels were stable there would be an attempt to wean off eltrombopag therapy. For repeat courses as 3rd line therapy the treatment duration would be 12 months after which a wean would be attempted. Dr Payne estimated that 10% of all patients may require long-term continuation of treatment.

In terms of paediatric cohorts, the main difference in treatment pathway is that patients would undergo an unrelated donor transplant ahead of receiving IST due to the small risk of relapse or transformation with IST, resulting in fewer patients requiring triple therapy. The applicant proposes use in a small cohort of patients aged >12 years old and the Committtee noted that patients>2 years old had been included within Townsley et al (2017), Patel et al (2022), Desmond et al (2014) and Winkler et al (2019) studies. The Committee noted that further clarity was being sought from NHS England regarding the commissioning route for the paediatric cohort.

In camera, the Committee discussed that:

i. In a first-line setting (eltrombopag as an adjunctive therapy with IST in patients < 60 years), the RACE trial (RCT) reported earlier transfusion independence with triple therapy compared to dual therapy, but did not provide evidence that triple therapy will alter the likelihood of a patient requiring a transplant and improved overall survival compared to dual therapy. The Committee were clinically supportive of use of eltrombopag as a first-line adjunctive therapy in patients who will receive immunosuppressive therapy [IST (anti-thymocyte globulin; ATG + ciclosporin; CSA)] in patients ≥12 years old and <60 years old to reduce platelet and red cell transfusion requirements.

ii. In the first-line setting in patients ≥60 years old, there is no evidence that eltrombopag in combination with CSA therapy is as efficacious as triple therapy. Based on the RACE trial, patients over 60 years old received ATG in both arms. Therefore, the Committee deemed there was an evidence base to support the use of triple therapy in a first-line setting in ≥60 years provided ATG was not cautioned or contraindicated in patients. The Committee were therefore clinically supportive of amending the indication to support the use of eltrombopag as a first-line adjunctive therapy in patients who will receive immunosuppressive therapy [IST (anti-thymocyte globulin; ATG + ciclosporin; CSA)] in patients ≥60 years old, provided ATG or CSA was not cautioned or contraindicated in order to reduce platelet and red cell transfusion requirements.

iii. In refractory patients, observational non-comparative data signalled a treatment effect in terms of improved blood cell counts and through extrapolation from the RACE trial, transfusion requirements may fall. The Committee were clinically supportive of using eltrombopag as a repeated course in the third-line setting as an adjunctive therapy with IST (ATG + CSA) in patients ≥2 years old and <60 years old, who have had an inadequate response to IST with or without eltrombopag at first-line and are unfit for transplant or have no suitable donor.

iv. In terms of cost-effectiveness, the Committee noted that the significant drug costs would be offset by savings in transfusion requirements for a 6-month course of treatment. However, the cost-effectiveness of long-term treatment for 10% of patients who could not be weaned off therapy was less convincing and would exert a potentially unsustainable cost pressure. The Committee noted that eltrombopag supports blood counts but is not disease modifying. Taking into account the limitations in the evidence base, the Committee noted that clinical approval would be contingent on a robust cost-analysis that demonstrated low or no cost-impact. The Committee noted that a business case seeking commissioner funding would be more likely to succeed with a limit on duration of therapy and a transfusion threshold to support the case for cost-effectiveness and agreed to support the applicants to further develop this cost-analysis.

Therefore, the Committee have deferred the decision on approval pending:

i. A cost-effectiveness estimate
ii. Agreement on a ceiling of treatment duration
iii. A protocol for weaning eltrombopag treatment

Decision: Deferred pending i. A cost-effectiveness estimate, ii. An agreement on a ceiling of treatment duration and iii. A protocol for weaning eltrombopag treatment

11. Guidelines, Pathways and Position Statements

Nil

12. Next meeting

Thursday 21st March 2024

13. Any other business

Nil