North Central London
Medicines Optimisation Network

Joint Formulary Committee (JFC): Minutes

Minutes from the meeting held on 15th December 2022

		Present	Apologies
Prof A Hingorani	NCL JFC Chair	✓	
Dr B Subel	NCL JFC Vice Chair	✓	
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; NCL ICS, Interim Chief Pharmacist	✓	
Dr R Urquhart	UCLH, Divisional Clinical Director	✓	
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		
Mr V Raman	RNOH, DTC Chair		✓
Mr A Shah	RNOH, Chief Pharmacist	✓	
Prof A Tufail	MEH, DTC Chair		✓
Ms N Phul	MEH, Chief Pharmacist		✓
Ms K Delargy	BEH, Chief Pharmacist		✓
Ms L Reeves	C&I, Chief Pharmacist		✓
Dr L Waters	CNWL, Consultant Physician in HIV		✓
Ms R Clark	NCL ICB, Head of Medicines Management (Camden)		✓
Mr P Gouldstone	NCL ICB, Head of Medicines Management (Enfield)	✓	
Ms E Mortty	NCL ICB, Interim Head of Medicines Management (Haringey)	✓	
Ms M Singh	NCL ICB, Head of Medicines Management (Barnet)	✓	
Mr A Dutt	NCL ICB, Head of Medicines Management (Islington)	✓	
Dr D Roberts	NCL ICB, Clinical Director (Islington)	✓	
Mr T Dean	Patient partner		✓
Ms S Amin	IPMO Programme Team, JFC Principal Pharmacist	✓	
Mr G Grewal	IPMO Programme Team, JFC Support Pharmacist	✓	
Ms S Maru	JFC Support Pharmacist	✓	
Ms P Varu	JFC Support Pharmacist	✓	
Ms I Samuel	RFL, Formulary Pharmacist	✓	
Mr H Shahbakhti	RFL, Formulary Pharmacist	✓	
Mr A Barron	UCLH, Principal Pharmacist	✓	
Mr S O'Callaghan	UCLH, Formulary Pharmacist	✓	
Ms A Sehmi	NMUH, Formulary Pharmacist	✓	
Ms H Thoong	GOSH, Formulary Pharmacist		✓
Mr D Sergian	MEH, Formulary Pharmacist	✓	
Ms H Weaver	NHSE, Specialised Commissioning Pharmacist	✓	

Ms A Blochberger	NHSE, Specialised Commissioning Pharmacist	✓	
Ms A Fakoya	NCL ICB, Contracts & Commissioning Pharmacist		✓
Dr A Hosin	UCLH, Clinical Pharmacology Registrar	✓	
Ms EY Cheung	NCL ICB, Deputy Head of Medicines Management (Camden)	✓	
Ms K Mistry	RNOH, Formulary Pharmacist	✓	
Ms S Ahmed	WH, Formulary Pharmacist	✓	
Ms M Thacker	RFL, Clinical Lead Pharmacist	✓	
Dr G Pollara	UCLH, Consultant in Infectious Disease	✓	
Ms D Cunningham	RFL, Specialist Pharmacist	✓	
Mr G Purohit	RNOH, Formulary Pharmacist		✓
Prof A Salama	RFL, Consultant Nephrologist	✓	
Ms J Bloom	MEH, Associated Chief Pharmacist	✓	
Dr M Thomas	UCLH, Consultant Haematologist	✓	
Ms C Gates	UCLH, Anticoagulation Pharmacist	✓	
Dr P Mallia	RFL, Respiratory Consultant	✓	
Dr K Roy	UCLH, Respiratory Consultant	✓	
Dr D Thompson	UCLH, Clinical Pharmacology Registrar	✓	

2. Meeting observers and members

Prof Hingorani welcomed members, applicants and observers to the meeting (see above). Ms Gillian Smith (RFL, DTC Chair) was noted to have stepped down from the Committee membership and was thanked for her valuable contributions to the Committee meetings. Dr Parag Jasani (RFL, interim DTC Chair), Dr Katia Boleti (RFL, interim DTC Chair) and Dr Vishal Raman (RNOH, DTC Chair) were welcomed as new members of the JFC.

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. Dr Mallia declared interests from the manufacturer of Bevespi and Trixeo (AstraZeneca).

4. Minutes of the last meeting

Minutes and abbreviated minutes were accepted as an accurate reflection of the November 2022 meeting.

5. Matters arising

5.1 Uromune for UTI prophylaxis

In October 2022, the Committee deferred an application for the use of Uromune® under an 18-month evaluation, pending the development of a patient selection criteria flowchart, a data collection form, agreed outcomes and a statistical analysis plan. The RFL and UCLH clinical teams presented these documents to the Committee for review. The Committee were informed that the study would compare outcomes in the 12-month periods before and after Uromune use. The cross-site evaluation will be useful to understand the efficacy of Uromune in different populations at UCLH (difficult-to-treat UTI patients) and RFL (renal transplant patients). The number of patients anticipated to enrol into the evaluation phase would be sufficient to detect a clinically important difference in UTI rates with 90% power and a 5% false positive rate, (based on the Lorenzo-Gomez et al (2022) study) in both populations independently and together.

In summary, the Committee approved the use of Uromune under an 18-month evaluation period for patients who fulfil the following patient selection criteria:

- Uromune is initiated in patients attending specialist clinics that have requested to use it.
- It is initiated in patients with recurrent (i.e., at least 2 treated UTIs in the past 6 months and at least 3 treated UTIs in the past year), and severe (i.e., patients that require hospitalisation with IV antibiotics for treatment of acute episodes or patients with difficult-to-treat UTIs due to the presence of multi-resistant organisms in urine cultures) UTIs.
- Patients have tried non-antibiotic prophylactic treatment options where suitable.
- MDT approval granted.

Decision: Approved under evaluation at UCLH and RFL only
Prescribing: Secondary care only

Tariff status: In tariff
Funding: Trust
Fact sheet or shared care required: N/A

6. Review of action tracker

Action tracker included for information.

7. JFC Outstanding Items & Work Plan

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

8. Local DTC recommendations / minutes

8.1 Approved

DTC site	Month	Drug	Indication	JFC outcome
UCLH	Jan 2020	Erythropoietin	For planned surgery in patients who refuse blood transfusions	**Decision:** Added to the NCL Joint Formulary **Prescribing:** Secondary care **Tariff status:** In tariff **Funding:** Trust **Factsheet or shared care required:** N/A
NCEM/ NPIS	Nov 2022	Glucarpidase	Category C antidote –now sourced from Oxford Pharmacy Store	**Decision:** Added to the NCL Joint Formulary **Prescribing:** Secondary care **Tariff status:** In tariff **Funding:** Trust **Factsheet or shared care required:** N/A
NCEM/ NPIS	Nov 2022	Uridine Triacetate	Category C antidote –now sourced from WEP Clinical	**Decision:** Added to the NCL Joint Formulary **Prescribing:** Secondary care **Tariff status:** In tariff **Funding:** Trust **Factsheet or shared care required:** N/A
NCEM/ NPIS	Nov 2022	Pralidoxime	Category C antidote –now sourced from Botulinum Antitoxin Holding Centres	**Decision:** Added to the NCL Joint Formulary **Prescribing:** Secondary care **Tariff status:** In tariff **Funding:** Trust **Factsheet or shared care required:** N/A
NCEM/ NPIS	Nov 2022	Prussian blue	Category C antidote –now sourced from Pralidoxime Holding Centres	**Decision:** Added to the NCL Joint Formulary **Prescribing:** Secondary care **Tariff status:** In tariff **Funding:** Trust **Factsheet or shared care required:** N/A

† 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. * Subject to funding consideration.

9. New Medicine Reviews

9.1 Appeal: Apixaban for VTE thromboprophylaxis for ambulatory cancer patients (Appellant: Dr M Thomas, UCLH and Ms C Gates, UCLH)

The Committee considered an appeal for apixaban 2.5mg BD, a direct-acting oral anticoagulant (DOAC), for primary VTE thromboprophylaxis for:

1. Newly diagnosed pancreatic cancer patients receiving chemotherapy.
2. Newly diagnosed cholangiocarcinoma patients receiving chemotherapy.
3. Newly diagnosed stage III/IV ovarian cancer patients receiving neo-adjuvant chemotherapy (NACT) before interval debulking surgery (IDS).

In May 2019, the Committee considered apixaban for several indications relating to VTE prophylaxis in ambulatory cancer patients. The Committee agreed that whilst the 3 cohorts listed above were sufficiently

high-risk to justify offering thromboprophylaxis, the evidence-base for DOACs was less convincing than for LMWH at the time. Apixaban was rejected on several grounds (and LMWH was approved instead). The appellants have offered a counter opinion to the May 2019 JFC minutes:

i) On the grounds that the Committee considered the cancer community to be in equipoise to use anticoagulation with any agent in the three indications (due to the placebo-controlled design of clinical trials), the appellant has stated that DOACs are now recommended in international guidelines and therefore there is no longer clinical equipoise in this matter.

ii) On the grounds that the Committee raised concerns of inappropriate continuation of DOAC thromboprophylaxis after chemotherapy cessation, the appellant has stated apixaban will be prescribed in secondary care only and stopped after the last cycle of chemotherapy.

iii) On the grounds that the additional cost and risk reduction associated with the use of DOACs would only be justified if long-term thromboprophylaxis was required and there were concurrent issues with LMWH adherence, the appellant stated that since approval, in the pancreatic cancer cohort, patients are not receiving thromboprophylaxis with LMWH due to patient inconvenience and injection burden, thus leaving patients without adequate anticoagulation.

The appellants requested use of apixaban in all stage III/IV ovarian cancer patients receiving NACT pre-IDS which differs from the indication outlined in the original application which requested use only in the intermediate to high-risk (Khorana score (KS) $\geq$ 2) patients within the overall cohort. The Committee were informed that the KS, a validated VTE risk assessment score, was deemed by NICE to be insufficiently accurate to recommend in clinical practice due to the low sensitivity and the need to take other risk factors into account. The Committee was informed that the appellants consider the KS to underestimate VTE risk in ovarian cancer as it is associated with a KS score of 1 (low-risk) despite having a reportedly high VTE incidence of 14.1% in an audit at UCLH. In comparison, various meta-analyses in all cancer types reported a KS> 3 was associated with an incidence rate of just 4 – 11%.

The appeal was made on grounds of significant new information available requiring reconsideration of the evidence. The Committee were presented with evidence from an updated Cochrane review (2020) which included both double-blind, placebo-controlled RCTs previously considered by the Committee (AVERT 2019 and CASSINI 2019), analysed in a meta-analysis conducted by JFC Support in May 2019. The Cochrane review also included the Levine 2012 study; when the Cochrane review excluded this study to reduce inter-trial heterogeneity due to incomplete outcome data and non-approved apixaban regimens, conclusions from both the JFC meta-analysis and the Cochrane meta-analysis were the same. A pooled analysis of the CASSINI and AVERT studies showed DOACs were not superior to placebo in terms of reducing symptomatic VTE (RR=0.57 [95% CI:0.29-1.14]) or symptomatic PE (RR=0.53 [95% CI:0.13-2.10]), whereas LMWH was superior for both outcomes (RR=0.62 [95% CI:0.46-0.83] and 0.60 [95% CI:0.42-0.88] respectively). Both DOACs and LMWH were associated with an increase in major bleeding when compared to placebo and no thromboprophylaxis (RR=1.95 [95% CI:0.88-4.30] and RR=1.63 [95% CI:1.12-2.35] respectively). Conclusions from this analysis were that LMWH were preferred in terms of safety and efficacy given the available evidence. From the results of the Cochrane review, the NNT was 40 for DOACs and 36 for LMWHs, and the NNH was 77 for DOACs and 111 for LMWHs, therefore, a similar number of patients would benefit from DOACs, although the risk of bleeding was higher.

The Committee also considered recommendations for DOACs for ambulatory cancer patients receiving SACT with intermediate to high risk of VTE from the ITAC 2022, ASH 2021 and ASCO 2020 guidelines. The Committee was informed that ITAC 2022 guidelines also recommended DOACs for the pancreatic cancer cohort based on a sub-group analysis conducted by Vadhan-Raj et al (2019, n=273) of high-risk (KS$\geq$2) ambulatory pancreatic cancer patients from the phase IIIb double-blind, placebo-controlled CASSINI 2019 study. Patients were randomised to apixaban 2.5mg BD or placebo. The study reported a statistically significant decrease in the primary composite endpoint of symptomatic deep vein thrombosis, asymptomatic proximal deep vein thrombosis, pulmonary embolism and VTE-related death (HR 0.35 [95% CI 0.13–0.97]; NNT=16), without an increase in major bleeding or clinically relevant non-major bleeding during treatment with rivaroxaban compared with placebo.

The Committee was presented with a prospective cohort study conducted in an NCL centre by Sayar et al (2022, n=249) detailing the local experience in ambulatory multiple myeloma patients receiving chemotherapy. The study compared outcomes in a cohort of patients before JFC approval for apixaban in multiple myeloma, compared to a cohort following approval. The study showed comparable rates of thrombotic, major bleeding

and clinically relevant non-major bleeding events between patients using apixaban and LMWH in both the historic and prospective cohorts.

The final evidence base considered was a head-to-head, multi-centre, prospective, open-label, RCT by Guntupalli et al (2020, n=400), assessing the safety and efficacy of 28 days of apixaban 2.5mg BD against enoxaparin 40mg OD in post-operative women with suspected or confirmed gynaecologic cancer. The Committee was informed that the post-operative population from the Guntupalli study was different from the pre-operative population in which DOACs were intended to be used in by the appellant, although it represented a data set comparing apixaban to LMWH in a closely related group of patients in the absence of data in the intended population. There were no statistically significant differences between both arms for major bleeding (OR: 1.04 [95% CI:0.07-16.76]), clinically relevant non-major bleeding (1.88 [95% CI:0.87-4.1]) and VTE events (1.57 [95% CI:0.26-9.50]).

In terms of budget impact, apixaban is cost-saving by approximately £3500 compared to LMWH in 170 patients. Approximately 30% of the ovarian cancer cohort will require district nurses to administer LMWH, representing an additional cost.

The Committee heard from Dr Thomas that the analysis of NNT looked at symptomatic VTE only, however, asymptomatic events are just as important due to the potential for eventually requiring surgery or filter support. Approximate NNT and NNH for use of any anticoagulation was presented; the number of VTE events prevented per 100 treated patients were greater than the harm caused by bleeding, with benefits increased in cohorts with a higher baseline VTE risk; however, the Committee recognised there is a fine balance between benefit and risk as the patient's baseline risk of bleed becomes increasingly worse. Dr Thomas stated that these patient cohorts have an unacceptably high thrombotic risk but anticoagulation is only initiated in those who do not have a higher bleeding risk, which is factored into a locally developed protocol. The Committee was also informed that apixaban would be prescribed by an oncologist in clinic only, with patient suitability re-assessed at each chemotherapy cycle and treatment cessation for the pancreatic and cholangiocarcinoma patients (or prior to interval debulking surgery for the ovarian cancer cohort).

In camera, the Committee acknowledged that all 3 cohorts represented a sufficiently high risk for VTE such that anticoagulation is required. The Committee agreed that while the confidence intervals from the Cochrane review for DOAC efficacy included the null hypothesis, which may be accounted for by the smaller total population size in the DOAC studies compared to the LMWH studies, the point estimates are consistent with a treatment effect consistent with that from the use of DOACs in other settings. The updated international guidance also demonstrated that the cancer community were no longer in equipoise and favoured DOACs over LMWH. In viewing all the available evidence, the Committee took a pragmatic view that DOACs would be of at least similar efficacy to LMWH, although there may be a higher baseline risk of bleeding in certain patients. To mitigate against this risk, the Committee recommended implementation of the protocol developed by the appellant to outline clinical information, exclusions and practical aspects for consideration. The Committee acknowledged that apixaban also offered the important additional convenience of oral therapy over LMWH which was regarded as an important consideration in this group of cancer patients, and was also cost-minimising.

In summary, the Committee approved the use of apixaban as primary VTE thromboprophylaxis for:

- Newly diagnosed pancreatic cancer patients receiving chemotherapy.
- Newly diagnosed cholangiocarcinoma patients receiving chemotherapy.
- Newly diagnosed stage III/IV ovarian cancer patients receiving neo-adjuvant chemotherapy (NACT) before interval debulking surgery (IDS).

Decision: Approved
Prescribing: Secondary care only
Tariff status: In tariff
Funding: Trust
Fact sheet or shared care required: N/A
Additional information: Prescribing protocol to be developed and implemented in each NCL centre to mitigate against potential risks

9.2 pMDI inhalers used for COPD

The Committee considered parallel applications for two inhalers licensed for use in the maintenance treatment of COPD; a dual LAMA/LABA combination pMDI (Bevespi®) and a triple ICS/LAMA/LABA pMDI (Trixeo®), both administered as two inhalations twice daily. Both inhalers are formulated in a novel 'aerosphere', which the manufacturer has claimed to have benefits of consistent delivery (despite shaking technique), improved stability and homogeneity compared to other pMDI devices (although this cannot be confirmed as there is no head-to-head data).

The proposed place in therapy was as per NCL COPD guidelines; at the time of the meeting these were being updated. Current guidance aligns with NICE recommendations (i.e., dual LAMA/LABA for patients limited with breathlessness without asthmatic features, and triple-therapy for patients with ongoing symptoms impacting quality of life or who have 1 severe or 2 moderate COPD exacerbations in the previous year), however were subject to change due to new international consensus statements which are under review. The Committee were also informed of a plan from LPP to create a pan-London inhalers formulary, and were reassured that LPP will be focusing on retrospective formulary decisions only (and hence any decision made by the Committee will not require amendments to the formulary status in other London ICS regions).

9.2.1 Bevespi® (LAMA/LABA dual combination inhaler)

PINNACLE 1 was a 24-week, 5-arm, randomised, double-blind, controlled study to compare the efficacy and safety of Bevespi® and either placebo or bronchodilator monotherapy for moderate to severe COPD (n=2,103). Patients were randomised to Bevespi or placebo, glycopyrronium monotherapy, formoterol monotherapy (all via the aerosphere device) or open-label tiotropium monotherapy DPI (via handihaler). The primary endpoint, change from baseline in morning pre-dose trough FEV_1 at week 24, was significantly better with Bevespi® compared to placebo (150mL [95% CI:110mL-190mL]), glycopyrronium monotherapy (59mL [95% CI:30mL-90mL]), and formoterol monotherapy (64mL [95% CI:40mL-90mL]), but was not significantly better than open-label tiotropium (21mL [95% CI:-10mL-50mL]). Key limitations of the study were the use of an open-label comparator, lack of a dual therapy comparator and relatively short duration of treatment/assessment.

PINNACLE 2 was a 24-week, 4-arm, randomised, double-blind, controlled study to compare the efficacy and safety of Bevespi® and either placebo or bronchodilator monotherapy for moderate to severe COPD (n=1,615). Patients were randomised to Bevespi or placebo, glycopyrronium monotherapy or formoterol monotherapy (all via the aerosphere device). The primary endpoint, change from baseline in morning pre-dose trough FEV_1 at week 24, was significantly better with Bevespi® compared to placebo (103mL [95% CI 70mL to 140mL]), glycopyrronium monotherapy (54mL [95% CI 30mL to 80mL]) and formoterol monotherapy (56mL [95% CI 30mL to 90mL]). Key limitations of the study were the lack of a dual therapy comparator, the impact on exacerbations were not assessed and relatively short duration.

The current COPD guidance endorsed by the JFC lists current LAMA/LABA options as Anoro® Ellipta (DPI) or Spiolto® Respimat (SMI). In terms of convenience, Bevespi® is the first LAMA/LABA pMDI option for patients who have poor inspiratory flow. Bevespi® has a significantly higher carbon footprint compared with both Anoro® and Spiolto®, though it was acknowledged pMDIs are likely to be used in only 20-30% of patients. Additional claims of convenience from the aerosphere device could not be proven as there is no head-to-head data available.

9.2.2 Trixeo (ICS/LAMA/LABA triple combination inhaler)

KRONOS was a 24-week, 4-arm, randomised, double-blind, controlled study to compare the efficacy and safety of Trixeo® and dual combination bronchodilator therapy for moderate to severe COPD (n=1,902). Patients were randomised to Trixeo®, Bevespi®, budesonide/formoterol dual combination pMDI (all via the aerosphere pMDI device) or open-label budesonide/formoterol DPI (administered via a Turbohaler). Primary endpoints were selected based on regulatory requirements in the region it was conducted in. The first primary endpoint, FEV_1 for the area under the curve from 0 to 4 hours ($AUC_{(0-4)}$) over 24 weeks, was significantly better with Trixeo® compared to budesonide/formoterol pMDI (104mL [95% CI 77mL to 131mL]) and budesonide/formoterol DPI (91mL [95% CI 64mL to 117mL]). The second primary outcome, pre-dose trough FEV_1 over 24 weeks, was significantly better with Trixeo® compared to budesonide/formoterol pMDI (74mL [95% CI 52mL to 95mL]) and Bevespi® (22mL [95% CI 4mL to 39mL]). Key limitations of the study were the potential inclusion of asthmatic patients, the inclusion criteria (which was not limited to patients with recent exacerbations, and hence potentially easier to treat), lack of a triple therapy comparator, and relatively short duration.

ETHOS was a 52-week, 4-arm, randomised, double-blind, controlled study to compare the efficacy and safety of full-dose Trixeo®, Trixeo® with half the usual ICS dose and or dual combination bronchodilator therapy for moderate to severe COPD (n=8,590). Patients were randomised to Trixeo® full dose, Trixeo® lower dose,

Bevespi® or budesonide/formoterol dual combination pMDI (all via the aerosphere pMDI device). The primary endpoint, the annualised rate of exacerbations at 52 weeks, was significantly lower with Trixeo® compared with Bevespi® (RR = 0.76 [95% CI 0.69 to 0.83]) and budesonide/formoterol pMDI (RR = 0.87 [95% CI 0.79 to 0.95]). In key secondary outcomes, the rate of severe exacerbations at 52 weeks was not significantly lower compared with Bevespi® (RR = 0.84 [95% CI 0.69 to 1.03]) but was significantly lower compared with budesonide/formoterol pMDI (RR = 0.80 [95% CI 0.66 to 0.97]). In another key secondary outcome, the risk of all-cause mortality at 52 weeks was significantly lower compared to Bevespi® (HR = 0.54 [95% CI 0.34 to 0.87]) but was not significantly lower compared with budesonide/formoterol pMDI (HR = 0.78 [95% CI 0.47 to 1.30]). Key limitations of the study were the potential inclusion of asthmatic patients, the use of ICS at baseline in 80% of patients which was abruptly discontinued in the Bevespi® group (who continued throughout the study without using maintenance ICS) and no licensed triple combination therapy comparator. The Committee were informed of post-hoc analyses to demonstrate that inclusion of further mortality data in 384 patients demonstrated similar significant improvements in mortality data versus Bevespi® although no significant difference versus budesonide/formoterol pMDI. A further post-hoc analysis claimed abrupt withdrawal of ICS did not cause an increase in mortality in the 30-, 60- and 90-day period immediately following ICS discontinuation in patients who used ICS at baseline. It was acknowledged that post-hoc analyses are hypothesis generating rather than hypothesis testing, and results should be interpreted with caution.

The current COPD guidance endorsed by the JFC lists current ICS/LAMA/LABA options as Trelegy® Ellipta (DPI) or Trimbow® (pMDI), and more recently Trimbow® NEXThaler (DPI) has also been added to the Joint Formulary. In terms of convenience, Trixeo® is claimed to be advantageous in containing similar components in the same device as Bevespi and was therefore the logical step-up in therapy from Bevespi and compared to Trimbow had data to support the benefits in mortality. Trixeo® has a lower carbon footprint compared to Trimbow® but is significantly higher than Trelegy®. Additional claims of convenience from the aerosphere device could not be proven as there is no head-to-head data available.

9.2.3 Committee discussion

In terms of safety, Bevespi and Trixeo were not expected to have a different adverse effect profile compared to other dual/triple combination devices currently used in NCL. In terms of budget impact, the cost of Bevespi® and Trixeo® are the same as other dual/triple combination devices on formulary in NCL. However, the patents of Bevespi and Trixeo are expected to remain available for several years longer compared to inhalers currently on formulary; the Committee was reminded that this does not guarantee cost savings, but the opportunity to switch to branded generics will come sooner with inhalers currently on formulary. The Committee was also reminded that new inhalers are expected on market in the next 10 years, especially as manufacturers seek to produce devices and propellants with a lower carbon footprint.

The Committee heard from Dr Mallia and Dr Roy that DPIs are routinely considered as a first choice if appropriate for the patient. However, there is a cohort of patients, particularly in the COPD cohort, who may benefit from a pMDI and hence the application for Bevespi®. There is currently no pMDI option available in the LAMA/LABA setting; the only alternative is Spiolto® Respimat (SMI), which takes a substantial amount of strength to prime before use. Trixeo® is requested as clinicians feel the evidence for improvements in COPD incidence and mortality is overwhelming, and it is felt that this isn't a class effect given Trixeo is a fixed triple-combination delivered via the novel aerosphere device. Future practice will gravitate towards more use of LAMA/LABA and triple-therapy devices (rather than monotherapies and ICS/LABA dual combination devices), hence adding both options to formulary would strengthen the armamentarium against COPD.

The Committee queried the lack of innovation from the pharma companies in the individual components used, and whether the populations and comparators used in the studies were appropriate; whilst clinicians would ideally prefer innovative therapies, these are not available yet and both Bevespi® and Trixeo® have demonstrated promising results. The Committee also discussed the availability of Trimbow® (a triple-therapy combination pMDI) which is already on the Joint Formulary; the clinicians personal choice would be to opt for Trixeo® due to available data, and to retain Trimbow for its use in COPD as well as asthma patients.

In camera, the Committee discussed the limitations in the clinical trial data, including discontinuation of ICS in the Bevespi® group in the ETHOS study, the design of the studies resulting in the intervention groups received more inhaler therapies than the comparator groups (i.e., resulting in an unfair test), and that claims of superior mortality data came from secondary outcomes only and which were not superior compared with dual budesonide/formoterol pMDI. The Committee considered there to be a lack of innovation and reviewed the claims of unmet need. The Committee noted that Bevespi® represented the first and only available pMDI in the dual combination LAMA/LABA therapy treatment line and concluded Bevespi® fulfilled an unmet need for

patients who were unable to utilise a dual LAMA/LABA DPI or SMI. However, compared to other triple therapy combination devices on the NCL Joint Formulary, Trixeo® did not fulfil an unmet need.

In summary, the Committee agreed to add Bevespi® to the NCL Joint Formulary for patients with moderate to severe COPD in accordance with the current and future use of dual LAMA/LABA combination therapy (where DPI or SMI devices are not appropriate). However, based on the evidence available and concerns that it does not fulfil an unmet need, the Committee could not recommend the use of Trixeo®.

Medication: Bevespi®
Decision: Approved
Prescribing: Primary and secondary care
Tariff status: In tariff
Funding: Trust/ICB
Fact sheet or shared care required: In accordance with NCL COPD guidelines (currently under review)

Medication: Trixeo®
Decision: Not approved

10. For noting: COVID-19 CAS alerts

The Committee discussed the publication of five CAS alerts for COVID-19 treatments. Notable amendments include the use of sotrovimab in exceptional cases only for non-hospitalised patients (previously optional first-line treatment) and hospital-onset patients (previously third-line), the option for combination treatment of baricitinib with IL-6 inhibitor (previously advised against simultaneous use), and use of remdesivir in children of all ages (previously ≥12 years only).

The Committee discussed the challenges posed by the national remdesivir shortage, and how this impacts the other therapies available to patients. Sotrovimab remained a possible option after MDT discussion if alternative therapies were not available or inappropriate. To conserve supplies, patients on remdesivir should have their duration of treatment reviewed regularly and stepped down as appropriate.

11. For noting: Letter to NICE and NHSE regarding DOAC use in atrial fibrillation

At the November JFC meeting, the Committee discussed new evidence for the use of DOACs in atrial fibrillation which suggested positive associations between the use of apixaban compared with other DOACs. The Committee agreed to escalate their concerns toNICE and NHSE. The Committee was presented with the letter which was sent to both NICE and NHSE addressing these concerns; the Committee was reminded that until the position is reviewed, the NCL position of DOAC preference remained in place.

12. Amendment to the NCL glucose & ketone monitoring for adults with diabetes guideline

The Committee were informed of a minor amend to the glucose & ketone monitoring for adults with diabetes guideline. The lancet recommendations for GlucoFix Tech was updated which reflected a change to the lancet device which comes with the meter. The Committee approved the amendment.

13. Next meeting

Thursday 19th January 2023

14. Any other business

14.1 Cannabis-based Medicinal Products

The Committee were presented with a letter from NHSE requesting support from clinical teams across the country to complete a registry for patients who are prescribed a cannabis-based medicinal products. Three products are on formulary in NCL (Sativex®, nabilone and Epidyolex®). JFC Support have written to the Arden and GEM CSU to understand whether completion of the registry is needed at initiation only or on an ongoing basis. The cannabis-based medicinal products position statement and the Sativex® shared care protocol will be updated when further information is known.