Joint Formulary Committee (JFC): Minutes

Minutes from the meeting held on 21st November 2024

		Present	Apologies
Members			
Prof A Hingorani	NCL JFC Chair		✓
Dr B Subel (Chair)	NCL JFC Vice Chair	✓	
Ms L Coughlan	NCL ICB, Deputy Chief Clinical Officer & ICS Chief Pharmacist	✓	
Ms W Spicer	RFL, Chief Pharmacist	✓	
Dr P Jasani	RFL, DTC Chair		✓
Dr K Boleti	RFL, DTC Chair		✓
Dr A Scourfield	UCLH, DTC Chair	✓	
Mr J Harchowal	UCLH, Chief Pharmacist	✓	
Dr K Tasopoulos	NMUH, DTC Chair	✓	
Ms S Stern	NMUH, Chief Pharmacist		✓
Dr M Kelsey	WH, DTC Chair	✓	
Mr S Richardson	WH, Chief Pharmacist	✓	
Dr S Ishaq	WH, Consultant Anaesthetist	✓	
Dr A Worth	GOSH, DTC Chair		✓
Ms J Ballinger	GOSH, Chief Pharmacist		✓
Dr M Henley	RNOH, DTC Chair	✓	
Mr A Shah	RNOH, Chief Pharmacist	✓	
Prof A Tufail	MEH, DTC Chair		✓
Ms N Phul	MEH, Chief Pharmacist		✓
Ms K Delargy	NLMHP, Partnership Deputy Chief Pharmacist	✓	
Ms L Reeves	NLMHP, Chief Pharmacist		✓
Dr L Waters	CNWL, Consultant Physician in HIV		✓
Ms R Clark	NCL ICB, Assistant Director of Medicines Optimisation	✓	
Ms M Kaur-Singh	NCL ICB, Head of Medicines Planning & Operations	✓	
Dr D Roberts	NCL ICB, Clinical Director (Islington)	✓	
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 C Tse	IPMO Programme Team, JFC Principal 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 S Amin	IPMO Programme Team, Lead Pharmacist	✓	✓
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	✓	
Dr S Unadkat	UCLH, Consultant Rhinologist	✓	
Dr P Harrow	UCLH, Consultant Gastroenterologist	✓	
Ms J Pang	IPMO Programme Team, Lead Pharmacist	✓	
J H Yeo	UCLH, Gastroenterology Registrar	✓	
Dr D Ryan	Clinical Pharmacology Registrar	✓	
Ms A Blochberger	NHSE, Chief Pharmacist – Specialised Commissioning	✓	
Ms A Husain	UCLH, Lead women's Health and Neonates Pharmacist	✓	
Dr J Bignall	NMUH, Sexual Health Consultant	✓	

2. Meeting attendees

Dr Subel welcomed members, observers, and applicants to the meeting (see above). The Committee thanked Dr Dominic Roberts and Ms Katherine Delargy for their contribution to the Committee and wished them luck for their future endeavours. The Committee thanked Ms Sonali Sanghvi (IPMO Programme Team, JFC Principal Pharmacist) for her contributions to the Committee and extended their best wishes for her maternity leave. The Committee welcomed Ms Cecilia Tse who has been appointed to cover the role of JFC Principal Pharmacist.

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. Dr Bignall declared interests from the manufacturer for Slynd® (Exeltis).

4. Minutes and abbreviated minutes of meetings on 17th September and 21st October 2024

Minutes and abbreviated minutes of the September and October 2024 meeting were ratified.

5. Review of action tracker

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

6. JFC Outstanding items and workplan

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

7. Local DTC recommendations/minutes

Date	Drug and Indication	DTC Decision and Details	JFC recommendation
September 2024	Bleomycin injection for symptomatic vascular anomalies/ malformations	**Reviewed by**: RFL **Drug**: Bleomycin injection. Adults: Maximum of 15mg per sclerotherapy procedure. Maximum lifetime cumulative dose 100mg. Child: Maximum	To add to the NCL Joint Formulary

		0.25mg/kg in a single session. Maximum lifetime cumulative dose 1 mg/kg (upper weight limit of dosage restricted to 100kg, therefore maximum lifetime cumulative dose is 100mg). **Indication**: Symptomatic vascular anomalies/ malformations **Decision**: Approved **Prescribing status**: Restricted to secondary care only **Funding source**: Divisional budget **Additional information**: Include information wrt how Bleomycin will be prescribed on EPMA. Include cytotoxic waste management in the protocol. Provide update to the committee in one years' time on safety and efficacy of Bleomycin. **Fact sheet or Shared Care required**: N/A	
September 2024	[FOC Scheme] Lenacapavir (Sunlenca®) for multidrug resistant HIV*†	**Reviewed by**: RFL **Drug**: Lenacapavir (Sunlenca®); 600mg oral od for day 1 and 2. On treatment Day 8, the recommended dose is 300 mg taken orally. Then, on treatment Day 15, 927 mg administered by subcutaneous injection and every 6 months thereafter **Indication**: Multidrug resistant HIV **Decision**: Approved **Prescribing status**: Restricted to secondary care only **Funding source**: FOC scheme funded by the manufacturer on a named patient basis. **Additional information**: Ensure RFL Trust legal team has reviewed the FOC scheme agreement. **Fact sheet or Shared Care required**: N/A	FOC approved by RFL - NCL recommendation to await national (NHSE) guidance.
September 2024	[FOC Scheme] Sotatercept for pulmonary arterial hypertension*†	**Reviewed by**: RFL **Drug**: Sotatercept; subcutaneous injection every 3 weeks. Starting dose of 0.3 mg per kilogram at visit 1, escalated to a target dose of 0.7 mg per kilogram at visit 2 (day 21, with a window of ±3 days). Patients will continue to receive a dose of 0.7 mg per kilogram unless a reduction is warranted according to the protocol **Indication**: Pulmonary arterial hypertension **Decision**: Approved **Prescribing status**: Restricted to secondary care only **Funding source**: Compassionate access scheme (named patient FOC) **Additional information**: Confirm dosing in RFL protocol aligns with STELLAR trial and FDA Sotatercept guidance. Explore options for reimbursement of delivery costs of Sotatercept to patients. Provide update to the committee in one years' time on safety and efficacy of Sotatercept.	Reviewed by RFL without NCL circulation by JFC (applicability to other trusts to be confirmed)

		Fact sheet or Shared Care required: N/A	
September 2024	Sirolimus Gel (Hyftor®) for facial angiofibroma secondary to tuberous sclerosis complex disease	**Reviewed by**: RFL **Drug**: Sirolimus gel; 800mg gel (1.6mg sirolimus) BD **Indication**: Facial angiofibroma secondary to tuberous sclerosis complex disease **Decision**: Approved **Prescribing status**: Restricted to secondary care only **Funding source**: Divisional budget **Additional information**: Provide topical administration guidance for patients. Development and documenting of patient outcome measures. **Fact sheet or Shared Care required**: N/A	Reviewed by RFL without NCL circulation by JFC (applicability to other trusts to be confirmed)
October 2024	Ivabradine for postural orthostatic tachycardia syndrome (PoTs)	**Reviewed by**: UCLH **Drug**: Ivabradine **Indication**: Ivabradine for postural orthostatic tachycardia syndrome (PoTs) patients with predominant tachycardia or hyperadrenergic symptoms on the advice of cardiology or the autonomic unit **Decision**: Approved **Prescribing status**: Suitable for secondary care initiation, primary care continuation – referred to NCL JFC for review **Funding source**: In tariff **Additional information**: Requires discussion at NCL Shared Care Group **Fact sheet or Shared Care required**: Yes – to be discussed	To add to the NCL Joint Formulary – Prescribing status to be discussed at NCL Shared Care Group
October 2024	Clonidine for postural orthostatic tachycardia syndrome (PoTs)	**Reviewed by**: UCLH **Drug**: Clonidine **Indication**: Clonidine for postural orthostatic tachycardia syndrome (PoTs) patients with predominant hyperadrenergic symptoms on the advice of cardiology or the autonomic unit **Decision**: Approved **Prescribing status**: Suitable for secondary care initiation, primary care continuation – referred to NCL JFC for review. **Funding source**: In tariff **Additional information**: Requires discussion at NCL Shared Care Group **Fact sheet or Shared Care required**: Yes – to be discussed	To add to the NCL Joint Formulary – Prescribing status to be discussed at NCL Shared Care Group
October 2024	[FOC Scheme] Daratumumab for cold agglutin disease*†	**Reviewed by**: UCLH **Drug**: Daratumumab 1800mg subcutaneously as per license dosing in multiple myeloma, continued until disease progression or unacceptable toxicity **Indication**: ≥ 3rd line option for patients with cold agglutinin disease who have ongoing uncontrolled	To add to the NCL Joint Formulary

		haemolysis, transfusion dependence and/or disabling acrocyanosis who are refractory to rituximab and chemotherapy for their underlying proliferative condition, who are not eligible for enrolment into a clinical trial. **Decision**: Approved **Prescribing status**: Restricted to secondary care only (haematology service) **Funding source**: Free of Charge Scheme **Additional information**: Nil **Fact sheet or Shared Care required**: N/A	
October 2024	Bortezomib for Waldenström macroglobulinaemia	**Reviewed by**: UCLH **Drug**: Bortezomib **Indication**: Relapsed Waldenström macroglobulinaemia **Decision**: Not approved	Not approved
October 2024	Prolonged course of metronidazole for remission of Crohn's post-ileocolonic resection	**Reviewed by**: UCLH **Drug**: Metronidazole; 400mg twice daily for 3 months **Decision**: JFC approved in line with UCLH Trust Guidelines **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

*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.

7.1 Penthrox® (Methoxyflurane) Ratification

The Committee considered the conditional decision by the Use of Medicines Committee (UMC) at UCLH, to approve the use of methoxyflurane (Penthrox®) for the management of pain during colonoscopy in patients where IV sedation is preferred but an escort cannot be arranged.

In September 2024, the UMC decision for Penthrox® was presented at the October 2024 JFC meeting for ratification. At the time, the Committee raised concerns regarding the clinical appropriateness of the use of Penthrox® when an escort cannot be arranged, and applicability to other NCL Trusts. Following the October meeting, the UMC minutes and supporting evidence was circulated to the NCL stakeholders for feedback. In summary, UMC have conditionally approved the use of Penthrox® for this indication based on the conditions that a local standard operating procedure (SOP) was developed and submitted to UMC for approval. UMC have asked for the following to be reported back: results after implementation (six months of data or after the first 20 patients, whichever is sooner), their experience, and data collected regarding patient pain scores, colonoscopy success rate, and inpatient bed avoidance. UMC supported the applicants and application to ensure clinical appropriateness was thoroughly discussed and mitigations were put in place for an initial pilot.

The Committee agreed to ratify the conditional decision by UMC as a pilot to take place at UCLH. Following the 6-month pilot at UCLH, the results will be presented at JFC for the Committee to consider the appropriateness of ratifying this application across NCL.

Reviewed by: UCLH
Drug: Methoxyflurane (Penthrox®)
Indication: Management of pain during colonoscopy in patients where IV sedation is preferred but an escort cannot be arranged

Decision: Conditionally approved pending development of local SOP. Data to be reported back to UMC 6 months (or 20 patients) after implementation.
Prescribing status: Secondary care only
Funding source: In-tariff
Fact sheet or Shared Care required: N/A

8. Matters arising

8.1. Cortiment® (budesonide multimatrix tablets) appeal and management of acute ulcerative colitis flare pathway (Applicant: Dr P Harrow, UCLH)

In March 2019, the Committee considered Cortiment® (budesonide multimatrix tablets) for induction of remission in mild-to-moderate ulcerative colitis where mesalazine is not sufficient and patients have an intolerance or contraindication to prednisolone. The Committee did not approve the use of Cortiment® as the Committee agreed that Cortiment® is less effective and more expensive than oral prednisolone. Additionally, there was no direct or indirect evidence available to suggest Cortiment® would be associated with a lower risk of steroid-related side effects.

In September 2023, the Committee considered an appeal on the grounds that the original decision was based on inaccurate or incomplete information. During this appeal, four pieces of evidence was submitted focusing on 1) the mechanism of action and pharmacokinetic profile, 2) the cortisol level suppression relative to prednisolone, 3) the indirect corticosteroid-related adverse effect profile compared to prednisolone and 4) inclusion in the British Society of Gastroenterology (BSG) 2019 guidelines. In terms of the management of acute ulcerative colitis (UC) pathway, licensed, colonic-release Cortiment® was intended to be used in a second line setting after mesalazine and in place of off-label, ileal-release budesonide capsules (Budenofalk®), in patients intolerant or contraindicated to prednisolone or patients at a higher risk of developing steroid-related side effects (e.g., diabetes, osteoporosis, hypertension, obesity, major psychiatric disorder, cardiovascular disease, stroke or previous steroid side effects). The Committee deferred the application for the use of Cortiment® in the proposed cohort until a consensus on the place in therapy was reached by NCL gastroenterologists across all interested NCL Trusts.

Following NCL wide consultation, the updated acute UC flare pathway was presented to the Committee. The Committee heard from Ms Patel that the proposed place in therapy for Cortiment® is within the mild to moderate proctitis and left-sided UC pathway when treatment with mesalazine alone is insufficient. In line with the evidence, it is not proposed to be used in severe or extensive disease. Oral prednisolone will remain the first line treatment. Cortiment® is proposed to be second line for patients who are intolerant to prednisolone or patients who are at high risk of steroid-related adverse drug effects such as diabetes, osteoporosis, severe psychiatric diagnosis, and glaucoma.

In terms of budget impact, Cortiment® was noted to be more expensive than Budenofalk® rectal foam, but less expensive than oral Budenofalk®. Overall, the decision to adopt Cortiment® is anticipated to be cost neutral.

The Committee heard from Dr Harrow that there is strong evidence to show that budesonide is less suppressing of the hypothalamic pituitary axis (HPA), which is associated with greater risk of adverse effects.

In camera, the Committee acknowledged that Cortiment® offers comparable efficacy to prednisolone in managing UC flares, with fewer corticosteroid-related adverse reactions, and without compromising patient care. It is expected that the total budget impact will be cost neutral due to the specific cohort of patients Cortiment® is intended to be used in. The Committee discussed whether Budenofalk® capsules (off-label) will be replaced by Cortiment® as a treatment option and whether the term 'not preferred' is used over 'non-formulary' or 'not approved' to indicate the more costly mesalazine formulations such as Mezavant XL® and Asacol® MR tablets on the pathway.

In summary, the Committee agreed to add Cortiment® to the NCL Joint Formulary for initiation in secondary care only. Furthermore, the Committee agreed to approve the acute UC flare pathway pending clarification on the status of Budenofalk® and the appropriate terminology to indicate mesalazine formulations are included on the NCL Joint Formulary.

Drug: Cortiment® (budesonide multimatrix tablets)
Indication: For the induction of remission in mild to moderate ulcerative colitis
Decision: Approved
Prescribing status: Restricted to secondary care only
Funding source: In tariff
Fact sheet or shared care required: N/A

Additional information: Acute UC flare pathway approved pending clarification on the status of Budenofalk® and the appropriate terminology to indicate which mesalazine formulations are included on the NCL Joint Formulary

9 Medicine reviews

9.1 Drospirenone for contraception (Applicant: Dr J Bignall, NMUH)

The Committee considered an application for drospirenone (Slynd®), a fourth-generation progestin and spironolactone analogue for contraception. The licensed dose for drospirenone is one tablet to be taken daily for 28 consecutive days: one white (active) tablet daily during the first 24 days and one green (inactive or placebo) tablet during the following four days (known as the 'hormone-free interval').

Drospirenone is proposed to be used as a second-line progestin-only contraceptive pill (POP), alongside levonorgestrel for women requiring POP contraception who do not have risk factors for potassium elevation (e.g., renal impairment, hypoadrenalism, concomitant use of potassium-elevating medicines). Presently, women who have attempted to use desogestrel (first-line POP) for a minimum of six months and are unable to tolerate it have limited alternative options within this drug class. Drospirenone offers a 24-hour missed pill window compared to other POPs (i.e., desogestrel and levonorgestrel) which have narrower missed-pill windows of 12 hours and 3 hours respectively.

Palacios et al (2019; n= 1571) reported two prospective, multicentre Phase III studies which aimed to demonstrate the efficacy and safety of drosperinone as a contraceptive pill. Study 1 (n= 724) was a nonrandomised, single-arm, open-label trial. Study 2 (n= 858) was a double-blind active-controlled, randomised controlled trial (RCT). Both studies recruited healthy women at risk of pregnancy aged 18 to 45 years. The study medication was one tablet containing 4mg drospirenone per day, with consecutive administration of 24 active tablets and four placebo tablets with no tablet-free interval between consecutive cycles. In Study 1, the duration of treatment intake was 13 cycles of 28 days. In Study 2, women were randomised to receive drospirenone or desogestrel 0.075mg (28 active pills) for 9 cycles.

In both studies, the primary outcome of interest was overall Pearl Index (PI), which reflects the number of contraceptive failures (i.e., pregnancies) per 100 women years of use. The overall Pearl index for drospirenone in Study 1 and 2 was 0.5106 [95% CI: 0.1053 to 1.4922] and 0.9715 [95% CI: 0.3154 to 2.2671] respectively. The overall Pearl index for desogestrel in study 2 was 0.5227 [95% CI: 0.0132 to 2.9124]. No statistical difference was found between the Pearl index for drospirenone and desogestrel indicating drospirenone provides similar clinical efficacy to its comparator, desogestrel.

Rates of overall or unscheduled bleeding or spotting was a secondary endpoint in Study 2. There was a significantly lower median number of unscheduled bleeding or spotting days for drospirenone compared to desogestrel (79.9% vs 86.5% for overall bleedings, p= 0.0324; 67.9% vs 86.5% for unscheduled bleedings, p <0.001). The median number of total bleeding days was shorter for drosperinone compared to desogestrel (10.0 days vs 12.0 days, p <0.05) during cycles 2 to 4. However, at cycle 7 to 9, the difference in median number of total bleeding days per cycle for women on drospirenone and desogestrel was not statistically significant (6.0 days vs 7.0 days). Drospirenone (3.3%) was also associated with fewer early study withdrawals associated with abnormal bleeding compared to desogestrel (6.6%)

Kimble et al (2020; n= 993), a prospective, open-label, single-arm, multicentre, Phase III trial aimed to evaluate the contraceptive efficacy and safety of drospirenone in sexually active, healthy, non-pregnant women aged 15 years and older. The primary outcome of interest was the Pearl index, which was reported to be 2.4 [95% CI: 1.2 to 4.2]. A key limitation of the study was that this was a single-arm, open-label study.

In terms of safety, side effects reported in Palacious et al and Kimble et al were mostly known side effects of POPs such as headache, acne, and irregular bleeding patterns. There were no cases of VTE reported across Palacious et al and Kimble et al. However, Palacious et al was not statistically powered to draw conclusions regarding the risk of venous thromboembolism (VTE). Hyperkalaemia is an adverse event of interest due to antimineralocorticoid activity of drospirenone. Palacious et al reported one patient who presented with an elevated potassium level of 5.7 mmol/L following completion of the study treatment, drospirenone. However, the patient did not present with any clinical signs of hyperkalaemia, and this was resolved within a week without medical intervention. Kimble et al reported five cases of asymptomatic hyperkalaemia, defined as two serum potassium measurements higher than the reference range of 3.5–5.3 mmol/L. One case of

hyperkalaemia was lost to follow-up, all remaining cases of hyperkalaemia resolved without sequelae. A notable limitation highlighted was the difference in methods of detection of hyperkalaemia; Palacious et al did not perform any routine blood tests, whereas Kimble et al checked urea and electrolytes (U&Es) of each patient every cycle which may result in increased rate of detection of hyperkalaemia in the latter trial.

In terms of budget impact, drospirenone is more costly than other POPs and is expected to cost approximately £9,000 for 150 patients per annum. However, the Committee were informed that women who are started on drospirenone are likely to have few other contraceptive options, and in the absence of alternative options, there may be increased costs associated with unplanned pregnancies.

The Committee heard from Dr Bignall that in secondary care sexual and reproductive health services, long-acting reversible contraceptives (LARC) are encouraged as first-line options as they are more effective than short-acting contraceptive methods (e.g., oral contraceptives) where effectiveness is user-dependent. The Committee were informed that baseline or routine U&Es are not expected to be carried out as it is anticipated only a small cohort of young women, with no significant co-morbidities or polypharmacy will be started on drospirenone by sexual and reproductive health consultants. Therefore, the risks concerning abnormal or undetected renal dysfunction in appropriately selected patients initiated on drospirenone are considered low. Dr Bignall explained that missed pill instructions are extensively covered during the treatment initiation consultation, when the first supply of drospirenone is made. Patients receive written instructions, directed to a website with additional guidance, and provided contact details for the clinic should they require any advice. The Committee noted that the initial JFC application proposed for drospirenone to be suitable for initiation in both primary and secondary are settings. Dr Bignall acknowledged that concerns regarding initiation of drospirenone could be mitigated by amending its prescribing status to initiation in secondary care and continuation by primary care only. This will also promote equity of access, so patients do not experience any disparity in accessing drospirenone if their primary care clinicians were uncomfortable initiating it while also ensuring patients receive comprehensive counselling at the point of treatment initiation.

In camera, the Committee questioned the place in therapy of drospirenone and the clinical advantages over desogestrel. The Committee were unconvinced of the improved bleeding profile of drospirenone and noted that drospirenone offered similar efficacy compared to desogestrel despite its wider missed-pill window. Due to the significant costs associated with drospirenone compared to alternative POPs, the Committee felt that stricter initiation criteria would be required to ensure only patients who would benefit most from drospirenone would be initiated on it.

In summary, the Committee agreed to defer the decision requiring the applicants to provide written details on proposed place in therapy; definition of the eligible patient cohort, and itemisation on operating procedure for initiation and monitoring; and clear itemisation of responsibilities (if any) to be placed on primary care for ongoing prescribing and monitoring.

Drug: Drospirenone; as per licensed dose
Indication: Contraception
Decision: Deferred pending written details on: 1) proposed place in therapy; 2) definition of the eligible patient cohort; 3) itemisation on operating procedure for initiation and monitoring; and 4) clear itemisation of responsibilities (if any) to be placed on primary care for ongoing prescribing and monitoring.

9.2 Ryaltris® (oloptadine hydrochloride and mometasone furoate monohydrate) for allergic rhinitis (Applicant: Mr S Unadkat, UCLH)

The Committee considered an application for Ryaltris® Nasal Spray, a combination treatment containing an intranasal antihistamine (olopatadine hydrochloride 600micrograms) and a corticosteroid (mometasone furoate monohydrate 25 micrograms) for the treatment of moderate to severe nasal symptoms associated with allergic rhinitis. It is licensed for use in adults and adolescents aged 12 years and above at the dose of two actuations into each nostril twice a day.

The proposed place in therapy was as per NCL Primary Care prescribing pathway for allergic rhinitis, which at the time of the meeting was being updated, with Ryaltris® being a fourth-line option alongside Dymista® (azelastine hydrochloride and fluticasone propionate) as an alternative in patients who cannot tolerate Dymista® or experience intolerable adverse side effects.

There are no head-to-head studies directly comparing the efficacy and safety of Ryaltris® against Dymista®. However, three efficacy and safety studies reviewed by the Swedish medicines regulatory agency were accepted for licensing within the EU via the mutual recognition process. The two confirmatory phase 3 studies compared Ryaltris® with its individual components (olopatadine or mometasone) and placebo. Studies conducted by Gross et al., Hampel et al., and Segall et al. provide evidence for the short- and long-term efficacy and safety of Ryaltris® in patients with allergic rhinitis.

Gross et al (2019, n=1176) was a phase 3, randomised, double-blind, parallel-group, multi-site study in adolescents and adult patients with seasonal allergic rhinitis (SAR) during the autumn and winter (mountain cedar pollen) season. Patients aged 12 years and above with a positive skin prick test result for relevant allergens (wheal diameter ≥5 mm greater than negative control) and minimum average morning and evening 12-hour reflective Total Nasal Symptom Score (rTNSS) of 8 or higher (out of 12) and a morning congestion score of 2 or more were recruited. Patients were randomised 1:1:1:1 to intranasal twice-daily Ryaltris® (665 mcg of olopatadine and 25 mcg of mometasone), olopatadine (665 mcg), mometasone (25 mcg), or placebo for 14 days. Mean change from baseline in average morning and evening 12-hour rTNSS was the primary endpoint. Ryaltris® significantly improved the average morning and evening 12-hour rTNSS from baseline to the end of 14-day treatment compared to placebo (LSMD -1.09 [95% CI=-1.49 to -0.69; P<0.001) and compared to each individual monotherapy component (P=0.03 vs olopatadine, and p=0.02 vs mometasone). The average morning and evening 12 hours instantaneous TNSS (iTNSS), was assessed as a secondary endpoint. Ryaltris® improved average morning and evening 12-hour iTNSS from baseline to the end of 14-day treatment compared to placebo (LSMD= -0.94 [95% CI=-1.32 to -0.56; p<0.001) and both monotherapy components (p=0.035 vs olopatadine; P=0.008 vs mometasone). Limitations of the study include the short duration, seasonal specificity, and reliance on self-reported symptoms, which may introduce subjectivity and reporting bias.

Hampel et al (2019, n= 1180), a phase 3, double-blind, randomised, parallel-group study in patients with seasonal allergic rhinitis during the spring pollen season, is a follow up study to Gross et al. Patients aged 12 years who met the same inclusion criteria for Gross et al were recruited. Study participants were randomised to one of four intranasal treatments for 14 days (2 sprays per nostril twice daily): Ryaltris®, olopatadine monotherapy (665 mcg), mometasone furoate monotherapy (25 mcg), and placebo. The primary end point was the mean change from baseline in the average A.M. and P.M. 12-hour rTNSS. Additionally, the instantaneous TNSS (iTNSS), also assessed. The study reported that Ryaltris® significantly improved the average 12-hour morning and evening rTNSS from baseline to end of 14-day treatment compared to placebo (LSMD = -0.98 [95% CI = -1.38 to -0.57; p<0.001) and olopatadine (p=0.003), but this was not statistically significant compared to mometasone (p=0.059). Ryaltris® also demonstrated significant and clinically meaningful improvements in average morning and evening 12-hour iTNSS from baseline to the end of the 14-day treatment compared with placebo (LSMD= -0.93 [95% CI = -1.28 to -0.58; p<0.001) and when compared against monotherapy arms (p=0.005 versus olopatadine; p=0.041 versus mometasone).

Segall et al (2019, n=601), a randomized, double-blind, parallel-group study evaluated the efficacy and safety of Ryaltris® in patients with perennial allergic rhinitis (PAR). Patients aged 12 years and older were randomised to receive Ryaltris® (olopatadine 665 mcg and mometasone 25 mcg) or a placebo for 52-weeks. Patients were randomised 4:1:1 to twice-daily Ryaltris (olopatadine 665 mcg and mometasone 25 mcg [pH 3.7]) or two GSP301 vehicle formulations (placebo, pH 3.7 or 7.0). At weeks 6 and 30, Ryaltris® provided significant and clinically meaningful improvements in the average rTNSS and iTNSS versus placebo pH 3.7 ($p < 0.01$, all comparisons). Similarly, at week 52, GSP301 provided significant and clinically meaningful improvements in rTNSS (least-squares mean difference −0.91, [95% CI, −1.35 to −0.47]; $p < 0.001$), and iTNSS (least-squares mean difference −0.75 [95% CI, −1.17 to −0.33]; $p < 0.001$) versus placebo pH 3.7.

In terms of safety, Ryaltris® has a similar safety profile to Dymista®. The most common adverse reactions include dysgeusia, epistaxis and nasal discomfort; no serious treatment-related effects were reported in clinical trials. Hampel et al. reported dysgeusia to be the most common adverse event linked to Ryaltris (3.3%) compared to the placebo group (0%). Ryaltris® did not demonstrate any benefits of convenience over Dymista® as both preparations require twice daily dosing.

In terms of budget impact, Ryaltris® is less expensive than Dymista® respectively. The Committee were informed that Dymista® is expected to go off patent in August 2026, which may significantly reduce treatment costs when generic preparations are available. In an event of supply issue with Dymista®, an intranasal antihistamine and an intranasal corticosteroid can be prescribed separately resulting in a more cost-effective approach. However, there is a potential risk in causing compliance issues as patients are expected to use two separate preparations instead of one.

The Committee heard from Mr Unadkat that the aim of the NCL pathway was to standardise the treatment of allergic rhinitis across London. Mr Unadkat highlighted the request to have both Ryaltris® and Dymista® on the NCL Joint Formulary as an additional benefit in circumstances where there may be shortages of either preparation. The Committee also heard that anecdotally, Mr Unadkat has experience with prescribing Ryaltris® for patients in private practice and there was less incidence of bitter taste when compared to Dymista®.

In camera, the Committee discussed the lack of an unmet need for Ryaltris® as Dymista® was already on the NCL Joint Formulary. The Committee were not convinced of any additional therapeutic benefits of Ryaltris® compared to Dymista® and recognised that dysgeusia could be managed with patient counselling. It was recognised that Ryaltris® was currently the cheaper treatment option, however, concerns were raised regarding the challenges of switching patients to Ryaltris® and reverting to generic Dymista® preparations when Dymista® is expected to go off patent in 2026.

In summary, the Committee were unconvinced about the additional clinical benefits on patient outcomes of Ryaltris® over Dymista®; therefore, the Committee did not approve the use of Ryaltris® nasal spray in allergic rhinitis.

Drug: Ryaltris® nasal spray
Indication: Allergic rhinitis
Decision: Not Approved

10 Position Statements and Guidelines

10.1 NCL Choice of Direct Oral Anticoagulant (DOAC) Position Statement

The Committee approved the NCL JFC Position Statement on Choice of Direct Oral Anticoagulant (DOAC). This NCL JFC position statement supersedes two separate position statements on: 1) treatment of venous thromboembolism (VTE) and secondary prevention of VTE recurrence, and 2) prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation (NVAF). The NCL DOAC position statement recommends that generic apixaban and generic rivaroxaban should be considered as the first line treatment option across NCL where clinically appropriate for patients. There is currently no mandate to switch patients currently taking other DOACs, such as edoxaban or dabigatran, to apixaban or rivaroxaban Ms. Pang informed the Committee that an updated prescribing support document, which will provide further guidance on DOAC use in specific patient cohorts, is expected to be presented for sign-off in the coming months.

10.2 NCL JFC Terms of Reference

The Committee approved the updated NCL JFC Terms of Reference following a 2-week consultation period with NCL stakeholders.

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.

11.2 NCL Pathways Group

Nil

11.3 Shared Care Group Minutes and Updates

Minutes of the October Shared Care Group meeting was included for information.

12 Next meeting

Thursday 16th January 2025

13 Any other business

Nil