Joint Formulary Committee (JFC): Minutes

Minutes from the meeting held on 16th January 2025

		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 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 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		✓
Ms EY Cheung	NCL ICB, Head of Quality and Improvement	✓	
Ms K Petrou	NCL ICB, Community Pharmacy Clinical Lead		✓
Dr S Ghosh	Enfield Unity PCN, Clinical Director; Enfield GP Federation, Co-Chair	✓	
Dr D Heaney	UCLH, Consultant Neurologist		✓
Mr S Jenkinson	RFL, Lead Pharmacist Cancer Services		✓
Attendees			
Ms C Tse	IPMO Programme Team, JFC Principal Pharmacist	✓	
Ms S Amin	IPMO Programme Team, Lead Pharmacist	✓	
Ms K Leung	IPMO Programme Team, JFC Senior Pharmacist	✓	
Ms M Darjee	IPMO Programme Team, JFC Senior Pharmacist	✓	
Ms M Butt	IPMO Programme Team, Director	✓	
Ms I Samuel	RFL, Formulary Pharmacist	✓	
Mr H Shahbakhti	RFL, Formulary Pharmacist	✓	
Ms J Peralta	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 W Li	MEH, Formulary Pharmacist	✓	
Ms J Bloom	MEH, Associate Chief Pharmacist	✓	
Ms A Bathia	RNOH, Formulary Pharmacist	✓	

Ms S Ahmed	WH, Formulary Pharmacist		✓
Ms S Shah	NMUH, Formulary Pharmacist	✓	
M A Sehmi	NMUH, Formulary Pharmacist		✓
Ms Y Lam	UCLH, Formulary Pharmacist		✓
Ms M Thacker	GOSH, Deputy Chief Pharmacist	✓	
Mr J Modha	NHSE, Specialised Commissioning Pharmacist		✓
Mr J Flor	WH, Lead Pharmacist	✓	
Ms R Allen	UCLH, Commissioning Pharmacist		✓
Mr A Fazal	RFL, Principal Pharmacist		✓
Mr G Grewal	RFL, Deputy Chief Pharmacist		✓
Ms J Collins	WH, Rotational Pharmacist	✓	
Ms C Weaver	NCL ICB, Senior Prescribing Advisor – Quality and Improvement	✓	
Ms N Patel	NCL ICB, Senior Prescribing Advisor – High-Cost Drugs	✓	
Ms H Shah	NCL ICB, Senior Prescribing Advisor	✓	
Ms J Pang	IPMO Programme Team, Lead Pharmacist		✓
Dr R Maclean	Clinical Pharmacology Registrar	✓	
Ms A Khanom	RFL, Formulary Pharmacist	✓	
Ms M Patel	RNOH, Principal Pharmacist	✓	
Mr G Purohit	Deputy Chief Pharmacist (RNOH)	✓	
Dr S McBride	Consultant Dermatologist (RFL)	✓	
Ms O Odejide	NCL ICB, Prescribing Pharmacist – Quality and Improvement	✓	
Dr T Mahendrayogam	Consultant Anaesthetist (WH)	✓	
Dr R Zarnegar	Consultant Anaesthetist (RNOH)	✓	
M A Farook	NCL ICB, Prescribing Support Pharmacist (Observer)	✓	
Ms S Shah	RFL, Cancer Service Pharmacist (Observer)	✓	
Ms M Devani	UCL Medical Student (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 declared by members or attendees present.

4. Minutes and abbreviated minutes of meetings on 21st November

Minutes and abbreviated minutes of the November 2024 was deferred.

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 Tse.

7. Local DTC recommendations/minutes

Date	Drug and Indication	DTC Decision and Details	JFC recommendation
January 2025	Parecoxib for the short-term management of acute pain (post-operative)	**Reviewed by**: RNOH **Drug**: Parecoxib; IM or IV initially 40mg, then 20-40mg every 6-12 hours as required for up to 3 days (maximum 80mg per day) **Indication**: Short-term management of acute pain (post-operative) **Decision**: Approved	**To add to the NCL Joint Formulary**

		Prescribing status: Secondary care, hospital prescribing only **Funding source**: In tariff **Additional information**: N/A **Fact sheet or Shared Care required**: N/A	
October 2024	Tofacitinib (Xeljanz®) for pansclerotic morphoea	**Reviewed by:** RFL **Drug:** Tofacitinib, 5mg BD **Indication:** Pansclerotic morphoea **Decision:** Approved **Prescribing status:** Divisional budget **Funding source:** Internally divisionally funded **Additional information:** Provide DTC update in 6-months' time with clinical efficacy and safety feedback. Provide update on national clinical commissioning policy application progress. **Fact sheet or Shared Care required:** N/A	**Approved for RFL only**
February 2019	Lidocaine infusion for neonatal seizures (preservative-free injection only)	**Reviewed by**: UCLH **Drug**: Lidocaine infusion (preservative-free injections only) **Indication**: Neonatal seizures **Decision**: Approved **Prescribing status**: Secondary care, hospital prescribing only **Funding source**: In tariff **Additional information**: N/A **Fact sheet or Shared Care required**: N/A	**To add to the NCL Joint Formulary**
January 2025	Pyridoxine for neonatal seizures	**Reviewed by**: UCLH **Drug**: Pyridoxine **Indication**: Neonatal seizures **Decision**: JFC approved in line with UCLH Trust Guidelines **Prescribing status**: Secondary care, hospital prescribing only **Funding source**: In tariff **Additional information**: N/A **Fact sheet or Shared Care required**: N/A	**To add to the NCL Joint Formulary**
March 2022	Botulinum toxin A (Botox®) to aid closure of abdominal wall hernia	**Reviewed by:** UCLH **Drug:** Botulinum toxin A (Botox®) **Indication:** To aid closure of abdominal wall hernia **Decision:** Approved **Prescribing status:** Restricted to secondary care only **Funding source:** In tariff **Additional information:** N/A **Fact sheet or Shared Care required:** N/A	**To add to the NCL Joint Formulary**
November 2024	Eurartesim® (artenimol + piperaquine) for first-line treatment of non-severe falciparum malaria	**Reviewed by:** UCLH **Drug:** Eurartesim® (artenimol + piperaquine) **Indication:** First-line treatment of non-severe falciparum malaria in patients returning from countries with evidence of >10% artemisinin combination therapy (ACT) treatment failure as per WHO recommendations **Decision:** Approved **Prescribing status:** Restricted to secondary care only **Funding source:** In tariff **Additional information:** N/A **Fact sheet or Shared Care required:** N/A	**To add to the NCL Joint Formulary**

November 2024	[FOC Scheme] Vorasidenib for IDH mutant grade 2 oligodendroglioma or astrocytoma*†	**Drug:** Vorasidenib tablets (unlicensed): 40mg once daily, continued until disease progression requiring treatment or grade 4 toxicity **Indication:** Adult patients (≥18yrs) with residual or recurrent IDH mutant low grade glioma, oligodendroglioma or astrocytoma, with measurable non-enhancing disease, who have had surgery (biopsy, sub-total resection or gross total resection), who have adequate performance status (Karnofsky PS≥80), hepatic and renal function, no previous chemotherapy, are appropriate candidates for active surveillance and not in immediate need of chemotherapy or radiotherapy as determined by the NHNN neurology service **Decision:** Approved pending assurances on service delivery model, impact assessment and risk mitigation **Prescribing status:** Restricted to secondary only **Funding source:** Free of Charge Scheme **Additional information:** N/A **Fact sheet or Shared Care required:** N/A	**Conditionally approved for UCLH only**
December 2024	Rezafungin for the treatment of candidaemia or invasive candidiasis	**Reviewed by:** UCLH **Drug:** Rezafungin **Indication:** Treatment of candidaemia or invasive candidiasis. Restricted to outpatient use only in patients who require ongoing echinocandin antifungal therapy on the advice of ID or microbiology, and where an oral antifungal product is unsuitable **Decision:** Approved **Prescribing status:** Restricted to secondary care only **Funding source:** In tariff **Additional information:** N/A **Fact sheet or Shared Care required:** N/A	**To add to the NCL Joint Formulary**
December 2024	[FOC Scheme] Capivasertib plus fulvestrant for locally advanced or metastatic breast cancer*†	**Reviewed by:** UCLH **Drug:** Capivasertib plus fulvestrant **Indication:** Relapsed/refractory hormone receptor (HR) positive, human epidermal growth factor 2 (HER2) negative locally advanced or metastatic breast cancer with PIK3CA alterations **Decision:** Approved **Prescribing status:** Restricted to secondary care only **Funding source:** FOC scheme **Additional information:** N/A **Fact sheet or Shared Care required:** N/A **Reviewed by:** UCLH **Drug:** Capivasertib plus fulvestrant **Indication:** Relapsed/refractory Hormone Receptor (HR) Positive, Human Epidermal Growth Factor 2 (HER2) Negative Locally Advanced or Metastatic Breast Cancer with AKT1 or PTEN alterations **Decision:** Not approved	**To add to the NCL Joint Formulary** **Not approved**

*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 Ustekinumab Dose Escalation (Applicant: Dr S McBride, UCLH)

The Committee considered an application to include ustekinumab dose escalation prior to switching to an alternative 2nd line biologic for the treatment of moderate to severe psoriasis. Ustekinumab is an established treatment option for psoriasis, which suppresses IL-12– and IL-23–mediated inflammation associated with psoriasis. The licensed dose is weight dependent. For patients weighing less than 100kg ustekinumab is dosed as 45mg on week 0 and week 4, then 45mg 12 weekly. For patients weighing over 100kg, ustekinumab is dosed as 90mg on week 0 and week 4, then 90mg 12 weekly. At week 16 assessment, patients who have achieved a 75% reduction in their Psoriasis Area and Severity Index (PASI) score from baseline will continue with the licensed maintenance dose.

The committee considered a new proposal that patients with an inadequate response (i.e., those achieving 50% reduction in their PASI score and a 5-point reduction in DLQI score with ongoing significant disease burden) to ustekinumab at 16 weeks patients weighing more than 100kg, should be eligible for a dose escalation to 90mg every 8 weeks. For patients with an inadequate response who weigh less than 100kg, the proposed dose escalation is to increase the dose to 90mg every 12 weeks initially. Dose intensification to 90mg 8 weekly would be offered if after a second 16-week assessment (i.e. at week 52 after initiation) good disease control is achieved but patients report symptoms reappearing prior to the next dose administration.

The committee considered statements from the American Academy of Dermatology National Psoriasis Foundation (AAD-NSF) 2019, which recommends an alternative dosing regimen for ustekinumab by increasing the frequency of injection to every 8 weeks during the maintenance phase) for patients showing a partial response to treatment prior to changing treatment to an alternative biologic. This is also supported by the European (EuroGuiDerm) 2020 guidance which recommends modifying treatment by either increasing the dose or reducing dose interval for patient who achieve a PASI score ≥ 50 or ≤ 75, and a DLQI > 5. Additionally, the British Association of Dermatologist (BAD) rapid review 2020 recommends escalating the dose of or reducing the interval for biologic therapy in adults when an inadequate primary response is achieved.

The committee considered evidence from the PHOENIX II trial (Papp et al, 2008), which was a multicentre, phase III, double-blind, placebo-controlled study which investigated the efficacy and safety of dose intensification at week 28 to week 52. A re-randomisation phase (n=159) assessed the response of dose escalation in participants who partially responded (identified by achieving PASI ≥ 50% but <75% improvement at week 28) to the standard dose of ustekinumab. The participants were re-randomised to receive ustekinumab 45mg 12 weekly (n=48), 45mg 8 weekly (n=45), 90mg 12 weekly (n=33) or 90mg 8 weekly (n=32). The secondary end point was the number of visits with PASI 75 response between weeks 40 to 52 in the group of participants receiving the drug every 8 weekly versus every 12 weekly. The dose intensification in partial responders receiving ustekinumab 90 mg resulted in a greater number of visits with PASI 75 response (mean 2·63 visits versus 1·58 visits; p=0·014) and higher PASI 75 response rate (22 [68·8%] patients with dosing every 8 weeks versus 11 [33·3%] patients with dosing every 12 weeks. A limitation of this phase of the study was that the dosing was not based on participant's weight, however it was stated 70% of participants weighed <100kg.

An observational analysis of registry data conducted by Svedbom et al showed that the prevalence of discontinuation of treatment the in ustekinumab group was much lower in comparison to adalimumab and etanercept whereby less than 10 % of patients discontinued treatment a year after starting ustekinumab. Furthermore, patients remained on escalated dose of ustekinumab for more than 5 years. However, this analysis had its limitations as the data collection was observational, and conducted over a long period of time over which there might have been potential changes in practice. At the time, ustekinumab was the most recently approved biologic treatment for psoriasis and due to limited experience, it might have been used as last line of therapy.

The European Medicines Agency (EMA) released a report on ustekinumab which supported that the higher serum concentration of drug, the higher the percentage of patients achieving PASI 75 or PASI 90. However, in practice trough levels of ustekinumab are not measured as the therapeutic trough levels for psoriasis have not yet been established.

In terms of safety, the PHOENIX II trial reported no additional adverse drug events associated with the dose intensification. During the dose escalation phase, 2/77 patients in the 8-weekly dosing group (without specified dose) reported malignancies. Additionally, 2/77 patients in this group experienced serious adverse events (AEs). In the 12-weekly dosing group (without specified dose), 1/81 patients had a serious infection, and 6

experienced serious AEs. This suggests that the frequency of adverse events, including serious events, were similar between the standard dose group and the intensified dosing regimen group.

The availability of ustekinumab means the cost implication of dose escalation is small. Increasing the dose from 45mg to 90mg every 12 weeks results in no additional cost *per se*. However, increasing the dosing frequency to every 8 weeks incurs an additional cost of £1,147 per patient per annum. Assuming the dose escalation protocol is effective in all eligible patients, there is an estimated cost avoidance of £37,857 per year 1 for the projected number of patients eligible for dose escalation, realised from the avoidance of more expensive next in line agents.

The Committee heard from Dr McBride that there is a view among specialists that the earlier dosing regimen results in underdosing of many patients. Reduced efficacy of ustekinumab has been demonstrated in patients weighing >90kg. Dr McBride agreed the evidence from the PHOENIX trial supported dose intensification in patients receiving 90mg has greater benefits than at the 45mg dose.

In camera, the Committee agreed that having the option of a dose escalation is clinically beneficial for patients, it does not pose additional risk to patient safety and is financially appropriate.

In summary, The Committee agreed that despite the lack of direct clinical evidence supporting the proposal for ustekinumab dose escalation, it appears sensible and safe to exhaust dosing options for ustekinumab prior to switching to a treatment with an alternative mode of action. The Committee approved the addition of ustekinumab dose escalation in the psoriasis pathway for the treatment of moderate to severe psoriasis.

Drug: Ustekinumab 45mg and 90mg subcutaneous injections (unlicensed), weight <100kg - 90mg every 12 weekly and/or 90mg every 8 weekly, weight >100kg – 90mg every 8 weekly)
Indication: Moderate to severe psoriasis
Decision: Approved
Prescribing status: Restricted to secondary care only
Funding source: ICB-commissioned High-Cost Drug
Additional information: N/A

9.2 Nefopam for acute and pharmacotherapy-resistant chronic pain (Applicant: Dr R Zarnegar, RNOH)

The Committee considered an application for nefopam, a licensed non-opioid analgesic with an uncertain mechanism of action for:

- The treatment of post-operative pain in those intolerant of opioids, and
- The treatment of pharmacotherapy-resistant chronic pain.

The Committee were informed nefopam is already prescribed without restrictions by RFL and NMUH based on historic inclusion on formularies. This application was brought for discussion at JFC following a request from RNOH to ratify this decision across all NCL Trusts and primary care.

i. Treatment of post-operative pain

In terms of efficacy for post-operative pain, the Committee considered Kakkar et al (2008), a Cochrane review of randomised, double-blind, placebo-controlled clinical trials of oral nefopam for relief of acute post-operative pain in adults. No studies were identified, and the authors concluded that "*in the absence of evidence of efficacy in acute post-operative pain, its use in this indication is not justified*".

ii. Treatment of pharmacotherapy-resistant chronic pain

Emery et al. (1986; n= 27) was a double-blind randomised placebo-controlled crossover trial in patients with rheumatoid arthritis who were already taking non-steroidal anti-inflammatory drugs (NSAIDs) at the maximal dose. The active comparator was nefopam 60mg three times a day versus placebo and the treatment time was 4 weeks with a 1-week washout period between treatment arms. The primary outcome was The Visual Analogue Score (VAS) for pain, nefopam was associated with improved pain symptoms compared to placebo (pain VAS -23mm versus +3mm). The study also investigated incidence of adverse events as a secondary outcome. Notably, 9 out of 27 patients experienced side effects including nausea, sweating, and insomnia with 5 patients withdrawing from the study due to significant adverse events. Key limitations of the study include the small study population, the placebo comparator group, high dropout rate due to adverse effects, and intention-to-treat (ITT) analysis was not reported.

Minotti et al (1989; n= 100), a double-blind randomised active comparator trial in cancer patients with moderate to severe chronic pain who were not on opioids, investigated the analgesic efficacy and toxicity of oral diclofenac versus nefopam versus aspirin and codeine. The study reported similar analgesic efficacy with

no significant difference in VAS difference reported between the three treatment arms. Discontinuation due to adverse events, a secondary outcome, patients receiving nefopam (n= 6) and aspirin with codeine (n= 6) had higher rates of discontinuation compared to diclofenac (n= 1). Limitations of the study include the short follow-up period and the high dropout rates due to adverse events and the deviation from routine practice in which cancer patients with pain are routinely prescribed opioid analgesia if pain is uncontrolled by other means.

Swinson et al (1988; n= 25), a double-blind, placebo-controlled non-randomised crossover trial in patients with rheumatoid arthritis who were receiving treatment with NSAIDs, investigated the analgesic efficacy of nefopam. The study reported no significant difference in pain VAS, however, there was significant dropout in the nefopam arm due to adverse events (40% versus 20%). The authors concluded that study was "marred by high dropout rate" and terminated early due to "*such poor toleration*" indicating the "*side effect profile* [of nefopam] *makes it an unsuitable analgesic for routine use*".

In terms of safety, nefopam was noted to have potential for abuse due to its psychostimulant-like effects. Case reports have also detailed patients experiencing depressive symptoms when attempting withdrawal following nefopam abuse (Villier et al., 2002). The Committee were informed that TOXBASE classifies nefopam as "potentially very toxic". It was also highlighted that an article published by the NHS Specialist Pharmacist Service (SPS) stated "nefopam appears no more potent than NSAIDs but is commonly associated with adverse drug reactions and is toxic in overdose". The product license lists symptoms of nefopam overdose such as coma, convulsions, hallucinations, agitation, and tachycardia with a hyperdynamic circulation. Additionally, the Committee were informed of drug-drug interactions with tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs) which may result in additive risk of anticholinergic effects and severe hypertension, respectively.

In terms of budget impact, it is estimated that the addition of nefopam to the NCL Joint Formulary would cost approximately £1000 per annum for 20 patients (10 patients with post-operative pain, and 10 patients with chronic pain).

The Committee heard from Dr Zarnegar that the cohort of patients seen at RNOH are highly complex given the nature of patients treated at the tertiary centre. From experience, many patients have tried other analgesics without success, or are keen to stop or reduce their opioid burden. Dr Zarnegar also emphasised the strict initiation criteria for nefopam to mitigate its adverse effects, acknowledging that only a small cohort of patients will be initiated on nefopam.

In camera, the Committee noted the lack of evidence of unmet need (i.e. a subgroup of patients who are opioid intolerant), the evidence that the analgesic efficacy of nefopam is approximately equivalent to an NSAID but not an opioid, the risk of drug-drug interactions, the high -dropout rate in the trials linked to adverse effects of nefopam, and risk of serious toxicity in overdose. The Committee noted the concerns of NHS Specialist Pharmacist Service. The committee noted that although nefopam was developed in the 1960s, there are no high-quality trials to form a robust evidence base for its use. Since then, a variety of other pharmacotherapy options for pain relief have emerged, making the current unmet need unclear, as NSAIDs, such as diclofenac have been shown to be equally efficacious. With respect to chronic pain, the committee noted that other pain services in the sector did not express an interest in its use. The committee were in agreement that the evidence did not support continued inclusion of nefopam in Trust formularies in the sector.

In summary, based the evidence and safety concerns, the Committee did not support the use of nefopam for post-operative pain and pharmacotherapy-resistant chronic pain, and were unconvinced of an unmet need that nefopam would fulfil. Consequently, the Committee requests that nefopam be removed from the RFL and NMUH formularies.

Drug: Nefopam, as per licensed dose
Indication: i) Post-operative pain, ii) Pharmacotherapy-resistant chronic pain
Decision: Not approved
Additional information: The Committee requests that nefopam be removed from the RFL and NMUH formularies.

9.3 Rapid Review: Naloxone for post-partum pruritus (Applicant: Dr T Mahendrayogam (in absentia); WH)

The Committee reviewed the use of naloxone as a second-line treatment option for post-partum pruritus. The proposed place in therapy is for naloxone to be used if chlorphenamine is ineffective. Pruritus a common side-effect following neuraxial opioid administration. The Committee were informed that the use of naloxone for this indication is an established practice at UCLH. A rapid review was conducted to assess the efficacy and

safety of naloxone for post-partum pruritus before its addition to the NCL formulary ensuring consistency of practice across NCL.

Evidence of naloxone for post-partum pruritus was identified in the Martindale, Micromedex, and UpToDate. Martindale references a literature review of opioid antagonists in the management of opioid-induced pruritus that found most evidence supporting the use of continuous infusions of low-dose naloxone with doses above 2 micrograms/kg/hour were generally not recommended due to the risk of reversal of analgesia. Micromedex lists this as an off-label, non-FDA use with mixed results in the literature on its efficacy. UpToDate concluded that the use of a small doses of intravenous naloxone was effective based on low-quality data. Currently, there is national guidance available for opioid-induced pruritus, however, local guidance from other NHS Trusts were identified with varying dosing schedules.

In terms of safety, the product licence lists side effects including nausea, dizziness, and headache. It was highlighted that naloxone is short-acting with a half-life of 1 to 1.5 hours therefore, the proposed use of naloxone would be for hourly administration based on patient reported symptoms.

Estimated patient numbers for NCL is approximately 1 to 5 patients per annum and the anticipated budget impact is expected to be minimal due to low patient numbers and the cost of naloxone.

The Committee discussed the discrepancy in dosing schedules in practice and it was noted that UCLH use a lower dose (50 to 100 micrograms per hour) compared to the dose proposed by the applicants.

In summary, the Committee approved the use of naloxone as a second-line treatment option for post-partum pruritus subject to clarification on: a) the wording to be utilised on the NCL Joint Formulary to ensure dosing will be standardised across NCL Trusts and b) whether there will be a maximum dose permitted within the 48-hour post-partum period.

Drug: Naloxone SC, dosing schedule to be confirmed (up to 48 hours post-partum)
Indication: Post-partum pruritus
Decision: Approved subject to clarification on: a) the wording to be utilised in the NCL Joint Formulary to ensure dosing is standardised across NCL Trusts and b) whether there will be a maximum dose permitted within the 48-hour post-partum period
Prescribing status: Restricted to secondary care only
Funding source: In tariff
Fact sheet or shared care required: No
Additional information: N/A
Post-meeting note: It was clarified with Dr Mahendrayogam (WH) and Dr Sampoe (UCLH) the wording will be *SC naloxone - Hourly PRN bolus dose of up to 100 micrograms (for up to 48 hours post-partum)*.

10 Position Statements and Guidelines

10.1 NCL Psoriasis HCD Pathway key updates

The Committee reviewed the rationale and evidence underpinning the proposed changes to the NCL pathway for moderate to severe psoriasis:

10.1.1 Exclusion of Ciclosporin

The Committee acknowledged that all NICE TA for psoriasis recommends biologics agents in patients for whom ciclosporin is contraindicated or intolerant or clinically inappropriate. However, clinical practice has changed whereby methotrexate is offered instead of ciclosporin prior to initiation of a biologic. This change is due to the adverse effect profile of ciclosporin and the significant reduction in cost of biologic agents given the availability of biosimilars. Ciclosporin is recommended to be excluded from the psoriasis treatment pathway.

10.1.2 Changing PUVA to Phototherapy

The Committee acknowledged that before NICE TA 575, biologics agents were recommended in patients for whom psoralen and long wave UVA radiation (PUVA) is contraindicated, intolerant or clinically inappropriate. Following the publication of NICE TA 575 (tildrakizumab) in April 2019, the recommendations have changed to provide phototherapy instead of PUVA. Trusts within NCL do not utilise PUVA as most clinicians prefer UVB, considering it more clinically appropriate and there is no anticipated budget impact.

10.1.3 Subcutaneous (SC) Infliximab

The Committee considered the proposal to include SC infliximab as an alternative to IV infliximab on the psoriasis pathway. The request for SC infliximab is based on the licensing for psoriasis, its cost- effectiveness compared to IV infusions resulting in lower administration costs and reduces infusion clinic requirement. Furthermore, SC infliximab has been approved for use in the NCL Inflammatory Bowel Disease (IBD),

Rheumatoid Arthritis (RA) and Ankylosing spondylitis (AS) pathways therefore, providing consistency across all pathways.

10.1.4 Absolute PASI score

The Committee noted that in patients with RA, who have failed a biologic therapy can be commenced on an alternative biologic treatment without having to deteriorate (which is assessed by the Disease Activity Score (DAS score) for the biologic pathway entry criteria. In contrast, in the current psoriasis pathway, patients can only be offered an alternative biologic treatment if their PASI and DLQI score are both greater than 10.

Similar to that for RA, it is necessary to act in the best interest of the patient by preventing deterioration of the condition, avoiding the anticipated cost implications of treating a worsen condition and aligning with the NCL RA pathway.

10.1.5 Updated Pregnancy and Breastfeeding advice

The Committee noted that certolizumab was previously the preferred option for pre-conception and pregnancy. However, the psoriasis pathway has been updated to align with the British Society for Rheumatology (BSR) guidance which includes recommendations for continuing or stopping all TNF inhibitors during pregnancy and breastfeeding including certolizumab. It is suggested that anti TNFs are compatible during peri conception, first, second and third trimester. However, depending on the specific agent and the risk of flare, treatment should be stopped in the second or early third trimester to ensure that full-term infants can follow a standard vaccination schedule.

The Committee noted that there is more data on pregnancy and breastfeeding in rheumatology than dermatology. The Committee noted that further work may be required by the clinical teams in collaboration with obstetrics department to support implementation including consideration of implications for childhood vaccination.

10.1.6 Apremilast as the preferred small molecule

The Committee approved the use of Apremilast as the preferred small molecule therapy instead of Dimethyl Fumarate (DMF). The NCL High-Cost Drugs (HCD) commissioning principles state that where two drugs with the same of mode of action are available, the cheapest drug should be used. The Committee noted that whilst DMF has the lowest cost, due to its poor safety profile and its extensive monitoring requirements, apremilast is the preferred small molecule in practice. DMF's safety concern include severe immunosuppression, progressive multifocal leukoencephalopathy and Fanconi syndrome (proximal tubal defect), however prevalence is unknown.

There are no head-to-head studies that compare the efficacy of apremilast against DMF however 4 multicentre placebo-controlled double-blind randomised controlled trials (the PSOR-005, -008, -009 and -010) studies demonstrated apremilast was more effective than placebo for key outcomes (including PASI75 response) at 16 weeks, and that this benefit was consistent across subgroups studied in people with moderate to severe chronic plaque psoriasis. An indirect network meta-analysis shows that systemic biological therapies and apremilast are more effective than DMF.

In terms of safety, apremilast has better safety profile with common side effects being diarrhoea, nausea or respiratory tract infections and requires less extensive monitoring in comparison to DMF.

In terms of budget impact, apremilast is already used as the preferred small molecule in clinical practice therefore the impact is expected to be minimal.

10.1.7 Bimekinzumab as an alternative mode of action

The Committee reviewed the proposal of adding bimekinzumab as an additional mode of action to the psoriasis pathway. Bimekinzumab acts on the interleukin (IL)-17 A&F inhibitor whereas the other second line treatment options act on the IL-17A or IL-17RA receptors.

The BE RADIANT trial (Reich et al, n=743) is a Phase 3b multicentre, randomised, double-blind, active-comparator–controlled, parallel-group trial which investigated the efficacy and safety of bimekizumab compared with Secukinumab in patients with moderate-to-severe plaque psoriasis. The primary end point was 100% reduction from baseline in the Psoriasis Area and Severity Index (PASI) score at week 16. The study showed that at week 16, a total of 230 patients (61.7%) in the bimekizumab group and 181 (48.9%) in the secukinumab group had a 100% reduction from baseline in the PASI score (PASI 100) (adjusted risk difference, 12.7 percentage points; 95% confidence interval [CI], 5.8 to 19.6); bimekizumab was shown to be noninferior and superior to secukinumab (P<0.001 for noninferiority and superiority). The study concluded that in patients with moderate-to-severe psoriasis, treatment with bimekizumab resulted in greater skin clearance than treatment with secukinumab over 16 and 48 weeks. There are no head to heads studies comparing

bimekizumab against brodalumab and Ixekizumab however a NICE network meta-analysis suggests that brodalumab and ixekizumab have similar efficacy to secukinumab, which implies that Bimekizumab is superior to all three treatment options.

10.1.8 Adalimumab dose escalation

The committee considered the addition of adalimumab dose escalation to the psoriasis pathway. The pathway recommends escalating the dose to 40mg weekly in patients with inadequate primary response, achieving PASI 50 but still having significant disease burden and if the drug level is known to be subtherapeutic (<7 micrograms/ml). National and international guidelines including the SPC for adalimumab supports the use of dose escalation prior to switching treatment.

In terms of safety, Gniadecki et al. 2018 reported that the incidence of adverse drug events in the adalimumab dose escalation was similar to the standard dose group. Therefore, the Committee noted that dose escalation does not pose any additional risk to patients experiencing adverse events.

In terms of budget impact, the dose escalation regimen will be ICB commissioned, and will result in a cost avoidance of £75,532 per annum for year 1 by delaying the use of more costly treatment options.

The Committee heard from Dr McBride that adalimumab will remain as the preferred anti-TNF therapy. However, due to the increased risk of side effect and poor drug survival, subcutaneous infliximab will be offered as a suitable option for patients with comorbidities such as inflammatory bowel disease, ankylosing spondylitis, or uveitis. In relation to bimekizumab, Dr McBride supports the addition to the pathway as an additional alternative mode of action for complex patients (i.e. those with psoriasis and psoriatic arthritis) who have failed treatment with secukinumab or ixekizumab. In comparison, bimekinzumab is more cost effective than secukinumab, ixekizumab and brodalumab.

In camera, the Committee agreed that the psoriasis pathway recommendations are evidence-based, reflective of current clinical practice, cost-effective and do not compromise patient safety.

In summary, the Committee approved the following changes in the psoriasis pathway:

i) The exclusion of ciclosporin from eligibility criteria of the pathway due to its adverse effects,

ii) To replace PUVA by phototherapy to align with NICE TA 575 and current clinical practice,

iii) The addition of subcutaneous infliximab as an alternative to IV infliximab, offering cost savings and consistency across multiple pathways,

iv) To use the absolute PASI score as this will not require patients to deteriorate back to baseline PASI and DLQI scores to access the next line of treatment,

v) The pathway follows BSR guidance on TNF inhibitors during pregnancy and breastfeeding, ensuring compatibility and safe vaccination schedules,

vi) The use of apremilast as the preferred small molecule inhibitor of phosphodiesterase 4 over dimethyl fumarate (DMF) due to better safety profile and less extensive monitoring requirements,

vii) To add adalimumab dose escalation as an option in the pathway for patients with inadequate primary response

viii) To add Bimekizumab (targets IL17A and IL17F) to the pathway and classified as an alternative mechanism of action to secukinumab, brodalumab, and ixekizumab due to its dual inhibition.

The potential impact of bimekizumab on other IL-17-related pathways was recognized by the committee, given its application in Psoriatic Arthritis and Ankylosing Spondylitis. As an interim measure, it was recommended that patients previously treated with an IL-17 inhibitor transition to a superior drug within the same class. For patients who have not yet received IL-17 inhibitor treatment, bimekizumab should be utilized. This decision will be reassessed by the Joint Formulary Committee (JFC) upon the availability of a biosimilar version of any IL-17 treatment.

11 Sub-Group Updates

11.1 NICE TA Implementation Group Report

The Committee heard from Ms Weaver who provided a summary of updates from the NICE TA Implementation Group. The Committee noted the current workplan, which was included in the agenda pack for information.

The following updates on NICE TAs with interface considerations were provided to support formulary teams and Trust DTCs with implementation:

- Atogepant for preventing migraine (NICE TA973): Prescribing status: unassigned. Ms. Weaver informed the JFC that NCL is overdue in implementing atogepant for migraine treatment. Although a primary care headache pathway exists for rimegepant, atogepant has not yet been included. This inclusion is pending

the development of an NCL system-wide migraine pathway, which will cover high-cost drugs. The implementation of atogepant will proceed as part of this broader initiative, with updates provided to the JFC accordingly. Additional considerations for tertiary centres will be addressed within the system-wide migraine pathway.

- Relugolix for treating hormone-sensitive prostate cancer (NICE TA995): An amber prescribing status has been assigned for this NICE TA (initiation will be restricted to oncology specialists, with continuation by primary care). The group has also made several recommendations:
  - Update the NCL factsheet for prostate cancer treatment to include relugolix as a support mechanism for primary care prescribing. The transfer of patients to relugolix is anticipated to occur after 2-3 months.
  - Maintain current patients on GnRH analogues (injectable treatment) without actively switching to relugolix, unless deemed clinically appropriate during reviews.
- Linzagolix for treating moderate to severe symptoms of uterine fibroids (NICE TA996) - An amber prescribing status has been assigned for this NICE TA (initiation should be by gynaecology specialists with continuation by primary care). To support primary prescribing, linzagolix should be included in the existing factsheet for relugolix. The group suggests offering linzagolix as a monotherapy for patients who cannot or do not want combined hormonal therapy containing relugolix, or when surgery is high risk. Linzagolix, without hormonal add-back therapy, is cost-effective for long-term use (over six months).
- Vibegron for treating symptoms of overactive bladder syndrome (NICE TA999): A green prescribing status (primary or specialist care initiation) has been assigned for this NICE TA in line with NICE recommendation. Vibegron is as effective and safe as mirabegron. NICE TA recommends using the medicine with the lowest acquisition cost first, which is currently vibegron. While active switching from mirabegron to vibegron is not anticipated, it can be considered during reviews if clinically appropriate.
- Latanoprost–netarsudil (Roclanda®) for previously treated primary open-angle glaucoma or ocular hypertension (NICE TA1009) - A amber prescribing status (specialist initiation and primary care continuation) has been assigned for this NICE TA in line with NICE recommendation. With agreement with the NICE TA implantation group and Moorfield Hospital, the glaucoma guidelines have been updated - to include this NICE TA. The guidelines define the place in therapy for Roclanda® and prefer multidose bottle (MDB) preservative-free (PF) eye drops over single-dose unit (SDU) PF eye drops for glaucoma and OHT in primary care. This preference will be added to the glaucoma pathway before final JFC approval.
- Tirzepatide for managing overweight and obesity (NICE TA1026): The first implementation date is 23 March 2025, for specialist weight management patients, followed by a phased implementation for other eligible patients starting 26 June 2025. This introduction is in line with the funding variation proposed by NHSE. Ongoing efforts are focused on establishing a uniform approach across the system, Local communications are being developed to manage patient enquiries to support primary care.

11.2 NCL Pathways Group

Nil

11.3 Shared Care Group Minutes and Updates

Nil

12 Next meeting

Thursday 20th February 2025

13 Any other business

Nil