Joint Formulary Committee (JFC): Minutes

Minutes from the meeting held on 19th February 2026

		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	✓	
Dr A Scourfield	UCLH, DTC Chair		✓
Mr J Harchowal	UCLH, Chief Pharmacist	✓	
Ms W Spicer	RFL, Chief Pharmacist	✓	
Dr J Cross	RFL, DTC Chair	✓	
Dr P Jasani	RFL, DTC Deputy Chair		✓
Dr K Boleti	RFL, DTC Deputy Chair		✓
Dr K Tasopoulos	RFL, DTC Deputy Chair	✓	
Ms S Stern	RFL, Deputy 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 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 S Sanghvi	IPMO Programme Team, JFC Principal Pharmacist	✓	
Ms K Leung	IPMO Programme Team, JFC Senior Pharmacist	✓	
Ms S Maru	IPMO Programme Team, JFC Senior Pharmacist	✓	
Ms M Butt	IPMO Programme Team, Director	✓	
Ms S Amin	IPMO Programme Team, Lead Pharmacist	✓	
Ms I Samuel	RFL, Formulary Pharmacist	✓	
Mr A Barron	UCLH, Deputy Chief 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 I Huda	WH, Formulary Pharmacist		✓

Ms M Thacker	GOSH, Deputy Chief Pharmacist		✓
Mr A Fazal	RFL, Principal Pharmacist	✓	
Mr G Grewal	RFL, Deputy Chief Pharmacist	✓	
Ms W Adelusi	IPMO Programme Team, Clinical Pharmacist	✓	
Ms Sedif Tasnim	NHSE, Specialist Commissioning Pharmacy Advisor	✓	
Dr C Zeicu	UCLH, Clinical Pharmacology Specialist Registrar	✓	
Dr S Sodha	RFL, Consultant Anaesthetist	✓	
Ms I Ibrahim	RFL, Specialist Surgical Specialities Pharmacist	✓	
Dr K Burke	CNWL, Palliative Care Consultant	✓	
Ms B Patel	GOSH, Specialist Pharmacist	✓	
Dr S De-Saram	UCLH, Consultant Microbiologist	✓	
Dr M Blank	UCLH, Microbiology Specialist Registrar	✓	
Ms P Panesar	UCLH, Lead Antimicrobial Pharmacist	✓	
Dr C Ashton	Islington Public Health, Public Health Consultant (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 15th January 2026

Minutes and abbreviated minutes of the 15th January 2026 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	JFC recommendation
February 2026	Denosumab biosimilar	**Reviewed by**: JFC **Drug**: Denosumab biosimilar **Indication**: As per existing approved indications **Decision**: Approved **Prescribing status**: In line with NICE TA/ NCL JFC approved indications **Funding source**: In-Tariff **Fact sheet or Shared care required**: N/A	**To add to the NCL Joint Formulary**
December 2025	Granisetron patches for chemotherapy-induced nausea and vomiting	**Reviewed by**: UCLH **Drug**: Granisetron transdermal patch **Dose**: 3.1mg/24-hour patch applied for up to 7 days (removed at least 24 hours after completing chemotherapy) **Indication**: Patients aged 13 years and above with a history of uncontrollable CINV, unable to tolerate oral anti-emetics and needing further cycles of chemotherapy requiring either: • Multiple SC/IV administrations of anti-emetics in ambulatory care, or • Admission for control of CINV via CSCI **Decision**: Approved under evaluation **Prescribing status**: Secondary care only (on the advice of palliative care) (Red)	**To add to the NCL Joint Formulary**

		Funding source: In tariff	
December 2025	Granisetron transdermal patch for patients with refractory CINV and a prolonged QTc who have not achieved adequate symptom control with cyclizine and aprepitant	**Reviewed by**: UCLH **Drug**: Granisetron transdermal patch **Dose**: 3.1mg/24-hour patch applied for up to 7 days (removed at least 24 hours after completing chemotherapy) **Indication**: In patients with refractory CINV and a prolonged QTc who have not achieved adequate symptom control with cyclizine and aprepitant **Decision**: Deferred	**Deferred**
December 2025	Modafinil for idiopathic hypersomnia [Historical review]	**Reviewed by**: UCLH **Drug**: Modafinil **Dose**: 200mg-400mg daily **Indication**: Idiopathic hypersomnia; initiated by specialist consultant at NHNN only **Decision**: Approved **Prescribing status**: Suitable for secondary care initiation ***(Prescribing status will be reviewed at the next NCL ICB Medicines CRG meeting)*** **Funding source**: In tariff	**To add to the NCL Joint Formulary**
December 2025	Methylphenidate for idiopathic hypersomnia [Historical review]	**Reviewed by:** UCLH **Drug**: Methylphenidate **Dose**: IR 10-60mg daily, PR tabs (XL) 18-72mg daily, MR caps 10-60mg daily **Indication**: Idiopathic hypersomnia; initiated by specialist consultant at NHNN only **Decision**: Approved **Prescribing status**: Suitable for secondary care initiation ***(Prescribing status will be reviewed at the next NCL ICB Medicines CRG meeting)*** **Funding source**: In tariff	**To add to the NCL Joint Formulary**
December 2025	Dexamfetamine for idiopathic hypersomnia [Historical review]	**Reviewed by**: UCLH **Drug**: Dexamfetamine **Dose**: 10-60mg daily **Indication**: Idiopathic hypersomnia; initiated by specialist consultant at NHNN only **Decision**: Approved **Prescribing status**: Suitable for secondary care initiation ***(Prescribing status will be reviewed at the next NCL ICB Medicines CRG meeting)*** **Funding source**: In tariff	**To add to the NCL Joint Formulary**
December 2025	Miltefosine for cutaneous leishmaniasis	**Reviewed by**: UCLH **Drug**: Miltefosine capsules **Dose**: • Adults and children over 12 (>50kg): 150mg/day • Children over 12 (25 to 50kg): 100mg/day • Children over 12 (<25kg): 50mg/day • Children under 12: 2.5mg/kg/day **Indication**: Cutaneous Leishmaniasis **Decision**: Approved **Prescribing status**: Secondary care only (on the advice of the Hospital for Tropical Diseases team) (Red) **Funding source**: In tariff	**To add to the NCL Joint Formulary**

*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

8.1. Strategic updates for NCL JFC

The Committee were informed that there are several important strategic changes happening at ICS and national level with implications for the JFC. The Committee discussed the following:

- North Central London (NCL) ICB and North West London (NWL) ICB are merging, and from April 2026 will jointly become the West and North London ICB (WNL ICB). NCL and NWL ICBs are currently undergoing a consultation on the new organisational structure which will impact medicines strategic commissioning, medicines primary care delivery, high-cost drugs (HCD) and formulary functions. The current aim is for NCL JFC meetings to continue from April 2026 until the formulary function can be aligned with WNL (timeframe TBC). The reporting line for JFC will need to be clarified within the WNL ICB governance structure. The HCD function has been hosted by the NCL IPMOP team under interim arrangements but will be transferred back to WNL ICB from April 2026.
- For 2025/2026 NCL ICB prioritised funding for medicines and indications covered by positive NICE Technology Appraisals (TAs), as statutorily required. The position for WNL ICB for 2026/2027 has not been confirmed but the current commissioning position is predicted to be maintained.
- The 10 Year Health Plan set out a commitment to move to a Single National Formulary (SNF). Further information on the SNF scope and timelines is required to understand the implication for JFC and DTCs.
- From April 2026, the threshold NICE uses to assess whether medicines are cost-effective will be increased from £20-30K per QALY gained, to £25-35K per QALY gained. This is likely to affect drug prices and therefore drug budget and affordability considerations.

Mr Harchowal and Ms Coughlan notified the Committee that an independent review of the NCL IPMOP team (which includes the JFC team) has been commissioned. Further details, including the terms of reference, will be shared with JFC members shortly. The Committee discussed setting out the core principles for the joint formulary, to support next steps with WNL alignment. The Committee agreed that strategic updates would be presented regularly to the JFC to ensure that Committee members remain appropriately informed.

8.2. Ratification of Information Leaflets

The Committee supported approval of the following information leaflets which were reviewed and approved via Chairman's actions:

- Drospirenone for contraception (information for primary care and community pharmacies)
- Drospirenone for contraception (information for patients)
- Nausea and vomiting in pregnancy

8.3 Denosumab biosimilar (Osvyrti®)

The Committee heard from Ms Sanghvi that a denosumab biosimilar (Osvyrti®) is available from January 2026. Whilst a full evidence evaluation by the JFC is not required for biosimilars, it was noted that risk assessments had been completed which identified no significant risks with the denosumab biosimilar. Implementation is currently underway in secondary care with additional work on interface prescribing requirements and primary care implementation ongoing.

Drug: Denosumab biosimilar (Osvyrti®)
Indication: In line with NICE TA/ NCL JFC approved indications
Decision: Approved
Prescribing status: In line with NICE TA/ NCL JFC approved indications
Funding source: In tariff
Fact sheet or shared care required: In line with NICE TA/ NCL JFC approved indications
Additional information: N/A

9. Medicine Reviews

9.1 Celecoxib for post-operative pain relief after hip and knee-replacement surgery (Applicant: Dr S Sodha, RFL)

The Committee considered an application for celecoxib 200mg daily, a selective COX-2 inhibitor, for off-label use to replace ibuprofen (oral) plus proton pump inhibitor (PPI) (or diclofenac suppositories + PPI when required as rescue therapy for severe patients) for post-operative pain relief after hip and knee replacement surgery for a 5-day course.

The Committee reviewed an in-house non-randomised, historic control study (2025, n=35) performed by RFL comparing baseline analgesia (modified-release opioids) to the trial period analgesia (immediate-release opioids +/- celecoxib). The results from this audit were inconclusive. The limitations of this study were that 1 analgesic agent at baseline was being compared to 2 analgesic agents in the trial, modified release opioids were being compared to immediate-release opioids and not all patients received celecoxib.

The Committee were informed of various studies submitted for review by the applicant but not considered relevant to the application as the relevant comparator was not included. These included studies by Jiang et al (2022), CLASS study (2000), Mammoto et al (2021), Huang et al (2008) and Gong et al (2013). The Committee also noted that there were no relevant studies published for the proposed indication, and therefore efficacy and safety data was drawn from trials in patients with osteoarthritis and rheumatoid arthritis.

Efficacy

The Committee reviewed the evidence base to assess if celecoxib is superior to non-selective NSAIDs (nsNSAIDs) for pain relief. A Cochrane review by Puljak et al (2017; n=11,271) was a systematic review and meta-analysis of randomised-controlled trials (RCTs) in osteoarthritis patients to compare the efficacy and safety of celecoxib 200mg daily to nsNSAIDs (naproxen/diclofenac). There was a lack of clarity on concomitant prescribing of PPIs across the included studies. The results of this review were inconclusive for the primary outcome of 100-point pain VAS score. CONDOR (2010, n=4484) was an active-controlled, double-blind study in osteoarthritis and rheumatoid arthritis patients comparing the efficacy and safety of celecoxib 200mg twice daily to diclofenac 75mg BD with omeprazole. The secondary outcome of the least-squares mean change from baseline to week 6 in Patients Global Assessment of Arthritis was not significantly better for the celecoxib arm compared to the diclofenac + omeprazole arm (0.75 vs 0.77; p=0.41). Park et al (2020; n=150) was an active-controlled, double-blind, double-dummy, non-inferiority study in osteoarthritis patients comparing the safety and efficacy of celecoxib 200mg daily with a placebo to naproxen/esomeprazole 500mg/20mg BD with a placebo. The secondary outcome of the pain VAS score for osteoarthritis was not significantly better for celecoxib compared to naproxen/esomeprazole.

GI safety

Clinical trials: In terms of safety, the Committee reviewed evidence to assess if celecoxib has a superior gastrointestinal safety profile than nsNSAIDs administered together with PPI as is standard practice. Three systematic review and meta-analyses were reviewed which compared gastrointestinal safety of celecoxib with nsNSAIDs. Rostom et al (2009; n=31,106) and NIHR Health Technology Assessment (2008) were systematic reviews and meta-analyses of randomised controlled trials in patients with osteoporosis, rheumatoid arthritis or other arthritic conditions comparing the efficacy and safety of celecoxib to nsNSAIDs. Rostom et al reported the composite safety outcome of 'strict ulcer complications' which included perforation, obstruction or bleeding (POBs) was significantly better for the celecoxib arm compared to the nsNSAID arm (RR: 0.23 [95% CI: 0.07 – 0.76]). The composite safety outcome of ulcer complications (which included perforation, obstruction and bleeding) and /or ulcer related symptoms (PUBs) was significantly better for the celecoxib arm compared to the nsNSAID arm (RR: 0.39 [95% CI: 0.21 – 0.73]). The NIHR Health Technology Assessment reported the composite safety outcome of POBs was significantly better for the celecoxib arm compared to the nsNSAID (RR: 0.57 [95% CI: 0.35 – 0.95]; NNT 723). The composite safety outcome of PUBs was significantly better for the celecoxib arm compared to the nsNSAID arm (RR: 0.55 [95% CI: 0.40 – 0.76]; NNT 225). However, the studies included in Rostom et al did not co-prescribe PPIs in the nsNSAID arm and, in the NIHR Health Technology Assessment, only had one out of twenty-two studies included a co-prescription of a PPI in the nsNSAID arm. Therefore, the findings of these were considered to be unfairly biased in favour of celecoxib and were therefore deemed unreliable for addressing the question of differential safety. Jarupongrapa et al (2012; n=7616) was a systematic review and meta-analysis of double-blind RCTs in osteoporosis, rheumatoid arthritis and healthy patients comparing the efficacy and safety of celecoxib to nsNSAIDs co-prescribed with a PPI. The primary safety outcome of POBs was significantly better for the celecoxib arm compared to the nsNSAID + PPI arm (RR: 0.38 [95% CI: 0.25 – 0.56]; p<0.001). However, the superiority of celecoxib to nsNSAID + PPI was confined to high risk patients only (RR 0.32 [95% CI: 0.2 – 0.51]). Celecoxib was not significantly superior to nsNSAIDs + PPI in the low-risk of major GI events sub-group (RR 0.66 [95% CI: 0.3 – 1.43]). Moreover, the superiority of celecoxib to nsNSAID was driven by the largest study in the high-risk category, the CONDOR (2010) study (RR 0.26 [95% CI: 0.15 – 0.46]), where the comparator nsNSAID was diclofenac. Diclofenac is known to have a higher rate of upper GI complications compared to ibuprofen (RR 3.34 vs 1.84) as reported by Castellsague et al (2012). In the Goldstein et al (2007) RCT included in the Jarupongrapa et al review, ibuprofen – the comparator nsNSAID – was used at approximately twice the usual clinical dose.

Observational studies: Abraham et al (2008; n=481,980) reported a single observational study using the UC Veterans Affairs database comparing the risk of NSAID-related upper GI events against the background rate of

upper GI events in non-users of NSAIDs. Both nsNSAIDs and COX-2 inhibitors had the same rate of upper GI events (RR 1.8) compared to no NSAID use. In both cases, the co-prescription of a PPI reduced the risk of GI complications to the same degree (RR 1.1 vs no NSAID use). Tawfik et al (2025; 25 studies; n=557,269) was a systematic review and meta-analysis of studies comparing the bleeding risk of NSAIDs, and included 19 case-control studies, 4 cohort studies and 2 IPD meta-analyses. The GI bleeding risk was reported as follows: celecoxib (OR: 1.16 [95% CI: 0.84 – 1.61]), ibuprofen (OR: 2.28 [95% CI: 1.71 -3.03]) and diclofenac (OR: 3.42 [95% CI: 2.58 -4.53]). The limitations of the study were that the studies were largely observational and did not specify concomitant PPI use.

Cardiovascular safety

The Committee reviewed evidence to assess if celecoxib has a worse cardiovascular safety profile than nsNSAIDs. The Coxib and traditional NSAID Trialists' (CNT) collaboration (2013; n=132, 809) study reported a systematic review and meta-analysis of RCTs comparing low-normal dose of COX-2 inhibitors to high-dose nsNSAIDs. The primary vascular outcome of major vascular events, defined as non-fatal myocardial infarction, non-fatal stroke or death from vascular cause, was significantly greater for COX-2 inhibitors and diclofenac compared to placebo (RR 1.37; p=0.0009 and RR 1.41; p=0.0036) but not significantly greater for ibuprofen or naproxen compared to placebo (RR 2.22; p=0.0253 and RR 0.93; p=0.66). The secondary vascular outcome of major coronary events, defined as non-fatal myocardial infarction or death from coronary disease, was significantly greater for COX-2 inhibitors, diclofenac and ibuprofen compared to placebo (RR 1.76; p=0.0001, RR 1.70; p=0.0032 and RR 2.22; p=0.0253 respectively) but not significantly greater for naproxen (RR 0.84; p=0.48). The main limitation of this study was that low-normal dose COX-2 inhibitors were compared to high-dose nsNSAIDs (ibuprofen, naproxen and diclofenac) which are not routinely used in clinical practice. PRECISION (2016; n=24,081) was an active-controlled, double-blind, non-inferiority study in patients at an increased risk of cardiovascular risk with osteoarthritis and rheumatoid arthritis which compared the safety profile of low-dose celecoxib with a PPI to high-dose ibuprofen or mid-high dose naproxen with a PPI. The primary composite outcome, defined as the first occurrence of an adverse event that met the ATPC criteria (i.e. death from cardiovascular causes) occurred in the celecoxib (2.3%), naproxen (2.5%) and ibuprofen (2.7%) arm (hazard ratio for celecoxib vs. naproxen, 0.93 [95% CI: 0.76 to 1.13]; hazard ratio for celecoxib vs. ibuprofen, 0.85 [95% CI: 0.70 to 1.04]; P<0.001 for noninferiority in both comparisons). The main limitation of the study was that low-dose celecoxib was compared to nsNSAIDs administered at mid-high doses for naproxen and high doses for ibuprofen that are not routinely used in clinical practice.

The Committee reviewed evidence to assess if celecoxib had a superior renal safety profile than nsNSAIDs. In the PRECISION study, the secondary outcome of serious renal events was significantly lower in the celecoxib arm compared to ibuprofen (HR 0.61 [95% CI: 0.44 – 0.85]; p=0.004) but not significantly better in the celecoxib arm compared to naproxen (HR 0.79 [95% CI: 0.56 – 1.12]; p=0.19). Chan et al (2002, n=287) was an active-comparator, double-blind study that compared celecoxib with diclofenac + omeprazole in patients with arthritis presenting with ulcer bleeding. The secondary outcome of other adverse events reported greater proportion of renal adverse events in the celecoxib arm (51.4%) compared to diclofenac + omeprazole arm (40.7%) although statistical significance was not assessed.

In terms of guidelines, both nsNSAIDs and COX-2 inhibitors are recommended for use by GIRFT (2023; endorsed by the British Association of Orthopaedics) in hip and knee surgery and the American Society of Anaesthesiologists 2016 for post-operative pain control.

In terms of budget impact, celecoxib is expected to cost £1350 per annum compared to £500 per annum for ibuprofen for an estimated 765 patients in NCL.

The Committee heard from Dr Sodha that there is an unmet need relating to suboptimal pain control in the post-operative patient cohort, which may contribute to delayed discharge. This is partly due to reluctance to prescribe ibuprofen because of perceived risks of gastrointestinal, renal, and bleeding complications in patients receiving concomitant VTE prophylaxis. She proposed that this may be addressed through multimodal analgesia strategies, including the use of celecoxib, which is considered to have a more favourable gastrointestinal adverse effect profile. The use of celecoxib is also thought to reduce the number of patients requiring diclofenac suppositories as rescue analgesia. Anecdotal evidence from other national centres, including the South-West Ambulatory Orthopaedic Centre, supports the use of celecoxib in this patient cohort.

In camera, the Committee noted that the design of the reviewed RCTs either did not include concomitant PPI therapy in the nsNSAID arm and/or compared higher-than-typical doses of nsNSAIDs, with low-to-moderate doses of celecoxib, thereby introducing potential bias in favour of celecoxib in relation to assessment of GI safety. The CONDOR trial compared celecoxib with diclofenac + PPI (an nsNSAID known to have a higher rate of GI adverse effects than naproxen or ibuprofen + PPI was in patients at high risk of GI bleeding, in whom all NSAIDs would likely be avoided. The Committee further noted that there is no direct comparative evidence

on analgesic efficacy in the specific setting of interest. The Committee also highlighted the possibility that patients initiated on celecoxib may be discharged on celecoxib, with subsequent requests to continue celecoxib in primary care beyond the intended 5-day course. Experience from the Royal National Orthopaedic Hospital indicates that adequate pain control has been achieved using a combination of opioids and ibuprofen with a PPI, without the need to prescribe celecoxib. Having considered the detailed evidence, the Committee also questioned whether there is a misconception among clinicians that celecoxib carries a lower risk of gastrointestinal adverse effects compared with the lower risk nsNSAIDs co-prescribed with PPI, and that this may warrant further education to ensure prescribing decisions are aligned with the evidence base and local guidance.

In summary, based on the evidence available and the Committee's concerns regarding potential bias in the supporting RCTs, the absence of consistent concomitant PPI use in studies, the risk of inappropriate continuation post-discharge, and the availability of effective multimodal analgesia alternatives with a similar risk profile to celecoxib, the Committee could not recommend the use of celecoxib for this indication. The Committee were supportive of developing and disseminating educational guidance to clinical teams summarising the Committee's evidence review, clarifying that the perceived superior gastrointestinal safety of celecoxib over ibuprofen co-prescribed with a PPI is not supported by robust comparative data and that real-world evidence demonstrates broadly similar GI complication rates.

Drug: Celecoxib 200mg daily tablets for a 5-day course
Indication: To replace ibuprofen (oral) with a proton pump inhibitor (PPI) (or diclofenac suppositories + PPI when required as rescue therapy for severe patients) for post-operative pain relief after hip and knee replacement surgery
Decision: Not approved
Additional information: Educational support to be provided to clinical teams on the perceived differential safety between celecoxib compared to ibuprofen + PPI.

9.2 Celecoxib for inflammatory cancer pain (Applicant: Dr K Burke, UCLH)

The Committee considered an application for celecoxib 200-400mg daily, a selective COX-2 inhibitor, for off-label use to replace ibuprofen or naproxen (oral) with a proton pump inhibitor (PPI) for inflammatory cancer pain (including but not limited to soft tissue and muscle infiltration particularly common in sarcomas or bladder cancer, pleural or diaphragmatic disease, liver capsular pain or necrotic abdominal tumours) of any severity for approximately 3-12 months for initiation by the palliative care team only.

The Committee reviewed the evidence base to support the use of NSAIDs in cancer pain. A Cochrane systematic review and meta-analyses of double-blind, single-blind and open-label studies by Derry et al (2017; 11 studies; n=949) in patients with cancer pain of any intensity compared NSAIDs to other NSAIDs or an NSAID with an opioid. It concluded that there is no high-quality evidence to support or refute the use of NSAIDs alone or in combination with opioids for the three steps of the WHO cancer pain ladder. A limitation was that only one study within this review (Mohammedinejad et al, 2015) reviewed the use of celecoxib compared to diclofenac without a PPI to reduce depressive symptoms (primary outcome) and pain (secondary outcome) in breast cancer patients with no significant reported difference in pain control. Magee et al (2019; 30 studies; n=2329) was another systematic review and meta-analyses of double-blind RCTs in adult patients with cancer pain. It compared NSAIDs to placebo, NSAIDs, opioids and NSAID + opioids but concluded that it was difficult to draw any meaningful conclusions from these studies due to heterogeneity in outcome measures.

Efficacy

The Committee reviewed the evidence base to assess if celecoxib is superior to non-selective NSAIDs (nsNSAIDs) for pain relief. A Cochrane review by Puljak et al (2017; n=11,271) was a systematic review and meta-analysis of randomised-controlled trials (RCTs) in osteoarthritis patients to compare the efficacy and safety of celecoxib 200mg daily to nsNSAIDs (naproxen/diclofenac). There was a lack of clarity on concomitant prescribing of PPIs across the included studies. with uncertainty on whether concomitant PPIs were co-prescribed. The results of this review were inconclusive for the primary efficacy outcome of 100-point pain VAS score. CONDOR (2010, n=4484) was an active-controlled, double-blind study in osteoarthritis and rheumatoid arthritis patients comparing the efficacy and safety of celecoxib 200mg twice daily to diclofenac 75mg BD with omeprazole. The secondary outcome of the least-squares mean change from baseline to week 6 in Patients Global Assessment of Arthritis was not significantly better for the celecoxib arm compared to the diclofenac + omeprazole arm (0.75 vs 0.77; p=0.41). Park et al (2020; n=150) was an active-controlled, double-blind, double-dummy, non-inferiority study in osteoarthritis patients comparing the safety and efficacy of celecoxib 200mg daily with a placebo to naproxen/esomeprazole 500mg/20mg BD with a placebo. The secondary outcome of

the pain VAS score for osteoarthritis was not significantly better for celecoxib compared to naproxen/esomeprazole.

GI safety

Clinical trials: In terms of safety, the Committee reviewed evidence to assess if celecoxib has a superior gastrointestinal safety profile than nsNSAIDs administered together with PPI as is standard practice. Three systematic review and meta-analyses were reviewed which compared gastrointestinal safety of celecoxib with nsNSAIDs. Rostom et al (2009; n=31,106) and NIHR Health Technology Assessment (2008) were systematic reviews and meta-analyses of randomised controlled trials in patients with osteoporosis, rheumatoid arthritis or other arthritic conditions comparing the efficacy and safety of celecoxib to nsNSAIDs. Rostom et al reported the composite safety outcome of 'strict ulcer complications' which included perforation, obstruction or bleeding (POBs) was significantly better for the celecoxib arm compared to the nsNSAID arm (RR: 0.23 [95% CI: 0.07 – 0.76]). The composite safety outcome of ulcer complications (which included perforation, obstruction and bleeding) and /or ulcer related symptoms (PUBs) was significantly better for the celecoxib arm compared to the nsNSAID arm (RR: 0.39 [95% CI: 0.21 – 0.73]). The NIHR Health Technology Assessment reported the composite safety outcome of POBs was significantly better for the celecoxib arm compared to the nsNSAID (RR: 0.57 [95% CI: 0.35 – 0.95]; NNT 723). The composite safety outcome of PUBs was significantly better for the celecoxib arm compared to the nsNSAID arm (RR: 0.55 [95% CI: 0.40 – 0.76]; NNT 225). However, the studies included in Rostom et al did not co-prescribe PPIs in the nsNSAID arm and, in the NIHR Health Technology Assessment, only had one out of twenty-two studies included a co-prescription of a PPI in the nsNSAID arm. Therefore, the findings of these were considered to be unfairly biased in favour of celecoxib and were therefore deemed unreliable for addressing the question of differential safety. Jarupongrapa et al (2012; n=7616) was a systematic review and meta-analysis of double-blind RCTs in osteoporosis, rheumatoid arthritis and healthy patients comparing the efficacy and safety of celecoxib to nsNSAIDs co-prescribed with a PPI. The primary safety outcome of POBs was significantly better for the celecoxib arm compared to the nsNSAID + PPI arm (RR: 0.38 [95% CI: 0.25 – 0.56]; p<0.001). However, the superiority of celecoxib to nsNSAID + PPI was confined to high-risk patients only (RR 0.32 [95% CI: 0.2 – 0.51]). Celecoxib was not significantly superior to nsNSAIDs + PPI in the low-risk of major GI events sub-group (RR 0.66 [95% CI: 0.3 – 1.43]). Moreover, the superiority of celecoxib to nsNSAID was driven by the largest study in the high-risk category, the CONDOR (2010) study (RR 0.26 [95% CI: 0.15 – 0.46]), where the comparator nsNSAID was diclofenac. Diclofenac is known to have a higher rate of upper GI complications compared to ibuprofen (RR 3.34 vs 1.84) as reported by Castellsague et al (2012). In the Goldstein et al (2007) RCT included in the Jarupongrapa et al review, ibuprofen – the comparator nsNSAID – was used at approximately twice the usual clinical dose.

Observational studies: Abraham et al (2008; n=481,980) reported a single observational study using the UC Veterans Affairs database comparing the risk of NSAID-related upper GI events against the background rate of upper GI events in non-users of NSAIDs. Both nsNSAIDs and COX-2 inhibitors had the same rate of upper GI events (RR 1.8) compared to no NSAID use. In both cases, the co-prescription of a PPI reduced the risk of GI complications to the same degree (RR 1.1 vs no NSAID use). Tawfik et al (2025; 25 studies; n=557,269) was a systematic review and meta-analysis of studies comparing the bleeding risk of NSAIDs, and included 19 case-control studies, 4 cohort studies and 2 IPD meta-analyses. The GI bleeding risk was reported as follows: celecoxib (OR: 1.16 [95% CI: 0.84 – 1.61]), ibuprofen (OR: 2.28 [95% CI: 1.71 -3.03]) and diclofenac (OR: 3.42 [95% CI: 2.58 -4.53]). The limitations of the study were that the studies were largely observational and did not specify concomitant PPI use.

Cardiovascular safety

The Committee reviewed evidence to assess if celecoxib has a worse cardiovascular safety profile than nsNSAIDs. The Coxib and traditional NSAID Trialists' (CNT) collaboration (2013; n=132, 809) study reported a systematic review and meta-analysis of RCTs comparing low-normal dose of COX-2 inhibitors to high-dose nsNSAIDs. The primary vascular outcome of major vascular events, defined as non-fatal myocardial infarction, non-fatal stroke or death from vascular cause, was significantly greater for COX-2 inhibitors and diclofenac compared to placebo (RR 1.37; p=0.0009 and RR 1.41; p=0.0036) but not significantly greater for ibuprofen or naproxen compared to placebo (RR 2.22; p=0.0253 and RR 0.93; p=0.66). The secondary vascular outcome of major coronary events, defined as non-fatal myocardial infarction or death from coronary disease, was significantly greater for COX-2 inhibitors, diclofenac and ibuprofen compared to placebo (RR 1.76; p=0.0001, RR 1.70; p=0.0032 and RR 2.22; p=0.0253 respectively) but not significantly greater for naproxen (RR 0.84; p=0.48). The main limitation of this study was that low-normal dose COX-2 inhibitors were compared to high-dose nsNSAIDs (ibuprofen, naproxen and diclofenac) which are not routinely used in clinical practice. PRECISION (2016; n=24,081) was an active-controlled, double-blind, non-inferiority study in patients at an increased risk of cardiovascular risk with osteoarthritis and rheumatoid arthritis which compared the safety

profile of low-dose celecoxib with a PPI to high-dose ibuprofen or mid-high dose naproxen with a PPI. The primary composite outcome, defined as the first occurrence of an adverse event that met the ATPC criteria (i.e. death from cardiovascular causes) occurred in the celecoxib (2.3%), naproxen (2.5%) and ibuprofen (2.7%) arm (hazard ratio for celecoxib vs. naproxen, 0.93 [95% CI: 0.76 to 1.13]; hazard ratio for celecoxib vs. ibuprofen, 0.85 [95% CI: 0.70 to 1.04]; P<0.001 for noninferiority in both comparisons). The main limitation of the study was that low-dose celecoxib was compared to nsNSAIDs administered at mid-high doses for naproxen and high doses for ibuprofen that are not routinely used in clinical practice.

In terms of budget impact, celecoxib is expected to cost £3200 per annum compared to £1800 per annum for ibuprofen and £3150 for naproxen for an estimated 70 patients in NCL.

The Committee heard from Dr Burke that patients with cancer are at particularly high risk of GI adverse effects. In this cohort, potential longer-term cardiovascular risks are considered in the context of limited life expectancy, with overall prognosis more likely to be determined by the underlying malignancy. Dr Burke noted that the palliative care team spend significant time with patients weighing risks and benefits and making nuanced care decisions as a result. Dr Burke advised that opioids alone are often insufficient to manage inflammatory cancer-related pain, highlighting a significant unmet clinical need. A perceived risk of GI adverse effects with nsNSAIDs, even when co-prescribed with a PPI, may contribute to clinician reluctance to prescribe them, resulting in suboptimal pain control. NCL is a national outlier in terms of access to celecoxib. The Palliative Care Formulary lists celecoxib as the NSAID of choice in this setting. However, the Committee noted that the Palliative Care Formulary concluded that the GI risks doubled with celecoxib and diclofenac but quadrupled with high-dose ibuprofen/naproxen without a PPI as per the CNT (2013) study and therefore, comparisons were not made with normal-dose ibuprofen/naproxen with a PPI.The Committee questioned what the treatment approach would be in patients at very high risk of GI complications and Dr Burke noted that in this cohort both celecoxibs and nsNSAIDS would likely be avoided.

In camera, the Committee agreed that there is an absence of robust comparative evidence in the relevant clinical setting. The Committee acknowledged that current practice appears to be influenced by a perception that ibuprofen is associated with greater gastrointestinal adverse effects. It was noted that there is an opportunity to provide educational support, setting out the Committee's review of the evidence. In particular, the apparent differential gastrointestinal safety between celecoxib and ibuprofen co-prescribed with a PPI was based on trials with methodological limitations and unfair comparisons. Furthermore, large real-world observational studies were noted to demonstrate broadly similar rates of gastrointestinal complications with celecoxib and nsNSAIDs, whether prescribed with or without a PPI.

In summary, based on the evidence available and the Committee's concerns regarding potential bias in the supporting RCTs, the absence of consistent concomitant PPI use in studies, and the availability of effective analgesia alternatives with a similar risk profile to celecoxib, the Committee could not recommend the use of celecoxib for this indication. The Committee were supportive of developing and disseminating educational guidance to clinical teams summarising the Committee's evidence review, clarifying that the perceived superior gastrointestinal safety of celecoxib over ibuprofen co-prescribed with a PPI is not supported by robust comparative data and that real-world evidence demonstrates broadly similar GI complication rates.

Drug: Celecoxib 200mg daily tablets for 3-12 months.
Indication: To replace ibuprofen or naproxen (oral) with a proton pump inhibitor (PPI) for inflammatory cancer pain (including but not limited to soft tissue and muscle infiltration particularly common in sarcomas or bladder cancer, pleural or diaphragmatic disease, liver capsular pain or necrotic abdominal tumours) of any severity.
Decision: Not approved.
Additional information: Educational support to be provided to clinical teams on the perceived differential safety between celecoxib compared to ibuprofen + PPI.

9.3 Cefepime for infections (Applicants: Dr S De-Saram, UCLH; Dr M Blank, UCLH)

The Committee considered an application for cefepime, a fourth-generation cephalosporin, for the treatment of infections caused by bacteria that are cefepime-sensitive. Cefepime can be administered via intravenous use (bolus and infusion) or intramuscular use. The licensed dose varies in accordance with the severity of the infection but can range from 500mg 12-hourly to 2 grams 8-hourly. Cefepime is proposed to be used in the following settings with prior microbiology/ infectious disease approval:

- Directed therapy: Cefepime sensitive organism identified on microbiology sample where first-line options (e.g. piperacillin-tazobactam, ceftazidime) are not appropriate (due to resistance [e.g. AmpC beta-lactamases], intolerance or drug allergy)

- Empirical therapy: In patients with infections in which Pseudomonas is a likely causative organism but other first-line options (e.g. piperacillin-tazobactam, ceftazidime) are not appropriate (due to intolerance or drug allergy)

The application proposes to add cefepime to the Joint Formulary to reduce prescribing of carbapenems and fluoroquinolones. From an antimicrobial stewardship perspective, the UK Health Security Agency, has designated meropenem as a 'last resort' antibiotic. Similarly, the Infectious Diseases Society of America (IDSA) guidance recommends 'carbapenem-sparing' agents to preserve the activity of carbapenems for future, increasingly drug-resistant infections. Fluoroquinolones should only be prescribed when other commonly recommended antibiotics are inappropriate following a 2024 MHRA alert that highlighted the risk of disabling and potentially long-lasting or irreversible side effects.

Yahav et al (2007; n= 57 trials), a systematic review and meta-analysis, aimed to investigate the efficacy and safety of cefepime compared with other beta-lactam antibiotics. The review reported that all-cause mortality, the primary outcome, was higher with cefepime than other beta-lactams (RR: 1.26 [95% CI 1.08 to 1.49]). The study reported no significant differences between groups in clinical treatment failure, superinfection, or adverse events. The study authors discuss possible explanations for the mortality signal. Firstly, neurological adverse events such as non-convulsive status epilepticus and encephalopathy can be difficult to recognise in elderly patients and delay in diagnosis may have contributed to increased mortality. Secondly, the authors attribute this to discrepancies between results in vitro and in vivo which have been described in other trials of cefepime.

Harris et al (2015; n= 11 trials), a systematic review and meta-analysis, compared the effects of different antibiotics on mortality in patients with bloodstream infectious caused by Enterobacteriaceae with chromosomal AmpC beta-lactamase. The study concluded that there was no strong evidence to suggest that cefepime was inferior to carbapenems. No statistical difference in mortality was found between cefepime versus carbapenems as definitive therapy (OR: 0.61 [95% CI 0.27–1.38]) or empirical therapy (OR: 0.60 [95% CI 0.17–2.20]).

In terms of safety, the Committee were informed that symptoms of neurotoxicity are a recognised adverse effect as listed in the product license. The SPC states that these symptoms "*resolved after discontinuation of cefepime*" and "*most cases occurred in patients with renal impairment who received doses of cefepime that exceeded the recommendations*".

The ACORN trial (2023, n= 2,511), an open-label, parallel-group, randomised comparative safety trial, investigated whether use of cefepime and piperacillin-tazobactam affects the risks of acute kidney injury (AKI) or neurological dysfunction. The trial recruited adults who were initiated on anti-pseudomonal antibiotics within 12 hours of presentation to the hospital. The study found treatment with cefepime or piperacillin-tazobactam did not increase the risk of AKI or death (OR: 0.95 [95% CI 0.80 – 1.13]; p= 0.56). However, treatment with cefepime was associated with increased risk of neurological dysfunction (OR: 0.79 [95% CI 0.65 – 0.95]), a secondary outcome. Key limitations of the study were the open-label design, and that the study was only conducted at one site.

In terms of budget impact, cefepime is more costly than meropenem and is expected to cost approximately £7,400 to £15,800 for 40 patients per annum.

The Committee heard from Dr De-Saram and Dr Blank that the intention is to use cefepime in a limited subset of patients requiring an antimicrobial agent with anti-pseudomonal activity where concomitant coverage for staphylococcal and Gram-positive organisms may also be necessary. The applicants highlighted that ceftazidime, currently the preferred agent for penicillin-allergic patients within this cohort, does not provide coverage for staphylococcal and Gram-positive organisms. In these circumstances, treatment will likely require escalation to meropenem, which clinicians are reserving as a last-line antimicrobial agent. Dr De-Saram and Dr Blank acknowledged the evidence regarding the risk of neurotoxicity with the use of cefepime. However, the Committee were informed that other antibiotics, such as carbapenems, piperacillin-tazobactam, and fluoroquinolones are also associated with neurotoxicity, a phenomenon documented within the available evidence. The applicants outlined measures to mitigate the risks of neurotoxicity and emphasised that initiation of cefepime will require prior approval from microbiology or infectious disease specialists following a patient-centred risk-benefit assessment. Dosing will strictly adhere to the licensed dosing regimens, including appropriate dose adjustment in renal impairment, with close monitoring of renal function throughout treatment. The applicants explained that cefepime use would predominantly occur in the ITU setting, where daily microbiology or infectious disease ward rounds would ensure the effects of cefepime would be closely monitored.

In camera, the Committee were satisfied that cefepime demonstrates comparable efficacy to that of piperacillin-tazobactam and meropenem. The Committee acknowledged the rationale underpinning the

application, particularly in relation to antimicrobial stewardship and motivations for reducing the use of carbapenems and fluoroquinolones, and were satisfied that appropriate mitigations were in place to reduce the risk of neurotoxicity

In summary, the Committee approved the addition of cefepime to the Joint Formulary subject to detailed clarification and specification of the target patient group and infection criteria.

Drug: Cefepime; as per licensed dose
Indication: See post-meeting note
Decision: Approved subject to details on the target patient group and infection criteria (see post-meeting note)
Prescribing status: Restricted to secondary care only (Red)
Funding source: In tariff
Fact sheet or shared care required: N/A
Additional information: N/A

Post-meeting note: The applicants provided an update for the proposed indication, which was approved via Chairman's Action:

- Directed therapy - Cefepime sensitive organism identified on microbiology sample where first-line options (e.g. piperacillin-tazobactam, ceftazidime) are not appropriate (due to resistance [e.g. AmpC beta-lactamases], intolerance or drug allergy) and where meropenem would otherwise be the treatment of choice.
- Empirical treatment - In patients with infections, e.g. HAP/CAP, neutropenic fever, in which Pseudomonas is a likely causative organism but other first-line options (e.g. piperacillin-tazobactam, ceftazidime) are not appropriate (due to intolerance or drug allergy or the need for broader spectrum cover compared to ceftazidime) and where meropenem might otherwise be used.

10. Position statements and guidelines

Nil

11. Sub-Group Updates

11.1. NICE TA Implementation Group Report

Nil

11.2. NCL Pathways Group

Nil

11.3. Interface Prescribing Group Updates

Ms Sanghvi notified the Committee that the Interface Prescribing Group has developed a new process for consulting and approving RAG statuses, and will now report into the NCL ICB Medicines CRG. Regular reports will therefore no longer be brought to NCL JFC however any decisions made by the IPG or Medicines CRG which impact on JFC decisions or ratifications will be brought back to JFC for noting.

12. Next meeting

Thursday 19th March 2026

13. Any other business

Nil