North Central London Integrated Care System

NHS
North Central London
Medicines Optimisation Network

Joint Formulary Committee (JFC): Minutes

Minutes from the meeting held on 20th July 2024

		Present	Apologies
Members			
Prof A Hingorani (Chair)	NCL JFC Chair	✓	
Dr B Subel	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 S Stern	NMUH, 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		✓
Dr M Henley	RNOH, DTC Chair	✓	
Mr A Shah	RNOH, Chief Pharmacist	✓	
Prof A Tufail	MEH, DTC Chair		✓
Ms N Phul	MEH, Chief Pharmacist		✓
Ms K Delargy	NLMHP, Partnership Deputy Chief Pharmacist	✓	
Ms L Reeves	NLMHP, Chief Pharmacist		✓
Dr L Waters	CNWL, Consultant Physician in HIV		✓
Ms R Clark	NCL ICB, Assistant Director of Medicines Optimisation	✓	
Ms M Kaur-Singh	NCL ICB, Head of Medicines Planning & Operations	✓	
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 K Leung	IPMO Programme Team, JFC Support Pharmacist	✓	
Ms M Butt	IPMO Programme Team, Director	✓	
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	✓	
Ms J Bloom	MEH, Associate Chief Pharmacist	✓	
Ms A Bathia	RNOH, Formulary Pharmacist	✓	
Ms S Ahmed	WH, Formulary Pharmacist	✓	
Ms N Patel	NMUH, Formulary Pharmacist	✓	
Ms M Thacker	GOSH, Deputy Chief Pharmacist		✓

Ms H Weaver	NHSE, Specialised Commissioning Pharmacist	✓	
Ms EY Cheung	NCL ICB, Head of Medicines Quality & Improvement		✓
Dr S Benafif	UCLH, Consultant Medical Oncologist	✓	
Ms J Pang	IPMO Programme Team, Lead Pharmacist (Observer)	✓	
Ms C Tse	LNWH, Formulary Lead Pharmacist (Observer)	✓	
Ms N Sakur	NCL ICB, Medicines Planning and Operation Pharmacy Technician (Observer)	✓	

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 relevant to the agenda were raised.

4. Minutes of the last meeting

Minutes and abbreviated minutes of the June 2024 meeting were ratified.

5. Review of action tracker

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

6. JFC Outstanding items and workplan

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

7. Local DTC recommendations/minutes

Date	Drug and Indication	DTC Decision and Details
May 2024	[FOC Scheme] Iptacopan capsules for C3 glomerulopathy*†	**Reviewed by**: RFL **Drug**: Iptacopan capsules 200mg twice daily **Indication**: C3 glomerulopathy **Decision**: Approved **Prescribing status**: Restricted to secondary care only **Funding source**: Free of Charge Scheme **Additional information**: RFL Trust legal team to review the FOC scheme contract from the manufacturer. **Fact sheet or shared care required**: N/A
May 2024	Clonidine patches for management of dystonia*	**Reviewed by**: RFL **Drug**: Clonidine patches (100 micrograms, 200 micrograms, 300 micrograms); initially 3 micrograms/kg/day, increased on a weekly basis according to response to a maximum dose of 2 micrograms/kg/hour in severe dystonia **Indication**: Management of dystonia **Decision**: Approved **Prescribing status**: Restricted to secondary care only **Funding source**: Internally funded – Divisional **Additional information**: Creating a localised RFL protocol for management of dystonia in paediatrics based on the Tertiary referral centre protocols. **Fact sheet or shared care required**: N/A
June 2024	[FOC Scheme] Fruquintinib capsules (unlicensed) for relapsed or refractory metastatic colorectal cancer†	**Reviewed by:** UCLH **Drug:** Fruquintinib capsules **Indication:** For adult patients with relapsed/refractory metastatic colorectal cancer after 3 or more prior lines of

		therapy (including trifluridine-tipiracil and regorafenib), with a good performance status (ECOG PS 0 to 2), who are not eligible for enrolment into a clinical trial. **Decision:** Approved **Prescribing status:** Restricted to secondary care only (GI cancer service) **Funding source:** Free of Charge Scheme **Additional Information:** N/A **Fact sheet or shared care required:** N/A
June 2024	[FOC Scheme] Venetoclax tablets (plus Dexamethasone +/- Bortezomib) for Relapsed/ Refractory Multiple Myeloma with t(11;14) chromosomal translocation†	**Reviewed by:** UCLH **Drug:** Venetoclax tablets (plus dexamethasone +/- bortezomib) **Indication:** Adult patients with relapsed/refractory multiple myeloma with t(11;14) chromosomal translocation after ≥4 prior therapies **Decision:** Not approved
June 2024	Bortezomib for severe refractory anti-NMDAR autoimmune encephalitis*	**Reviewed by:** UCLH **Drug:** Bortezomib subcutaneous injection: 1.3mg/m2 twice weekly for two weeks (days 1, 4, 8, and 11 of a 21-day cycle) and repeated for up to 3 cycles **Indication:** Adult patients with severe refractory anti-NMDAR autoimmune encephalitis as a third line treatment option after steroids (+/-IVIG or PLEX supportive care) and rituximab **Decision:** Approved pending development of SOP submitted and approved by Medication Safety Committee (in liaison with Chemotherapy Governance Group) **Prescribing status:** Restricted to secondary care only (Neurology/Haematology MDT approval only) **Funding source:** Internally funded high cost drug **Additional information:** N/A **Fact sheet or shared care required:** N/A
June 2024	Triptorelin for puberty suppression	**Reviewed by:** UCLH **Drug:** Triptorelin (Decapeptyl SR) 22.5mg intramuscular injection every 6 months **Indication:** Puberty suppression in patients with gender incongruence / dysphoria already receiving treatment or already referred to UCLH paediatric endocrinology service by the former NHS Gender Identity Development Service before 1st April 2024 (in line with NHSE policy) **Decision:** Approved following MDT assessment and in line with local protocol **Prescribing status:** Restricted to secondary care only (UCLH paediatric endocrinology service) **Funding source:** In tariff **Additional information:** N/A **Fact sheet or shared care required:** 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.

8. Matters arising

Nil

9. Medicine reviews

9.1. Famotidine for gastroprotection in patients on high-dose steroids for immune checkpoint inhibitor toxicities (Applicant: Dr S Benafif, UCLH)

The Committee considered an application for famotidine (20mg once daily up to 40mg twice daily), a histamine H2 receptor antagonist (H2RA), for gastroprotection in patients on high-dose steroids for immune checkpoint inhibitor (ICI) toxicities (≥ Grade 2). Current practice involves using proton pump inhibitors (PPIs) for gastroprotection in patients treated with ICIs experiencing immune-related adverse events and taking more than 30mg of prednisolone (or equivalent) daily. The application proposes that co-administration of PPIs and ICIs leads to a higher incidence of immune-related adverse events and poorer treatment outcomes, including shortened progression-free survival and overall survival, in cancer patients. The exact mechanism is unknown but is hypothesised to involve effects on the gut microbiome. This application is for the use of famotidine, instead of PPIs, for this patient cohort to allow gastroprotection during steroid treatment for immune-related adverse events, without compromising therapeutic outcomes.

Okamoto et al (2023) was a meta-analysis of observational studies that investigated the association of concomitant acid suppressant medication use, PPIs and H2RAs, on overall and progression free survival, and incidence of immune-related adverse events during immune checkpoint inhibitor treatment for a range of cancers. The study found any acid suppressants use was associated with reduced overall (HR 1.40 [95% CI 1.21 to 1.61]) as well as progression free survival (HR 1.39 [95% CI 1.21 to 1.59]. Subgroup analyses showed co-administration of ICIs and PPIs was associated with reduced overall survival (HR 1.43 [95% CI 1.21 to 1.69]) and progression free survival (HR 1.34 [95% CI 1.13 to 1.58]), whereas H2RAs use was not associated with a difference in survival (HR 0.80 [95% CI 0.38 to 1.67]).

The Committee discussed limitations of the evidence base, noting that all studies in the meta-analyses were observational (hence associations between acid suppressant use and survival might be confounded, e.g. use of acid suppressant therapy might be a marker for a group with a poorer prognosis), retrospective (hence provide estimates of acid suppressant use given an adverse outcome rather than adverse outcome given acid suppressant use) and small in size (hence the potential for small study bias; for example data on H2 receptor antagonist use was based on only 75 patients in the exposed group). Moreover, the studies in the meta-analysis were based on acid suppressant drug use outside the setting of steroid treatment of immune checkpoint related adverse effects. Taken together, there remains substantial uncertainty about a causal link between PPI co-administration and worse treatment outcomes in ICI-treated patients and, in terms of applicability to the proposed cohort, it was noted that the therapeutic rationale for acid suppression in the reported studies is different to the setting proposed in the application.

When evaluating the efficacy of PPIs versus H2RAs as gastroprotective agents more generally, the Committee considered a systematic review by Almufleh et al (2018). This review included RCTs of patients on dual antiplatelet therapy (DAPT) who received either PPIs or H2RAs and outcomes of interest included the incidence of GI complications. Although the population is not representative of the oncology cohort in question, the results were deemed sufficiently generalisable. The study found that PPIs were superior to H2RAs for gastroprotection in DAPT patients (OR 0.28 [95% CI 0.17 to 0.48]). The applicant acknowledged that H2RAs may offer a lower level of gastroprotection but deemed the risk-benefit balance to be appropriate for the cohort in question. The Committee noted that a very low proportion of patients on steroids for ICI-toxicity would require ICU support and have accompanying risk factors (e.g. ventilation support, renal impairment) for gastrointestinal bleeds.

In terms of safety, Famotidine is generally considered to be a well-tolerated drug and has been widely used.

In terms of budget impact, the anticipated annual spend for famotidine is £4,200 to £12,600 for 200 patients per annum. However, the number of patients is expected to increase in the coming years due to the expanding use of ICIs across more tumour groups.

The committee heard from Dr Benafif who acknowledged limitations in the evidence base and the lack of relevant RCTs examining the effect of PPIs or H2RAs on therapeutic outcomes for patients receiving ICIs. However, separate retrospective gut microbiome studies have suggested an impact on ICI treatment outcomes with drugs that alter the gut microbiome, such as antibiotics. Although international societal guidelines have not been recently updated, the oncology community recognises the influence of the gut microbiome on immunotherapy response and the growing body of evidence on this topic. Dr Benafif informed the Committee that the application for famotidine was intended for patients treated with ICIs whilst they were on a course of high-dose steroids only. A small sub-group of patients at high-risk of developing gastric or duodenal ulceration or gastrointestinal symptoms may require longer term gastric protection thereafter. The Committee suggested

that this cohort should be switched back to a PPI for longer-term therapy after ICI treatment, due to the superior efficacy and cost-effectiveness. Patients who were on a PPI pre-ICI treatment would require individual risk-benefit consideration regarding a short-term switch to famotidine.

In camera, The Committee noted the limitations of the data and additional uncertainty regarding impact of H2RAs on ICI therapy outcomes. However, overall, taking into account the safety and cost and famotidine, it was considered reasonable to allow famotidine as a treatment option for gastroprotection in patients on high-dose steroids for immune checkpoint inhibitor toxicities. The Committee encouraged a review if further data emerges on the effects of H2RAs as a gastroprotective agent in this patient cohort.

In summary, the Committee approved the use of famotidine as a treatment option for gastroprotection in patients on high-dose steroids for immune checkpoint inhibitor toxicities. The Committee recommended that patients requiring ongoing gastroprotection post ICI/steroid treatment, due to other gastrointestinal risk factors, should be switched to a PPI for longer term prescribing.

Drug: Famotidine; 20mg once daily up to 40mg twice daily
Indication: For gastroprotection in patients while on high-dose steroids for immune checkpoint inhibitor toxicities (≥ Grade 2)
Decision: Approved
Prescribing status: Secondary care only
Funding source: In tariff
Fact sheet or shared care required: No
Additional information: N/A

9.2. Famotidine for gastro-oesophageal reflux disorder (Applicant: Dr Sheena Mankodi; NMUH)

The Committee considered an application *in absentia* for famotidine 20-40mg twice daily, a H2 receptor antagonist (H2RA), for off-label use in patients with gastro-oesophageal reflux disease (GORD) i) intolerant to proton pump inhibitors (PPIs) or ii) requiring combination treatment with PPIs as symptoms are not controlled with PPIs alone.

Following the ranitidine shortage in 2019, the JFC issued a position statement outlining the indications where it was appropriate to switch patients to PPIs. The Committee were informed that although this application requests the use of famotidine for one of the indications covered by the position statement (GORD), there are several other indications for which similar criteria may be applicable.

The Committee noted that NICE Guideline CG184 (2019), recommends the use of PPIs ahead of H2RAs in patients with GORD.

The Committee considered the comparative evidence for efficacy of H2RAs, noting that ranitidine was previously on the formulary for GORD. McCullough et al (1996; n =980) was a double-blind, randomised, active-controlled trial comparing the efficacy of famotidine with ranitidine in patients with active duodenal ulcer disease. Patients were randomised to famotidine 20mg twice daily, famotidine 40mg twice daily, famotidine 40mg once daily or ranitidine 150mg twice daily. The primary end point, duodenal ulcer healing rate, was not statistically significantly different across the different arms (famotidine 20mg twice daily (92%), famotidine 40mg twice daily (92%), famotidine 40mg once daily (87%) or ranitidine 150mg twice daily (90%)). The Committee noted that the total daily dose and administration in divided doses (are likely to be more important determinants of efficacy than the choice of H2-antagonist (Drugs and Therapeutics Bulletin review, 1996).

For patients requiring combination therapy with a PPI and a H2RA, NICE Guidelines CG184 (2019) do not mention combination therapy for patients with GORD. The BMJ Best Practice guideline for GORD (2024) recommends the use of combination therapy in patients with an incomplete response to PPIs if they have GORD with a nocturnal component. Wang et al (2009; n=274) reported a Cochrane review of 8 randomised controlled trials comparing the efficacy of PPIs in combination with H2RAs to placebo or PPI monotherapy in patients with nocturnal gastric acid breakthrough. The review reported that additional bedtime H2RA in combination with a PPI can decrease the prevalence rate of nocturnal gastric acid breakthrough (RR: 0.48 (95% CI: 0.3 – 0.75), $p<0.05$). However, the authors reported that this was based on low-quality evidence with a lack of long-term efficacy data and the safety profile was not reported. The authors therefore concluded that the use of combination therapy should be used in a research setting only.

In terms of cost, famotidine is significantly more expensive than omeprazole (£42-£84 per patient per month versus £1-2 respectively) but is currently the most cost-effective H2RA. The Committee noted it was challenging to determine an NCL-wide budget impact as the estimated patient numbers that would be initiated on famotidine for GORD had not been received from all Trusts, the budget impact of extending the use of famotidine to other indications was unknown and the proportion of patients currently already prescribed famotidine where PPIs are inadequate/unsuitable is unclear. In particular for the latter point, the current prescribing of famotidine in NCL (despite a highly restricted formulary position) was approximately £81,000 in secondary care and £1 million in primary care. The Committee noted that famotidine prescriptions currently represented 40% of the pre-ranitidine shortage usage of H2RAs but at 5 times greater spend due to the significantly higher cost of famotidine compared to ranitidine.

In summary, the Committee agreed that given the potential applicability of the same H2RA prescribing criteria to several other indications, and the associated high cost pressure associated with famotidine, it was not appropriate to consider the use of famotidine for GORD in isolation. Primary care members noted that cost improvement schemes for H2RA prescribing were under consideration, and welcomed a review of criteria for appropriate H2RA prescribing across a broader range of indications. Therefore, the Committee deferred a decision on the use of famotidine for the treatment of GORD, pending a consultation on patient selection criteria for indications for which PPIs are currently used (as per previous JFC position statement) where H2RAs may be suitable as i) PPIs are not tolerated or ii) dual therapy with a PPI + H2RA is required following an insufficient response to PPIs alone. The Committee agreed that:

i. The proposed initiation criteria for all potential indications would be circulated for NCL-wide consultation as an update to the 'Ranitidine Supply Disruption Position Statement'.
ii. A proposal for concise wording to be updated on NetFormulary should be included as part of the consultation.
iii. Due to comparable efficacy, the choice of H2RA in NCL should be based on lowest drug acquisition cost in primary care.

Drug: Famotidine
Indication: GORD in patients i) intolerant to PPIs or ii) requiring combination therapy with PPIs as a PPI alone is insufficient at controlling symptoms including patients with significant Barrett's disease
Decision: Deferred pending an update of the 'Ranitidine Supply Disruption Position Statement' and tighter decision on place in therapy and patient selection criteria through NCL-wide consultation for all potential indications for which PPIs are currently used and H2RAs may be suitable in patients in whom i) PPIs are not tolerated or ii) dual therapy with a PPI + H2RA is required following an insufficient response to PPIs alone.

10. Position Statements and Guidelines

10.1. High Cost Drug Rheumatoid Arthritis Pathway: Update

The Committee approved an update to the NCL High Cost Drug Pathway for Rheumatoid Arthritis to incorporate the following changes:

- Subcutaneous tocilizumab biosimilar (Tyenne®) was added to the pathway as the preferred subcutaneous IL-6 inhibitor in line with NCL commissioning principles. The Committee noted that there is currently a supply constraint with tocilizumab biosimilar (Tyenne®), so this new pathway will not be implemented until the supply constraint has been resolved.

11. NHSE Updates

11.1. NHSE Specialised Commissioning NICE Appraisals Update

The Committee noted an NHSE Circular (SSC2660) providing an update on Specialised Commissioning from June 2024. This was included for information only.

12. Next meeting

Thursday 15th August 2024

13. Any other business

Nil