Joint Formulary Committee (JFC): Minutes

Minutes from the meeting held on 16th November 2023

		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	✓	
Ms H Bouattia	RFL, Formulary Pharmacist		✓
Mr A Barron	UCLH, Principal Pharmacist	✓	
Mr S O'Callaghan	UCLH, Formulary Pharmacist	✓	
Ms R Allen	Commissioning Pharmacist, UCLH	✓	
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 H Muhammad	WH, Specialist Biologics and Homecare Pharmacist	✓	
Ms N Patel	NMUH, Formulary Pharmacist	✓	
Mr J Flor	WH, Finance, Business and Performance 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 C Weaver	Senior Prescribing Advisor, NCL ICB (Camden)	✓	
Mr A Fazal	Commissioning Pharmacist, RFL	✓	
Dr M Ehrenstein	Rheumatology Consultant, UCLH	✓	
Dr M Castelino	Rheumatology Consultant, UCLH	✓	
Dr P Harrow	Gastroenterology Consultant, UCLH	✓	
Dr C Murray	Gastroenterology Consultant, RFL	✓	
Ms N Taherzadeh	Principal Pharmacist, Gastroenterology & Nutrition, RFL	✓	
Ms J Toft	Specialist IBD Pharmacist, UCLH	✓	

2. Meeting attendees

Dr Subel 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 September and October meeting were ratified.

5. Matters arising

Nil

6. Review of action tracker

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

7. JFC outstanding items & work plan

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

8. Local DTC recommendations/minutes

DTC site	Month	Drug	Indication	JFC outcome
MEH	September 2023	Roclanda® (latanoprost + netarsudil) eye drops	Glaucoma	**Decision**: Approved **Prescribing**: Secondary care only **Tariff status**: In tariff **Funding**: Trust **Fact sheet or shared care required**: N/A **Additional information:** pending treatment pathway, financial considerations, guideline updates and monitoring/audit of use in practice.
UCLH	October 2023	Bortezomib, lenalidomide and dexamethasone (VLd) followed by lenalidomide and dexamethasone (Ld)	Maintenance as 1st line treatment for transplant ineligible patients	**Decision**: Not approved **Additional information:** was approved in Sept 2023, but NICE TA for DLd is now published therefore VLd/Ld will not be added to the formulary

UCLH	September 2023	Intratympanic dexamethasone	Sudden sensorineural hearing loss	**Decision**: Approved – UCLH only **Prescribing**: Secondary care only **Tariff status**: In tariff **Funding**: Trust **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

9. New medicine reviews

9.1 Principles for Commissioning high-cost drug pathways for ICB commissioned indications

The Committee reviewed the proposed changes to the document, which was previously approved in March 2023 by NCL JFC and subsequently by NCL IMOC. The Committee approved the following:

i) Removal of the requirement for anti-drug antibody (ADA) monitoring prior to initiating a second biosimilar anti-TNF for patients who experienced secondary loss-of-response to the first anti-TNF. The rationale for this was due to differences in the evidence base for ADA monitoring across different specialties (whereby ADA monitoring reflects clinical practice in gastroenterology but not rheumatology). Additionally, it was noted that the cost of anti-TNF biosimilars has significantly reduced and a trial of a second anti-TNF may prevent the use of other more expensive therapies. ADA monitoring may still be clinically appropriate, for example in gastroenterology, but would not be enforced as a commissioning principle.

ii) New principle to support the management of adverse drug reactions. This will be added to all pathways.

iii) Commissioning position on the concurrent use of biologic treatments for the same disease and for different diseases. This will be added to all pathways.

The document was approved and will be taken to the November NCL Integrated Medicines Optimisation Committee (IMOC) meeting for commissioning approval.

9.2 Ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-AxSpA)

The Committee reviewed the NCL pathway for Ankylosing Spondylitis (AS) and Non-radiographic Axial Spondyloarthritis (nr-axSpA) and supporting documents and discussed the following:

9.2.1 Secukinumab Dose Escalation

The Committee noted that the 'temporary' secukinumab dose escalation is not ideal and that RFL clinicians are pursuing an NCL FOC scheme application to support ongoing secukinumab dose escalation if a patient responds. This would need to be reviewed by NCL JFC and commissioners.

9.2.2 Subcutaneous Infliximab

The Committee approved the proposal to include SC infliximab as an alternative option to IV infliximab across the rheumatology (RA and AS) pathways. The rationale for this was because SC infliximab is licensed for RA and AS, is cheaper than IV infusions resulting in lower administration costs and reduces infusion clinic requirement. Additionally, it is approved for IBD pathways and will therefore provide consistency across pathways.

9.2.3 BSR Pregnancy & Breastfeeding Recommendations

The Committee also noted that certolizumab was previously the preferred option for pre-conception/pregnancy. However, the pathways now reflect the updated guidance from the British Society for Rheumatology (BSR) which outlines continuation and stopping recommendations for all TNF inhibitors during pregnancy and breastfeeding including certolizumab. The Committee approved these updates. The UCLH Rheumatology team added their support for the BSR guidance, and noted that further work may be required by clinical teams in collaboration with obstetrics and pregnant patients to support implementation of the guidance into practice, including consideration of implications for childhood vaccination.

In summary, the Committee approved the NCL pathway for Ankylosing Spondylitis (AS) and Non-radiographic Axial Spondyloarthritis (nr-axSpA). This will be taken to the November NCL Integrated Medicines Optimisation Committee (IMOC) meeting for commissioning approval. The Committee also recommended that NCL pre-biologic pathways for the rheumatology pathways (RA and AS) should be developed to support appropriate use of high cost drugs.

9.3 Rheumatoid arthritis (RA)

The Committee reviewed the NCL pathway for Rheumatoid Arthritis (RA) and supporting documents and discussed the following:

9.3.1 Delayed Rituximab During COVID-19 Pandemic

In October 2021, the Committee extended the interim approval for biosimilar rituximab to be paused or delayed during the COVID-19 pandemic, with alternative agents made available for second-line use. The Committee noted that: i) COVID-19 is no longer in the pandemic stage, ii) the observational studies assessed by JFC in October 2021 reflect risk data from before the availability of COVID-19 vaccinations and COVID-19 treatments, iii) NICE TAs published since COVID-19 still specify eligibility or ineligibility based on 2nd -line rituximab use (e.g. TA676) and assess cost-effectiveness on this basis and iv) NICE NG167 COVID-19 rapid guideline has been withdrawn. Based on the above rationale, the Committee approved the withdrawal of the interim decision to allow delayed use of biosimilar rituximab in rheumatoid arthritis during the COVID-19 pandemic and agreed that rituximab should be the preferred 2nd-line option in the RA pathway as per NICE.

Prof Ehrenstein stated that he would like the option to avoid rituximab in exceptional patients with low immunoglobulin levels or who cannot receive COVID-19 vaccinations and that these would be considered contra-indications to rituximab within the pathway.

In summary, the Committee:

i) Approved the withdrawal of the interim decision to allow delayed use of biosimilar rituximab in rheumatoid arthritis during the COVID-19 pandemic and agreed that rituximab should be the preferred 2nd-line option in the RA pathway as per NICE.
ii) Approved the proposal to grant long-term approval for SC infliximab as an alternative option to IV infliximab across the rheumatology (RA and AS) pathways as discussed in item 9.2.2.
iii) Approved inclusion of the updated guidance from the BSR (2022) regarding pregnancy and breastfeeding advice with TNF-inhibitors as discussed in item 9.2.3.
iv) Recommended that NCL pre-biologic pathways for the rheumatology pathways (RA and AS) should be developed to support appropriate use of high cost drugs.
v) Approved the NCL pathway for Rheumatoid Arthritis. This will be taken to the November NCL Integrated Medicines Optimisation Committee (IMOC) meeting for commissioning approval.

9.4 Ulcerative colitis (UC)

The Committee reviewed the NCL pathway for Ulcerative colitis (UC) and supporting documents and discussed the following:

9.4.1 Definition of Conventional Treatment prior to Biologics

The Committee approved a change in the criteria for conventional treatments required prior to biologics from 'corticosteroids and thiopurines' to 'corticosteroids or thiopurines'. The rationale for this was: i) to bring this in line with the NCL CD pathway, ii) Recognition that newer NICE TAs do not specify the requirement for both corticosteroids and thiopurines (e.g. NICE TA 342) and iii) NICE and BSG guidelines are supportive of the term 'or' despite lack of clarity from ECCO guidelines.

Dr Harrow stated that other drivers to support this are the significant reduction in cost of TNF-inhibitors and that evidence suggests patients are more likely to achieve clinical remission with anti-TNFs compared to thiopurines. Earlier disease control leads to better long-term outcomes. Dr Harrow noted that this will not be a change from real-world clinical practice as there has been a significant reduction in thiopurine use over recent years.

The Committee requested development of a pre-biologic pathway to clarify conventional treatment options and support appropriate use of high-cost drugs within the pathway. The UCLH and RFL clinical team agreed that this could be supported.

9.4.2 Exclusion of Ciclosporin from Pathway

The Committee acknowledged that NICE TA 163 recommends infliximab in patients in whom ciclosporin is contraindicated or clinically inappropriate. However, clinical practice has changed and ciclosporin is not routinely offered because of its adverse effect profile and the significant reduction in cost of infliximab given the availability of biosimilars. Therefore, the Committee approved the proposal to exclude ciclosporin (NICE TA 163) from the UC treatment pathway.

9.4.3 Upadacitinib after Failure on Filgotinib or Tofacitinib

The Committee reviewed a proposal to initiate upadacitinib (UPA; a JAK-1 inhibitor) in patients who have experienced primary or secondary failure on filgotinib (FIL; a JAK-1 inhibitor) or tofacitinib (TOF; a JAK-1 and -3 inhibitor).

In April 2023, the JFC approved the use of UPA in preference to FIL for the induction and maintenance of UC in a second-line setting in a restricted cohort of patients at high-risk of severe disease and colectomy. This was based on indirect comparisons made from network meta-analyses (NMAs) reporting the superiority of UPA 45mg daily compared to FIL 200mg daily at inducing clinical remission and endoscopic improvement. For the maintenance of remission, the superiority of UPA 30mg daily was uncertain as it was significantly superior than FIL 200mg daily at maintaining endoscopic improvement but not clinical remission. UPA 15mg daily was not significantly superior to FIL 200mg daily for maintaining endoscopic improvement or clinical remission.

The Committee noted that although UPA appears to be superior to FIL/TOF from the indirect comparison, there is uncertainty regarding the potential sub-optimal dosing of FIL/TOF in the induction phase. As all three medicines are JAK-inhibitors, the response would be expected to be similar, however this was not observed in the NMAs. The Committee considered that a potential reason for this may be that the licensed dose of FIL/TOF is sub-optimal compared to the licensed induction dose of UPA.

The Committee noted that there was no published evidence to support the use of UPA after FIL.In terms of the evidence base to support the use of UPA after TOF, the Committee noted the evidence was limited to 5 studies (2 prospective observational studies and 3 retrospective case series). These included patients with UC after failure/exposure to TOF (n=3-18) who were administered UPA with no comparator arm. The outcomes assessed across most of the studies were: i) clinical remission (20 – 100%, although majority of the studies ranged from 60-100%), ii) clinical response (60 – 100%) and iii) steroid-free remission (40 – 100%). The main limitations of these studies were that 4 of the studies were abstracts only, 3 of the studies had a retrospective study design, the studies included small patient numbers, long-term data was not available and outcomes reported were for incomplete datasets. Additionally, there were concerns of selective reporting as majority of the studies reported clinical remission rates of 60-100% which were much greater than the clinical remission rates reported in the pivotal phase 3 clinical trials for UPA (26-33%).

In terms of convenience, the oral JAK-inhibitors provide improved patient convenience compared to injectable therapies (the next mechanism of action).

In terms of cost, a full budget impact analysis was not conducted due to the complexity of the model. If UPA was effective in this cohort (for which the evidence base is limited), it would delay the requirement for more expensive injectable biologics (the next mechanism of action). However, access to a second JAK-inhibitor may increase the overall pathway budget impact.

Dr Harrow acknowledged the limited evidence base to date and stated he has recently submitted an abstract (n=99) to ECCO reporting a multi-centre retrospective cohort study whereby 60% of patients were induced in remission following the use of a second JAK-inhibitor. The Committee asked whether the cohort who are most likely to benefit from UPA could be defined, but Dr Harrow noted this could not yet be determined from the current evidence base. Dr Harrow expressed concerns about restricting access to UPA as a first-line JAK-inhibitor despite acknowledging a degree of superiority over other JAK-inhibitors and therefore suggested access to UPA should be allowed if an inferior JAK-inhibitor treatment does not work.

Ms Toft and Ms Taherzadeh stated that they have treated patients with UPA following FIL/TOF with positive outcomes, and these patients have been included in the abstract submitted to ECCO.

In camera, the Committee heard that the recently submitted ECCO abstract had not been available for the evidence review. The Committee noted that a full review of methodology and results would be required (which would not be possible from an abstract alone) to assess the impact of the results and exclude the risk that similar limitations were applicable as per the other evidence reviewed. The Committee agreed that there was a lack of convincing evidence to support the use of UPA after FIL/TOF failure but that there was a theoretical basis for allowing UPA to be used after primary failure of FIL/TOF, where potency of dosing is a more significant factor for treatment success. This would be assessed at the 12-16 week assessment point. Based on the limited evidence base currently available, secondary failure to JAKi would warrant moving to a different mechanism of action.

The Committee decided on the basis of a vote to approve the use of UPA after primary failure of FIL/TOF only.

In summary, the Committee approved:

i) The criteria of conventional treatments required prior to biologics to change from 'corticosteroids and thiopurines' to 'corticosteroids or thiopurines'.
ii) The proposal to exclude ciclosporin (NICE TA 163) from the UC treatment pathway.
iii) The use of UPA after primary failure of FIL/TOF only.
iv) The recommendation to develop an NCL pre-biologic pathway for the gastroenterology pathways (UC and CD) to clarify conventional treatment options and ensure appropriate use of high cost drugs.
v) The NCL pathway for Ulcerative Colitis. This will be taken to the November NCL Integrated Medicines Optimisation Committee (IMOC) meeting for commissioning approval.

9.5 Crohn's Disease (CD)

The Committee reviewed the NCL pathway for Crohn's Disease (CD) and supporting documents and discussed the following:

9.5.1 Dose Escalation in Fistulising Crohn's Disease

The Committee noted the advice on dose escalation of anti-TNFs applies equally to moderate to severe Crohn'sdisease as it does to fistulising Crohn's disease. The requirement to assess response at 12-16 weeks is retained, but there is no requirement to drop back to the standard dose of anti-TNF after dose escalation. The original requirement in the pathway was not evidence-based, but rather a negotiated position between providers and commissioners in 2017 when anti-TNF costs were high. The Committee acknowledged that dosing guided by therapeutic drug monitoring is in the patient's best interest.

9.5.2 Pre-biologic treatment in fistulising Crohn's Disease

The Committee noted that pre-treatment with azathioprine/mercaptopurine (6-MP/AZA) is not required in patients with fistulising Crohn's disease. This recommendation is based on the ECCO guidelines 2019 (recommendation 3.7) advising against the use of thiopurine monotherapy for fistula closure in patients with CD and complex perianal fistulae.

9.5.3 Treatment Options for Fistulising Crohn's Disease

The Committee considered the evidence base for the efficacy of upadacitinib (UPA), vedolizumab (VDZ) and risankizumab (RZB) for treating fistulising Crohn's disease. U-EXCEL and U-EXCEED were the phase 3 induction trials for UPA (45mg OD) vs placebo (PBO) for 12 weeks. Patients who achieved clinical response after 12 weeks of induction were eligible for U-ENDURE, the maintenance study where patients received UPA 30mg, 15mg or PBO for 52 weeks. Colombel et. al is a poster presentation/abstract assessing rates of fistulas and fistula improvement with UPA in patients who had fistulas or fissures at baseline in the phase 3 induction and maintenance trials. 143 patients had fistulas and 54 had perianal fistures at baseline. Among patients with Crohn's disease complicated with fistulas and/or fissures at baseline, UPA treatment led to higher rates of external closure of fistula openings, resolution of draining, and healing of fissures, along with clinical remission and improvements in luminal disease compared with PBO.

Feagan et. al is a report of exploratory data analysis from the GEMINI 2 (pivotal) trial for VDZ. 461 responders to 6-week VDZ induction therapy received maintenance placebo [VDZ/PBO, N = 153] or VDZ [VDZ/VDZ, N = 308]. Fistula closure rates were assessed at weeks 14 and 52, and the time to fistula closure was analysed. 33% of patients had a history of fistulising disease and 12% had ≥1 active draining fistula at entry into the maintenance period. Patients who received VDZ/VDZ had greater fistula closure compared to VDZ/PBO (week 14; 28% vs. 11%; ARR: 17.1%, 95% CI -11.4 to 43.9, week 52; 31% vs. 11%; ARR: 19.7%, 95% CI -8.9 to 46.2). Patients who continued treatment with VDZ were more likely to have fistula closure by week 52 than those who received placebo (HR 2.54, 95% CI, 0.54 to 11.96).

The data for the use of RZB in patients with active fistulising disease is limited to the phase 3 induction trials (ADVANCE; n=911, MOTIVATE; n =618). Among patients with draining fistulas at baseline (ADVANCE; n=27, MOTIVATE; n=29), the absence of draining fistulas at week 12 was assessed as a secondary endpoint. There was no significant difference between PBO and RZB in patients with no draining fistulas at week 12 (ADVANCE; 22.2, 95% CI: 0 to 49.4 vs. 27.8, 95% CI: 7.1 to 48.5, MOTIVATE; 13.3, 95% CI: 0 to 30.5 vs. 7.1, 95% CI: 0 to 20.6). The Committee agreed that there is insufficient data to support the use of risankizumab in patients with fistulising active Crohn's disease.

In summary, the Committee acknowledged that although the data is limited, there is some evidence to support the efficacy of upadacitinib and vedolizumab in treating fistulising Crohn's disease. The Committee agreed that there is insufficient data to support the use of risankizumab in patients with fistulising active CD.

In summary, the Committee:

i) Agreed that dose escalation of anti-TNFs applies equally to moderate to severe Crohn's disease as it does to fistulising CD.
ii) Agreed that pre-treatment with azathioprine/mercaptopurine (6-MP/AZA) is not required in patients with fistulising CD.
iii) Approved the use of upadacitinib and vedolizumab to treat fistulising CD.
iv) Did not approve the use of risankizumab for patients with fistulising active CD.
v) Recommended development if an NCL pre-biologic pathway for the gastroenterology pathways (UC and CD) to clarify conventional treatment options and ensure appropriate use of high cost drugs.
vi) Approved the NCL pathway for Crohn's Disease. This will be taken to the November NCL Integrated Medicines Optimisation Committee (IMOC) meeting for commissioning approval.

10. Next meeting

Thursday 18th January 2024

11. Any other business

Ms Weaver informed the Committee that she will circulate a new NHSE Specialised Commissioning monthly summary letter which notifies Trusts of new medicines, and request feedback at January JFC on whether this would be useful to include as a regular item on the JFC agenda.