Joint Formulary Committee (JFC): Minutes

Minutes from the meeting held on 16th April 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	✓	
Mr S Richardson	WH, Chief Pharmacist		✓
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 S Amin	IPMO Programme Team, Lead Pharmacist	✓	
Ms I Samuel	RFL, Formulary Pharmacist	✓	
Ms N Patel	RFL, Formulary Pharmacist	✓	
Ms A Abdullahi	RFL, Formulary Pharmacist	✓	
Mr K Cahill	RFL, Deputy Chief Pharmacist	✓	
Mr S O'Callaghan	UCLH, Formulary Pharmacist	✓	
Mr A Barron	UCLH, Deputy Chief Pharmacist	✓	
Mr D Sergian	MEH, Formulary Pharmacist	✓	
Mr W Li	MEH, Formulary Pharmacist	✓	
Ms A Bathia	RNOH, Formulary Pharmacist	✓	
Ms N Mistry	RNOH, Formulary Pharmacist	✓	
Mr J Flor	WH, Lead Pharmacist	✓	
Ms J Collins	WH, Formulary Pharmacist	✓	
Ms B Balci	WH, Formulary Pharmacist	✓	

Ms M Thacker	GOSH, Deputy Chief Pharmacist	✓	
Ms H Thoong	GOSH, Formulary Pharmacist	✓	
Ms J Modha	NHSE, Specialist Commissioning Pharmacy Advisor	✓	
Dr R Shah	UCLH, Clinical Pharmacology Specialist Registrar	✓	
Dr C Zeicu	UCLH, Clinical Pharmacology Specialist Registrar	✓	
Ms A Khanom	RFL, Lead Specialist Clinical Commissioning Pharmacist	✓	
Dr C Primus	UCLH, Consultant Cardiologist	✓	
Dr B Freudenthal	RFL, Consultant Endocrinologist	✓	
Ms G Glass	RFL, Endocrinology Pharmacist	✓	
Dr A Lima Soares	UCLH, Specialist Doctor in Medical Microbiology	✓	
Ms P Panesar	UCLH, Lead Antimicrobial Pharmacist	✓	
Ms C Cleetus	UCLH, Senior Rotational Pharmacist (Observer)	✓	
Ms A Niemet	UCLH, Lead Pharmacist (Medicine and Emergency Services) (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 19th March 2026

Minutes and abbreviated minutes of the 19th March 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	DTC Decision and Details	JFC recommendation
April 2025	**Reviewed by:** JFC **Drug:** Combined hormone contraception (CHCs) **Dose:** 30mcg ethinylestradiol preparation preferred for 21/7 regimen or extended/tricycling regimen; avoid within first 12 months post-menarche unless contraception required. **Indication:** i) First-line treatment of menstrual dysfunction in adolescents and ii) First-line treatment of androgen excess in adolescents **Decision:** Approved **Prescribing status:** **GREEN** – suitable for primary care initiation **Funding source:** In tariff **Additional information:** Approved as historical standard of care practice based on the April 2025 JFC application for drosperinone. Proposed green status in line with NCL primary care pathways for heavy menstrual bleed and chronic pelvic pain.	**To add to the NCL Joint Formulary**
April 2025	**Reviewed by:** JFC **Drug:** Desogestrel **Dose:** 75mcg daily in line with license **Indication:** Second-line treatment of menstrual dysfunction in adolescents **Decision:** Approved **Prescribing status:** **GREEN** – suitable for primary care initiation **Funding source:** In tariff	**To add to the NCL Joint Formulary**

	Additional information: Approved as historical standard of care practice based on the April 2025 JFC application for drosperinone. Proposed green status in line with NCL primary care pathways for heavy menstrual bleed and chronic pelvic pain.	
November 2024	**Reviewed by:** GOSH **Drug:** Enoxaparin **Dose:** As per BNFc and GOSH guidelines (available for local adaptation) **Indication:** Prophylaxis and treatment of symptomatic VTE in paediatric patients ≥ 2 months old and ≥ 10kg **Decision:** Approved **Prescribing status:** **RED** – restricted to secondary care prescribing only **Funding source:** In tariff **Additional information:** Update to the May 2024 JFC decision based on updated GOSH guidelines (Nov 2024). Dosing and recommendation match BNFc recommendation.	**To add to the NCL Joint Formulary**
November 2024	**Reviewed by:** GOSH **Drug:** Dalteparin **Dose:** As per BNFc and GOSH guidelines (available for local adaptation) **Indication:** Prophylaxis and treatment of symptomatic VTE in patients < 10kg **Decision:** Approved **Prescribing status:** **RED** – restricted to secondary care prescribing only **Funding source:** In tariff **Additional information:** Update to the May 2024 JFC decision based on updated GOSH guidelines (Nov 2024). Dosing and indication match BNFc recommendation.	**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. NCL JFC Strategic Updates

Ms Coughlan provided an update on developments with the Single National Formulary (SNF) and the merger of the NCL and North West London ICBs into West & North London ICB.

9. Medicine Reviews

9.1 Acetazolamide for acute decompensated heart failure (Applicants: Dr C Primus, UCLH; Dr C Whelan, RFL (in absentia))

The Committee considered an off-label application for acetazolamide, a carbonic anhydrase inhibitor, for the following indications:

- In patients admitted with acute decompensated heart failure (ADHF), presenting with severe congestion or anasarca, requiring high doses of intravenous loop diuretics,
- In patients admitted with furosemide-induced metabolic alkalosis, often with hypernatremia

ADHF is a progressive and often rapid worsening of symptoms of heart failure with high rate of emergency admission for intravenous therapy with loop diuretics such as furosemide. Acetazolamide is licensed for abnormal retention of fluid, in conjunction with other diuretics, at doses of 250-375mg daily. However, this application proposes to use 500mg IV acetazolamide daily for up to 5 days, which is higher than the licensed dose for this indication but within the dose range for other indications such as glaucoma and epilepsy.

Acute decompensated heart failure

The proposed place in therapy is as an adjunctive option with IV furosemide with or without metolazone where there is an insufficient response to maximal dose, or where limiting or reducing the dose of other diuretics would be advantageous. Acetazolamide will only be initiated under the advice of the cardiology or heart failure team, and its use will be reviewed daily by the team. The use of acetazolamide for this indication is acknowledged by the European Society of Cardiology (ESC) in the 2023 Focused Update; however, it notes that "*further data on outcomes and safety are needed*"

In terms of efficacy, the ADVOR trial (2022, n= 519) was a randomised placebo-controlled trial, that investigated whether the addition of acetazolamide to standardised intravenous loop-diuretic therapy would improve the incidence of successful decongestion among patients with acute decompensated heart failure. The trial recruited patients with ADHF with clinical signs of volume overload, NT-proBNP over 1000 pg/mL or a BNP level of more than 250 pg/mL to receive either IV acetazolamide (500mg once daily) or placebo added to standardised loop diuretics (at a dose equivalent to twice the oral maintenance dose). For the primary endpoint, the study reported that the addition of acetazolamide to standardised loop diuretic therapy was associated with a higher incidence of successful decongestion within 3 days after randomisation compared to placebo (42.2% versus 30.5%; RR: 1.46 [95% CI 1.17 to 1.82], p<0.001). The addition of acetazolamide was also associated with a shorter duration of hospital stay (secondary endpoint) compared to patients who received placebo (8.8 days versus 9.9 days; RR: 0.89 [95% CI 0.81 to 0.98]). However, there was no statistically significant difference between the two groups for death from any cause or rehospitalisation for heart failure (secondary outcome). The study reported that treatment with acetazolamide was associated with higher cumulative urine output and natriuresis. Subgroup analysis showed that patients who were receiving a higher maintenance dose of loop diuretics (over 60mg furosemide equivalent) appeared to have less benefit (RR of successful decongestion: 1.08 [95% CI 0.76 to 1.55]) than those who were receiving a lower maintenance dose (RR: 1.78 [95% CI 1.33 to 2.36]).

The Committee heard the key limitations of the ADVOR trial. It was noted that patients may have been under-dosed in the comparator arm as the dose of loop diuretics was capped at twice the daily oral maintenance dose of diuretics for the first two days after enrolment. In clinical practice, substantially higher doses or continuous infusions are utilised, therefore, the under-dosing of the comparator arm may result inflation of the benefit of acetazolamide. Although escalation of therapy was permitted from day 3 after enrolment, the primary study outcome was assessed one day later, which may be too soon for the loop diuretic dose escalation to have become fully effective. Finally, the absolute difference in congestion score between the acetazolamide and placebo group was noted to be small with overlapping 95% confidence intervals.

The Committee also heard results from the ORION-A trial (2025, n= 416), an open-label, prospective, multi-centre, randomised trial that assessed the efficacy and safety of oral acetazolamide in addition to standard therapy in patients with ADHF. Patients were randomised to receive either 250mg oral acetazolamide three times a day or standard therapy, defined as an increasing dose of loop diuretics with no cap. The study reported that there was no statistically significant difference in successful decongestion within 72 hours of randomisation (primary outcome) between the acetazolamide group and the standard therapy group (39.6% versus 39.7%, p= 0.983). However, the addition of acetazolamide to standard therapy resulted in increased diuresis in the first 72 hours (p= 0.028), and increased natriuresis on the second day (p= 0.04) after randomisation compared to those who received standard therapy. The key limitations of the ORION-A trial were that the acetazolamide was administered orally, with the theoretical concern of lower bioavailability.

In terms of safety, the ADVOR trial reported that the incidence of adverse events was similar across both arms during the treatment phase and during the 3-month follow-up. Similarly, the ORION-A trial that reported the incidence of adverse events were similar in the two trial groups.

The anticipated budget impact is estimated to be approximately £1,800 per annum for 24 patients across NCL. However, this cost is likely to be offset by reduction in the length of hospital stay, as per the ADVOR trial.

Furosemide-induced metabolic alkalosis

Loop diuretics can cause hypokalaemic metabolic alkalosis, an electrolyte disorder characterised by low potassium, raised serum bicarbonate and associated with symptoms such as muscle cramps, twitching, numbness, and confusion. The application proposes the use of acetazolamide, which increases renal bicarbonate excretion, for the treatment of furosemide-induced metabolic alkalosis in a level 2 setting (CCU or ITU). It would be used in patients who have failed to decongest and require intensification of diuretic therapy, with acetazolamide either added to, or substituted for, furosemide - alongside down-titration or cessation of furosemide — depending on the severity of the alkalosis until biochemical resolution is achieved. Acetazolamide will be initiated only under the guidance of the cardiology or heart failure team, with daily review.

In terms of efficacy, the Committee noted the dearth of available literature for this indication. Addison et al (2023, n= 35), a multi-centre retrospective cohort study, aimed to determine the effectiveness of IV and oral acetazolamide for patients with heart failure and diuretic-induced metabolic alkalosis. The study reported that IV acetazolamide resulted in significantly decreased bicarbonate within 24 hours of administration. The Committee were informed that there was no head-to-head evidence against potassium replacement or the addition of potassium sparing diuretics such as amiloride or spironolactone where not already taken.

In terms of safety, the safety profile of acetazolamide was extrapolated from the ADVOR trial which reported that the incidence of adverse events was similar across both arms.

The Committee heard from Dr Primus that in clinical practice, patients with ADHF do not receive sufficiently high doses of diuretics or reach a limit of effect to loop diuretics. The European Society of Cardiology has attempted to standardise the management of ADHF by recommending starting IV loop diuretics at 1-2 times the patient's chronic oral dose on admission. Therefore, the application seeks to encourage earlier involvement of cardiology and specialist heart failure teams upfront with the intention of initiating acetazolamide, alongside a loop diuretic at the outset in admitted patients with ADHF, as per the ADVOR trial.

The Committee discussed the results of the two trials in ADHF, which yielded different findings. The ADVOR trial, which capped the loop diuretic dose for the first 48 hours, concluded that the addition of acetazolamide resulted in more rapid decongestion. In contrast, the ORION-A trial, which permitted escalation of loop diuretics to the maximum tolerated dose, found no significant benefit from the addition of acetazolamide. It is therefore possible that up-titration of loop diuretics alone may achieve a degree of decongestion comparable to that obtained with the combination of furosemide and acetazolamide. Dr Primus explained, however, that patients hospitalised with ADHF and significant fluid retention (defined as oedema above the knee), reach a limit of effect with IV loop diuretics, and that the rationale for this application is to enhance diuresis early in the admission, prior to the onset of diuretic resistance thereby reducing their length of stay. The Committee also noted that, in the ADVOR trial, all patients received an intravenous magnesium infusion as part of the study protocol. Dr Primus clarified, however, that the overall incidence of hypomagnesaemia in this patient population is low, and that routine magnesium supplementation is unlikely to be required during the three days of acetazolamide administration proposed in this application.

Regarding the metabolic alkalosis indication, Dr Primus noted that the use of acetazolamide is already established practice at other centres, including Barts Health NHS Trust, a major tertiary cardiology centre. On its place in therapy, Dr Primus clarified that conventional approaches to correcting metabolic alkalosis, namely reduction of the loop diuretic dose, addition of a potassium-sparing diuretic, or potassium replacement, would be attempted first. Acetazolamide would be reserved for patients in whom potassium cannot be adequately managed by these measures, such as those with deteriorating renal function.

In camera, the Committee acknowledged the substantial limitations of the evidence base, including the suboptimal comparator used in the ADVOR trial and the null findings of the ORION-A trial where an appropriate comparator was used. The possibility that the null findings in ORION-A might have been due to the oral route of administration rather than the lack of superiority of acetazolamide compared with clinical uptitration of loop diuretics was also discussed. The use of acetazolamide to increase diuresis and natriuresis in patients with ADHF is supported by its mechanism of action and pharmacokinetic profile. The Committee further noted that acetazolamide is an inexpensive and relatively safe agent with a long-established clinical track record and was reassured by the safeguards proposed, initiation under cardiology input only, and daily review. Finally, the Committee recognised that this represents established practice across cardiology centres in London, and that alignment by NCL would be the most pragmatic approach to ensure equity of access for heart failure patients.

In summary, the Committee approved the addition of acetazolamide to the Joint Formulary subject to detailed clarification and specification of the patient cohort and initiation criteria.

Drug: Acetazolamide IV, 500mg daily for up to 3 days
Indication: See post-meeting note
Decision: Approved subject to clarifications on the place in therapy and initiation criteria for both indications
Prescribing status: Restricted to secondary care only (Red) – Cardiology or heart failure teams only
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:

- For ADHF (initiation by HF/Cardiology only) in patients presenting with severe congestion or anasarca (oedema above the knee), requiring high doses of IV loop diuretics, in whom concurrent optimisation of mineralocorticoid receptor antagonist has already taken place based on renal function, the inpatient admission episode is anticipated exceed 7 days and where one or more of the following apply:
  a. patients have reached a limit of effect with IV loop diuretics
  b. where limiting or reducing the dose of loop diuretics would be advantageous
  c. there is contraindication to SGLT2i as another drug class acting on the proximal tubule i.e. TIDM, catheter, intolerance/ allergy

- In patients admitted with furosemide-induced metabolic alkalosis, where hypokalaemia and metabolic alkalosis have failed to correct either by down titration of the loop diuretic, potassium replacement, mineralocorticoid receptor antagonist therapy, amiloride or some combination.

9.2 Lithium for thyrotoxicosis (Applicant: Dr B Freudenthal, RFL)

The Committee considered an application for lithium modified release (MR) in the short-term management of thyrotoxicosis where thioamides (carbimazole, propylthiouracil) have failed or are contraindicated. Thyrotoxicosis is a clinical syndrome arising from an excess of circulating thyroid hormones, most commonly attributable to Graves' disease, toxic multinodular goitre, or solitary toxic adenoma. Although mortality is low when definitive treatment is administered, untreated disease is associated with increased mortality owing to complications including atrial fibrillation, heart failure, and thyroid storm.

The proposed lithium dose is 400 mg nightly, titrated to a serum lithium concentration of 0.2–0.6 mmol/L. The proposed place in therapy is second line, where thioamides have failed or are contraindicated. The use of lithium for thyrotoxicosis is recognised by the American Thyroid Association (2016) and is included in guidance from UpToDate (2026) and BMJ Best Practice (Graves' disease, 2024). The Committee was informed that the use of lithium for this indication is established practice at RFL, where treatment is initiated and monitored by endocrinologists, with repeat prescriptions issued in primary care.

In terms of efficacy, Kristensen et al (1976, n= 24), conducted an open label randomised controlled trial recruiting patients with newly diagnosed and untreated thyrotoxicosis who were randomised for treatment with either methimazole 40mg, or lithium carbonate titrated to serum lithium level 0.5 - 1.3 mmol/L. The study reported that lithium carbonate and methimazole both resulted in a reduction in free thyroxine after 10 days (primary outcome) with mean falls of 38.1% and 43.3% respectively. Both lithium carbonate and methimazole also resulted in reduction in serum thyroxine iodine after 10 days (secondary outcome), with mean falls of 27.0% and 30.3%, respectively.

In terms of safety, McKnight et al (2012, n= 385 studies), a systematic review and meta-analysis of the toxicity profile of lithium, reviewed trials of patients with mood disorders treated with lithium. The study authors reported that the incidence of grade 3 or higher adverse drug reactions greater was low, with nephrogenic diabetes insipidus and hypothyroidism identified as the most clinically significant. However, the review was limited by inconsistent or incomplete reporting of doses and serum concentrations, and by target serum lithium levels typically higher than those proposed in the present application. Therefore, the review cannot establish the relative safety of low doses of lithium. It was further noted that the SmPC states that "*side effects are usually related to serum lithium concentrations and are less common in patients with plasma lithium concentrations below 1.0 mmol/L.*"

In terms of budget impact, the anticipated cost is approximately £1000 per annum for 15 patients, but it was recognised that this is historical practice and therefore already within existing drug spend.

The Committee heard from Dr Freudenthal that lithium serves as a second-line bridging therapy for these patients who are intolerant of thioamides whilst they await definitive treatment with radioactive iodine or thyroidectomy. Definitive treatment may be delayed for a variety of reasons, including patient-specific factors and capacity constraints within the service. During this time, patients typically attend community clinics for blood tests, with follow-up appointments conducted via telephone consultation under the endocrinology service. Dr Freudenthal highlighted that, although the use of lithium in thyrotoxicosis is unlicensed, it is established practice at RFL and endorsed by several guidelines. At RFL, serum lithium monitoring and dose adjustments are undertaken solely under the advice of the endocrinology team in secondary care. It was further noted that some peripheral sites do not have on-site inpatient pharmacies, precluding local dispensing, which may inconvenience patients. Interruption of treatment carries clinically significant consequences, potentially resulting in deterioration and further delays in accessing definitive treatment, as patients are required to remain stable and euthyroid in the interim. The Committee discussed the proposal that prescribing of lithium in thyrotoxicosis be transitioned from secondary to primary care, with monitoring and dose adjustment advice being retained in secondary care. The committee expressed reservations with this proposed approach because the proposed use is anticipated to be short-term pending definitive treatment, for a very small cohort of patients, for the off-label use of a drug that requires therapeutic dose monitoring.

In camera, the Committee was satisfied that there was evidence of clinical benefit for lithium carbonate in the treatment of thyrotoxicosis. The Committee acknowledged the interface issues highlighted by Dr Freudenthal; however, it was strongly felt that prescribing should remain within secondary care, with implementation and delivery of medicines addressed by pharmacy teams at Trust-level to ensure that patients do not encounter undue challenges in obtaining their medicines.

In summary, the Committee agreed to clinically approve the addition of lithium for thyrotoxicosis to the NCL Joint Formulary for secondary care prescribing only. The Committee further noted that the implementation of this decision, and any arrangements for the delivery of medicines to patients, should be addressed by acute Trust pharmacy teams.

Drug: Lithium, 400mg nightly titrated to a serum lithium concentration of 0.2–0.6 mmol/L
Indication: Treatment of thyrotoxicosis where thioamides have failed or are contraindicated
Decision: Approved
Prescribing status: Restricted to secondary care only (Red)
Funding source: In-tariff
Fact sheet or shared care required: N/A
Additional information: N/A

9.3 Aztreonam with Avibactam for infection caused by carbapenem resistant Gram-negative bacteria (most commonly MBLs) in patients where alternatives cannot be used (Applicant: Dr A Soares, UCLH)

The Committee considered an application for aztreonam-avibactam (loading dose: 2g/0.67g followed by a maintenance dose of 1.5g/0.5g every 6 hours), a monobactam antibiotic combined with a B-lactamase inhibitor, for licensed treatment of infections caused by carbapenem resistant Gram-negative bacteria where alternatives cannot be used (most commonly those producing metallo-beta-lactamases (MBLs)).

The Committee heard that treatment options are currently limited to ceftazidime-avibactam with aztreonam or cefiderocol for all patients including those with a mild penicillin allergy (rash). However, MBLs are increasingly resistant to cefiderocol based on local resistance profiles (Baltas et al (2024)). For patients with severe penicillin allergy (anaphylaxis), patients currently receive combination therapies which include amikacin or colistin. These are not preferred due to their toxicity profiles and the need for combined use of multiple antibiotics.

The rationale for omitting ceftazidime from the combination therapy is to reduce the risk of C. diff and to allow use in patients with penicillin allergy. Omission of ceftazidime is not considered detrimental to achieving the same therapeutic effect. Additionally, ceftazidime-avibactam needs to be co-administered at the same time as aztreonam due to a synergistic clinical effect. However, co-administration is challenging in practice if there is not enough line space or there are vascular issues which may result in sub-therapeutic efficacy. However, the Committee noted that ceftazidime-avibactam with aztreonam appear to be physically compatible when diluted to 100mL using compatible diluents (0.9% sodium chloride or 5% dextrose or lactated ringer's) and given via a Y-site. While there was no data on the chemical stability of the combination it was deemed to have an overall theoretical low risk of clinically meaningful chemical degradation because the Y-site contact time is brief (seconds to minutes), which is substantially shorter than known degradation half-lives (hours) of the individual components.

The Committee noted that aztreonam–avibactam is proposed for use in paediatric patients, although it is not currently licensed for this population. Two dose-determination studies are ongoing, with both trials actively recruiting outside the UK. Aztreonam and avibactam (in combination with ceftazidime) are individually licensed for paediatric use. The Committee was informed of anecdotal experience from Great Ormond Street Hospital indicating favourable outcomes with aztreonam–avibactam, and that the proposed dosing is consistent with the trial protocol. However, differences between the trial protocol and existing licensed paediatric dosing were noted. Specifically, the trial protocol uses a combination of weight and creatinine clearance (CrCl) to determine dosing for all patients; the CrCl-based dosing is lower than in current licensed regimens, which may present a risk of subtherapeutic exposure and potential resistance; and aztreonam and avibactam are administered four times daily in the trial protocol, compared with three times daily in licensed use.

The Committee noted that there is no direct efficacy data comparing ceftazidime-avibactam with aztreonam to aztreonam-avibactam. The Committee noted indirect efficacy data by Falcone et al (2021; n=102) comparing ceftazidime-avibactam with aztreonam to other antibiotics, but did not focus on this small, observational study as the intervention and comparators were not considered relevant and the study design was subject to bias.

REVISIT (2025; n=422) was a, Phase III, active-comparator controlled, open-label, central assessor masked, parallel group trial to compare the efficacy and safety of aztreonam-avibactam and meropenem ± colistin for adult patients with complicated intra-abdominal infection or HAP/VAP with confirmed/suspected Gram-negative bacteria (of which 64% of patients had a Gram-negative pathogen). Patients were randomised to aztreonam-avibactam or meropenem ± colistin via block randomisation. The primary endpoint, clinical cure at the test-of-cure visit in the intention-to-treat group, was not better with aztreonam-avibactam compared to meropenem ± colistin (68.4% vs. 65.7). Key limitations of the study were the open-label design, low patient

numbers with MBLs in each arm, the comparator arm was not a suitable comparator for MBLs, the study sponsor was involved in all aspects of the study and potential confounding from additional use of antibiotics for other micro-organisms.

ASSEMBLE (2025; n=15) was a Phase III, active-comparator controlled, open-label, central-assessor-blinded, randomised study for hospitalised patients with confirmed MBL-positive Gram-negative bacteria. Patients were randomised to aztreonam-avibactam (n=12) or best available therapy (n=3; of which 1 patient did not receive treatment due to patient decision). The primary endpoint, adjudicated clinical cure rate at the test-of-cure visit on day 28, was better with aztreonam-avibactam compared to best available therapy (42% vs 0%). Key limitations of the study were the small sample size, open-label design and unknown medicines used in the best available therapy arm which may not have been truly representative of current clinical practice.

In terms of safety, aztreonam-avibactam had a lower risk of adverse drug reactions compared to ceftazidime-avibactam with aztreonam. This is because the omission of ceftazidime is deemed to result in a reduced risk of *C. difficile* and is useful in patients with allergy to beta-lactams and cephalosporins.

Aztreonam–avibactam is considered more convenient because it involves administration of a single agent. However, it is given four times daily, compared with three times daily for the combination of ceftazidime–avibactam plus aztreonam. In the dual-agent regimen, the total daily dose of aztreonam is the same, while the total daily dose of avibactam is 25% lower.

In terms of budget impact, aztreonam-avibactam is expected to cost an additional £315,000 per annum across NCL, compared to ceftazidime-avibactam with aztreonam.

The Committee heard from Dr Soares that aztreonam-avibactam will be particularly beneficial in patients with severe penicillin allergy due to limited alternatives that are associated with additional toxicities, resistance or may not be suited to the micro-organism being treated. The Committee asked further about the clinical unmet need, considering the significant cost of the proposal, and heard that in the current patient cohort treated with ceftazidime-avibactam with aztreonam there has not been any discontinuation of treatment due to intolerance, toxicities or incidents of *C. difficile* as a result of treatment. To prevent further prescribing creep, a report can be generated on a regular basis from an existing registry to ensure treatment is restricted to the approved patient cohort. Treatment with aztreonam-avibactam would be recommended by infection specialists only, usually following MDT approval, and closely monitored with a clear stopping criteria (resistance, lack of efficacy, adverse drug reactions or resolution of symptoms). For patients with an unknown penicillin allergy status or severity of allergy, an alternative therapy would be used, or a test dose of the existing option of ceftazidime-avibactam with aztreonam would be considered to see if it is tolerated.

Great Ormond Street Hospital representatives reported that aztreonam-avibactam was approved for paediatric use locally at the end of 2024, based on the trial dosing protocol, which has not been associated with subtherapeutic exposure in their experience. However, they are awaiting further evidence before confirming the proposed dosing for routine clinical practice.

In camera, the Committee raised concerns about whether the significant cost of aztreonam-avibactam was justified by the marginal advantages in safety and convenience. On the convenience aspect, it was noted that investigations into compatibility suggested line access challenges can be mitigated by co-administration of ceftazidime-avibactam and aztreonam via a Y-site. From a safety perspective the Committee noted that alternative treatment options with amikacin or colistin-based combinations are available for patients with severe penicillin allergy (documented anaphylaxis). Ceftazidime-avibactam with aztreonam is still proposed to be used for patients with mild allergy or as a potential test dose for patients with uncertain allergy status. . There have been no documented discontinuations of current ceftazidime-avibactam with aztreonam therapy due to intolerance, toxicity, or incidents of *C. difficile* infection.

In summary, based on the available evidence, and the lack of a clear unmet clinical need that justifies the high cost of treatment, the Committee was unable to recommend aztreonam–avibactam for routine use. However, it was acknowledged that, in rare cases, for patients with severe penicillin allergy (documented anaphylaxis) who are contraindicated for, resistant to, or have failed suitable alternative therapies, aztreonam-avibactam may be appropriate on an individual, case-by-case basis, subject to one-off Trust approval. The Committee also recommended that Great Ormond Street Hospital review their formulary position on aztreonam-avibactam, considering the JFC outcome.

Drug: Aztreonam-avibactam infusion (loading dose: 2g/0.67g followed by a maintenance dose of 1.5g/0.5g every 6 hours)
Indication: For the treatment of infections caused by carbapenem resistant Gram-negative bacteria where alternatives cannot be used (most commonly those producing metallo-beta-lactamases (MBLs))
Decision: Not approved

Additional information: Aztreonam-avibactam may be considered on an individual case-by-case basis for patients with severe penicillin allergy (documented anaphylaxis) who are contraindicated for, resistant to, or have failed suitable alternative therapies (amikacin and colistin combination therapies), subject to one-off Trust approval.

10. Position statements and guidelines

Nil

11. Sub-Group Updates

11.1. NICE TA Implementation Group Report

Nil

11.2. NCL Pathways Group

Nil

12. Next meeting

Thursday 21st May 2026

13. Any other business

Nil