North Central London
Medicines Optimisation Network

JOINT FORMULARY COMMITTEE (JFC) – MINUTES

Minutes from the meeting held on 16 September 2019
G12 Council Room, South Wing, UCL, Gower Street, WC1E 6BT

Present:	Dr R Sofat	NCL JFC Chair	(Chair)
	Dr M Kelsey	WH, DTC Chair	
	Ms R Clark	Camden CCG, Head of Medicines Management	
	Mr S Semple	MEH, Chief Pharmacist	
	Dr R Urquhart	UCLH, Chief Pharmacist	
	Mr P Gouldstone	Enfield CCG, Head of Medicines Management	
	Ms I Shaban	Islington CCG, Deputy Head of Medicines Management	
	Ms P Taylor	Haringey CCG, Head of Medicines Management	
	Ms K Delargy	BEH, Deputy Chief Pharmacist	
	Ms W Spicer	RFL, Chief Pharmacist	
	Dr K Tasopoulos	NMUH, DTC Chair	
	Mr S Richardson	WH, Chief Pharmacist	
	Dr A Stuart	Camden CCG, GP Clinical Lead Medicines Management	
	Mr C Daff	Barnet CCG, Head of Medicines Management	
In attendance:	Dr P Bodalia	UCLH, Principal Pharmacist	
	Ms M Kassam	NCL JFC, Support Pharmacist	
	Mr G Grewal	NCL JFC, Support Pharmacist	
	Ms I Samuel	RFL, Formulary Pharmacist	
	Mr F Master	RFL, Formulary Pharmacist	
	Ms H Mehta	NMUH, Formulary Pharmacist	
	Ms Y Al-Hayali	MEH, Formulary Pharmacist	
	Mr G Purohit	RNOH, Deputy Chief Pharmacist	
	Dr J Sun	UCLH, Foundation Year 2 Doctor	
	Dr D Thompson	UCLH, Specialist Registrar in Clinical Pharmacology	
	Ms A Fakoya	NEL CSU, Senior Prescribing Advisor	
	Ms J Bloom	MEH, Associate Chief Pharmacist	
	Ms L Restrik	WH, Consultant Respiratory Physician	
	Mr S O'Callaghan	UCLH, MI and Governance Pharmacist	
	Mr E Khan	ULCH, Rheumatology Consultant	
	Mr J Sun	UCLH, Foundation Year 2 Doctor	
Apologies:	Ms K Davies	NEL CSU, Deputy Director Medicines Management	
	Prof D Hughes	RFL, Consultant Haematologist	
	Ms L Reeves	C&I, Chief Pharmacist	
	Prof L Smeeth	NCL JFC Vice-Chair	
	Dr A Bansal	Barnet CCG, GP Clinical Lead Medicines Management	
	Prof A Tufail	MEH, DTC Chair	
	Mr A Shah	RNOH, Chief Pharmacist	
	Mr S Tomlin	GOSH, Chief Pharmacist	
	Dr S Yardley	CNWL, Consultant in Palliative Medicine	
	Dr S Ishaq	WH, Consultant Anaesthetist	
	Mr T Dean	Patient Partner	
	Dr A Sell	RNOH, DTC Chair	
	Mr A Dutt	Islington CCG, Head of Medicines Management	

2. Meeting observers

There were no meeting observers.

3. Minutes of the last meeting

Alprostadil cream (Vitaros®) for erectile dysfunction was considered by the applicant to be suitable for initiation in primary care. The NCL STP Erectile Dysfunction pathway (version 10.7) recommends sildenafil and tadalafil are trialled in primary care and patients should be referred to urology if no response after 8 weeks "only if patient wishes to consider MUSE". The NCL STP pathway therefore does not allow for alprostadil cream to be initiated in primary care therefore the pathway should be updated in one or two directions; (1) update to allow initiation in primary care or; (2) update to remove the statement "only if patient wishes to consider MUSE" so that it is initiated in secondary care only. Camden CCG offered to liaise with the authors of the pathway and inform them of the addition of alprostadil cream to the NCL Joint Formulary and request that the pathway is updated. Whilst the pathway is updated, alprostadil cream should remain restricted to Secondary care initiation and suitable for *continuation* only in Primary care.

4. Matters arising

The July JFC minutes were updated to reflect the Committee's decision to ratify spironolactone for hirsutism in Polycystic ovary syndrome for use in UCLH.

4.1 Letrozole – switch to first line agent for ovulation induction

JFC support has contacted Professor Conway to address the action points raised during the last JFC and are awaiting a reply.

4.2 Cannabis-based medicinal products – NCL position statement

JFC Support informed the Committee that NICE has produced a draft guideline for cannabis-based medicinal products. This is currently under consultation, with the full guideline expected to be published in November 2019. The NCL position statement will be reviewed once the full NICE guideline has been published.

5. JFC Work Plan & outstanding actions

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

6. Declarations of relevant conflicts of interest

No additional declarations were noted for the new medicine applications.

7. Local DTC recommendations / minutes

7.1 Approved

DTC site	Month	Drug	Indication	JFC outcome
RFL	Jul-19	Tafamadis (Vyndaqel®)	EAMS: Treatment of transthyretin amyloidosis in adult patients with wild type or hereditary cardiomyopathy	Decision: RFL only Prescribing: Secondary care Tariff status: N/A Funding: FoC Fact sheet or shared care required: No
RFL	Jul-19	Bupivacaine 0.125% infusion via perineural stump catheter	Post-operative pain management following limb amputation for peripheral arterial disease to reduce post-operative opioid requirement	Decision: RFL only Prescribing: Secondary care Tariff status: In tariff Funding: Trust Fact sheet or shared care required: No

C&I	Sep-12	Oxazepam	Management of acute alcohol withdrawal in patients with severe liver disease where chlordiazepoxide is not appropriate	Decision: Added to NCL Joint Formulary Prescribing: Secondary care Tariff status: In tariff Funding: Trust Fact sheet or shared care required: No

8. New Medicine Reviews

8.1 Benzbromarone for treatment resistant gout (Applicant: Dr V Morris, UCLH)

The Committee reviewed an application for benzbromarone for treatment resistant gout. Benzbromarone was proposed for use in patients refractory or intolerant to prior treatment with allopurinol or febuxostat.

A randomised, un-blinded controlled trial compared benzbromarone to allopurinol both in combination with colchicine 0.5-1 mg daily for the first 6 months. The primary outcome was the proportion of participants who achieved a serum urate of ≤0.36 mmol/L. Seven patients crossed over from the allopurinol group to the benzbromarone group due to failure to achieve target serum uric acid. Target serum urate level was achieved in 94% of those treated with benzbromarone and 63% of those treated with allopurinol, p = 0.0442. Frequency of gouty bouts did not differ between the groups.

A separate but similar study had a primary outcome of proportion of participants who tolerated serum urate-lowering medication without adverse events and attained a serum urate ≤0.30 mmol/L. The primary outcome was achieved in 26% of allopurinol patients and 52% of benzbromarone patients (p= 0.049). There were no significant differences in the frequency of acute gout attacks observed between benzbromarone and allopurinol arms after 4 months.

A third study included a 2 months allopurinol monotherapy run in period. Participants who had not reached serum urate normalisation ≤0.30 mmol/L were randomised to benzbromarone or probenecid. The primary end point was the proportion of patients tolerating the drug and the proportion attaining target serum uric acid of ≤0.30 mmol/l. Target serum urate levels was achieved with 92% of those treated with benzbromarone and 65% of those treated with probenecid (p=0.03). Correspondingly the mean reduction of serum urate concentration from baseline was higher with benzabromarone than for probenecid (64% vs. 50%; p<0.001). There were no significant differences in the frequency of acute gout attacks observed between benzbromarone and probenecid.

With regards to safety, benzbromarone has not received FDA approval owing to concerns around hepatotoxicity. It has been approved in Europe, however the application has subsequently been withdrawn in 2003 by Sanofi due to further case reports of hepatotoxicity. There is no evidence that an approval is currently being sought again. Other common adverse effects include gastrointestinal adverse effects, especially diarrhoea.

Currently few agents are available for lowering of uric acid levels and patient intolerance is common. Febuxostat is available and on the treatment algorithm , although it was noted that a recent MHRA drug safety update issued this year has cautioned use of feboxostat in patients with pre-existing cardiovascular disease. Lesinurad, a similar URAT-1 inhibitor was rejected by NICE in 2018. This further limits the options available for treatment of gout.

Dr Khan informed the Committee that following treatment with allopurinol and febuxostat, patients may be offered a uricosuric agent: probenecid, sulphinphyrazone or benzbromarone. These uricosuric agents are not licensed in the UK. The main comparator to benzbromarone is probenecid, limited trials show superiority of benzbromarone over probenecid; however probenecid is favoured due to past reports of hepatotoxicity with benzbromarone. Sulphinpyrazone is poorly tolerated and therefore is not considered as a routine treatment option.

In term of annual treatment costs, benzbromarone costs £40 - £161 per patient compared with probenecid costs of £203 - £815 per patient.

In camera, the Committee agreed the evidence base for benzbromarone lacks high quality studies that inform on its efficacy and safety. The studies available were carried out with an open-label design which introduces bias and the primary outcomes were serum uric acid reduction rather than clinically relevant

endpoints, such as reduction in frequency or severity of gout attacks. The Committee agreed that there are very few pharmacological treatments available for this group of patients with drug intolerance being commonplace further limiting treatment options. There was concern over hepatotoxicity associated with benzbromarone and subsequent removal of its licence, however benzbromarone has been adopted elsewhere in the UK following a Specialist recommendation for use as second-line in guidelines issued by the British Society of Rheumatologist (for mild to moderate renal insufficiency) and EULAR. The Committee agreed benzbromrone should be prescribed only by a named consultant for a named patient; and due diligence is necessary to monitor patients appropriately particularly for hepatotoxicity.

The Committee requested that the following action points be clarified prior to approval to establish the preceding treatment options:

- ***Clarification on maximum dose of allopurinol***
- ***Clarification on treatment algorithm***

Decision: Deferred subject to development of an NCL treatment algorithm for gout.

8.2 Trelegy® & Trimbow® triple therapy inhalers for Chronic Obstructive Pulmonary Disease (Applicant: Dr L Restrick, WH)

The Committee considered an application for two separate combination inhalers, each containing a long-acting beta2 agonist (LABA), a long-acting muscarinic antagonist (LAMA), and an inhaled corticosteroid (ICS) to treat moderate to severe COPD in accordance with COPD NICE Guidance from July 2019; Trelegy®, a dry-powder inhaler (DPI) in an Ellipta device, and Trimbow®, a pressurised metered-dose inhaler (pMDI).

Supporting evidence from six randomised, double-blind, active-comparator studies (three for each inhaler). Trimbow demonstrated statistically significant improvements versus ICS/LABA pMDI Fostair® in mean difference from baseline of pre-dose FEV1 (81mL [95% CI 52mL to 109mL; p<0.001]) and 2-hour post-dose FEV1 (117mL [95% CI 86mL to 147mL; p<0.001]), and a non-significant improvement in dyspnoea score (transitional dyspnoea index score (0.21 [95% CI −0.08 to 0.51; p=0.160]). Trimbow also demonstrated a significantly reduced rate of moderate to severe COPD exacerbation compared to the LAMA DPI Spiriva® (RR = 0.80 [95% CI 0.69 to 0.92; p=0.0025]) and the LAMA/LABA combination DPI Ultibro® (RR = 0.85 [95% CI 0.72 to 0.99; p=0.043]). Trimbow demonstrated non-inferiority versus a combination of Spiriva® and Fostair given as triple-therapy in multiple devices (RR = 1.01 [95% CI 0.85–1.21]; p=0.89).

Trelegy was compared to the ICS/LABA DPI Symbicort® and was found to significantly improve mean pre-dose FEV1 from baseline (171mL [95% CI 148mL to 194mL; p<0.001]) and mean change in St. Georges' Respiratory Questionnaire score from baseline (−2.2 units [95% CI −3.5 to −1.0 units; p<0.001]); only the former reached the minimal clinically important difference. Trelegy demonstrated statistical significance in reducing the rate of moderate to severe COPD exacerbations compared to an ICS/LABA DPI Relvar® (0.85 [95% CI 0.80 to 0.90; p<0.001]) and a LAMA/LABA DPI Anoro® (0.75 [95% CI 0.70 to 0.81; p<0.001]). Trelegy was also compared to triple therapy administered in multiple DPI devices with Relvar® and LAMA DPI Incruse®, and this found non-inferiority in the mean change of pre-dose FEV1 from baseline (18mL [95% CI -12mL to 50mL]).

Adverse effects of the triple therapy inhalers are already well known in NCL as the components are available in mono- and dual- therapy devices already. Pneumonia is a particularly harmful adverse effect associated with COPD inhaler use. A meta-analysis found no difference in pneumonia rate between triple therapy given in a single device or multiple devices however there was a significantly increased risk of pneumonia when triple-therapy was compared to LAMA/LABA, due to the ICS component.

The drug acquisition cost of triple therapy in a single device is lower than that given in multiple devices (cost savings in NCL estimated to be £9,000 to £19,000 per annum). A NICE evidence-review on triple therapy, which reviewed all studies of triple therapy use (in single or multiple devices), stated that adding an ICS to a COPD regime gives less clinical benefit than adding a LAMA – therefore recommended that LAMA/LABA patients whose symptoms interfere with daily living should only be offered a three month trial of triple therapy.

Dr Restrick discussed the approach of the NCL Responsible Respiratory Prescribing Group (RRP) in focusing on the fundamentals of COPD care, aligned with the approach by NICE, which is a cost- and

clinically- effective strategy in improving care for COPD patients. Dr Restrick clarified that a significant proportion of participants within the six studies were current smokers (up to 50%), and due to the NICE approach there would be a large focus of smoking cessation, vaccination and pulmonary rehab before resorting to inhaled therapies. However, a single-device triple therapy inhaler device is needed to make prescribing and patient adherence as easy as possible. The RRP has also undertaken work with a patient centred approach to determine preferred devices by patients, of which the pMDI and Ellipta were the first and second most preferred. The proposal for both triple therapy inhalers would be to suggest that patients with asthmatic features would already be stabilised on pMDI therapy, and would therefore benefit from escalation to Trimbow®; patients with features of COPD only would be stabilised on an Ellipta device and would therefore benefit from escalation to Trelegy®.

In camera, the Committee were supportive of the inclusion of both inhalers on the NCL Joint Formulary in line with NICE recommendations to suit patient preference in order to improve adherence rates. The Committee however were unclear as to how patients on LAMA/LABA therapy initiated on a trial of triple-therapy would be appropriately followed up, and also requested that all inhalers on the NCL Joint Formulary for COPD to be reviewed and rationalised where possible. The Committee were informed that the RRP are updating their COPD guideline, which includes an inhaler guide that rationalises inhaler choices for COPD. Both matters will be addressed in the guideline and will be brought to a future meeting before other COPD inhalers will be considered for addition to the Joint Formulary. In summary, the Committee approved the addition of both Trelegy® and Trimbow® to the NCL Joint Formulary for use in moderate to severe COPD, but requested for the aforementioned details of follow-up and rationalisation of inhalers be brought back to a future meeting.

Decision: Approved
Prescribing: Primary and Secondary care
Tariff status: In tariff
Funding: Hospital/CCG
Fact sheet or shared care required: No

8.3 Hydrocortisone sodium phosphate eye drops (Softacort®) for mild non-infectious allergic or inflammatory ocular surface diseases

The Committee considered an application for the use of hydrocortisone sodium phosphate eye drops for mild non-infectious allergic or inflammatory ocular surface diseases (OSD) and control of scar tissue formation *in absentia*. The ocular surface includes the cornea, the conjunctiva, the eye lids and the lacrimal glands.

The Committee heard that steroids are widely used in ophthalmology to suppress inflammation, reduce symptoms and minimise scarring. Hydrocortisone eye preparations were available between 1950s-90s however were withdrawn from the market for commercial reasons as specialists preferred the unlicensed preparations of low strength prednisolone manufactured by Moorfields pharmaceuticals. Moorfields Pharmaceuticals ceased production in 2013 leaving unlicensed prednisolone 0.1% as the only remaining low potency steroid preparation available, which is costly and has an in-use expiry of seven days. The applicant proposes low potency steroid preparations are required to treat mild inflammatory or allergic OSD and minimise adverse effects and Softacort® is the least potent licensed product available.

Softacort was licensed as a generic to an Italian product Idracemi® which was licensed in Italy in 1958 without conventional large RCTs. Softacort is preservative free in a unit dose form whereas Idracemi contains paraben preservatives (which may alter absorption and distribution of the hydrocortisone) and is in multi-dose form. There is an absence of human comparative studies between the Softacort formulation and any other hydrocortisone products on the European market, but it is assumed that Softacort will act in a similar way to Idracemi or the discontinued hydrocortisone acetate eye drops.

The main adverse effects of the topical ophthalmic corticosteroids include cataract, ocular hypertension, glaucoma, secondary infection and delayed corneal wound healing. Ocular hypertension can lead to damage to the optic nerve and resulting visual field loss (steroid-induced glaucoma) may ensue. The propensity of different corticosteroids to induce ocular hypertension is thought to be related to the steroid potency and ability to cross the cornea and distribute in the ocular structures. One study found dexamethasone 0.1% eye drops caused a seven-fold less pressure rise compared to hydrocortisone 0.5% eye drops however were many limitations including inadequate description of patient characteristics,

medications and study methodology. Softacort is expected to be less well absorbed into the anterior chamber compared with other corticosteroid products on the UK market since it is in the form of the ionised phosphate salt and does not contain the preservative benzalkonium chloride. Therefore, Softacort may theoretically have a lower potential to cause ocular hypertension and other adverse effects.

In terms of cost, hydrocortisone sodium phosphate (£10.99/30 SUD) is less expensive than unlicensed prednisolone 0.1%, however more expensive than the preserved multi-dose fluorometholone eye drops (£1.71/5mL). The estimated budget impact for 30 patients initiated in MEH is estimated at a minimum of £1,100 per annum.

The Committee expressed hesitancy on an additional steroid eye drop to the NCL Joint Formulary, particularly given the absence of evidence to show comparative benefit in terms of safety or efficacy against the current weakest steroid eye drop - FML®. The Committee however were accepting of the principal that the lowest potency steroid should be available provided specialists provide adequate communication to GP for course duration and/or date for review.

Decision: Approved
Prescribing Secondary care initiation, primary care continuation
Tariff status: In tariff
Funding: Trust/CCG
Fact sheet or shared care required: No

9. HRT shortages

The Committee were informed of a UK-wide long term shortage of several hormone replacement therapy (HRT) preparations summarised in the below table (OOS = out of stock).

Ingredient (s)	Manufacturer	Brand	Strength	Current Availability	Anticipated resupply date
OESTROGEN ONLY					
Oral Preparations					
Estradiol	Resource Medical UK	Bedol	2mg	Long term OOS	Unknown
Transdermal patches					
Estradiol	Janssen-Cilag	Evorel	25 mcg	In stock until Feb 2020	Mid 2020
			50mcg	Long term OOS	
			75mcg	Long term OOS	
			100mcg	Long term OOS	
PROGESTOGEN ONLY					
Oral Preparations					
Medroxyprogesterone	Resource Medical UK	Climanor	5mg	Long term OOS	Unknown
COMBINATION HRT – CONTINUOUS THERAPY					
Oral Preparations					
Estradiol valerate/ medroxyprogesterone	Orion	Indivina	2mg/5mg	OOS	Dec 2019
Transdermal patch					
Estradiol hemihydrate/ norethisterone acetate	Janssen-Cilag	Evorel Conti	3.2mg/ 11.2mg	Long term OOS	Mid 2020
Estradiol hemihydrate/ levonorgestrel	Theramex	FemSeven Conti	1.5mg/ 0.525mg	Long term OOS	Q2 2020
COMBINATION HRT – SEQUENTIAL THERAPY					
Oral Preparations					
Estradiol [X,X] / norethisterone acetate	Resource Medical UK	Clinorette	[2mg, 2mg]/ 1mg	Long term OOS	Unknown

Estradiol/norgestrel	Mylan	Cyclo-progynova	2mg/500mcg	Long term OOS	Unknown
Transdermal patch					
a) Estradiol hemihydrate and b) estradiol hemihydrate/ norethisterone acetate	Janssen-Cilag	Evorel Sequi	a)3.2mg b) 3.2 mg /11.2 mg	Long term OOS	Mid 2020
a) 1.5mg of estradiol hemihydrate b) Estradiol hemihydrate /levonorgestrel	Theramex	FemSeven Sequi	a) 1.5mg b) 1.5mg /1.5mg	Long term OOS	Late 2019

While a number of alternative brands are available to sufficiently address the above 'out of stock' or 'in short supply' for oestrogen only oral and transdermal HRT and combination oral HRT, there is *no directly equivalent alternative combination transdermal HRT for sequential or continuous therapy available*. NICE guidance (NG23) recommends combination (oestrogen + progestogen) HRT for women with a uterus and that transdermal oestrogen should be considered for patients at an increased risk of VTE.

The only licensed option for combination HRT for women with a uterus who require transdermal oestrogen due to increased risk of VTE is a combination of a transdermal oestrogen preparation plus the only currently available oral progestogen, Utrogestan®. Utrogestan is licensed for adjunctive use with oestrogen in post- menopausal women with a uterus as HRT, and is a recommended option by the international Menopause Society, British Menopause Society and European Society of Human Reproduction and Embryology.

Utrogestan was previously reviewed by the Committee (May 2018) under the confines of an application to switch from the current formulary synthetic progestins when used as adjunctive therapy due to proposed improved tolerability (i.e. oral/transdermal combination HRT plus oral utrogestan). At the time of the review, the Committee found there was insufficient data to support superior efficacy of Utrogestan or claims of improved tolerability due to a lack of direct comparison studies, whilst also representing a significant increase in cost; on this basis the Committee did not approve the application.

At the present meeting the Committee reviewed a draft local memo prepared by UCLH in consultation with the gynaecology clinical team proposing the use of oral Utrogestan in combination with transdermal oestrogen for women with a uterus at increased risk of VTE (i.e. in line with the previous application) on the basis that the current formulary option is long term out of stock. As the significant majority of prescribing of HRT therapy occurs in primary care the memo was brought to the JFC rather than being considered at the local DTC. Summary of recommendations provided below.

It was noted that the advice within the memo reflects that published by Specialist Pharmacy Service on "Shortage of Evorel hormone replacement therapy (HRT) patch range". Further, it was highlighted that by only switching combination transdermal HRT to transdermal oestrogen plus oral Utrogestan it would realise a cost saving, however introduced a risk of reduced adherence due to the intermittent dosing schedule of utrogestan.

Although not previously approved, the Committee agreed that appropriate licensed alternatives should be used in response to acute shortages and therefore approved the addition of Utrogestan onto the NCL Joint formulary for the purpose of providing an alternative supply as described above for women with a uterus who require transdermal oestrogen HRT due to increased risk of VTE and the above information will be communicated to primary and secondary care to facilitate the switch and inform patients. It was also agreed that Utrogestan should *not* be offered where oral combination HRT is indicated, and that when the shortage of combination transdermal HRT products has resolved, the Committee would consider reports of reduced adherence and whether or not there would be value in switching patients back to previously available options.

COMBINATION HRT - Transdermal preparations Only for women at increased risk of VTE [NICE NG23]		
Brand	Current Availability	Approved (Available) Alternatives
Evorel Conti 3.2mg/11.2mg (Estradiol hemihydrate/ norethisterone acetate) FemSeven Conti 1.5mg/ 0.525mg (Estradiol hemihydrate/ levonorgestrel)	Long term Out of Stock (possible return mid-2020)	No alternative combination patches or progestogen only patches available For women who can have oral combination HRT (i.e. low risk of VTE), available alternatives are: - Elleste Duet Conti 2mg/1mg - Kliofem 2mg/1mg - Kliovance 1mg/ 500mcg - Femoston Conti 1mg/5mg - Premique 300mcg/1.5mg - Indivina 1mg/2.5mg, 1mg/5mg For women with a uterus who cannot have oral combination HRT due to oral oestrogen (i.e. high risk of VTE as per NICE NG23), switch to: - Utrogestan oral capsule 100mg at night (Day 1 to 25) PLUS either: - Estradot 50mcg/24hrs, Estraderm MX 50mcg/24hrs, Femseven Mono 50mcg/24hrs, or Progynova TS 50mcg/24hrs
Evorel Sequi a) 3.2mg b) 3.2 mg /11.2 mg (a) Estradiol hemihydrate and b) estradiol hemihydrate / norethisterone acetate FemSeven Sequi (a) 1.5mg of estradiol hemihydrate b) Estradiol hemihydrate /levonorgestrel	Long term Out of Stock (possible return mid-2020)	No alternative combination patches or progestogen only patches available For women with a uterus who can have oral combination HRT (i.e. low risk of VTE), available alternatives are - Elleste Duet 1mg/1mg, 1mg/2mg - Femoston 1mg/10mg, 2mg/10mg - Novofem 1mg/1mg - Trisequens [2mg, 2mg, 1mg]/ 1mg - Tridestra 2mg/20mg For women with a uterus who cannot have oral combination HRT due to oral oestrogen (i.e. high risk of VTE as per NICE NG23), switch to: - Utrogestan oral capsule 200mg at night (Day 15 to 26) PLUS either: - Estradot 50mcg/24hrs, Estraderm MX 50mcg/24hrs, Femseven Mono 50mcg/24hrs, or Progynova TS 50mcg/24hrs

10. Zanamivir IV for treatment of complicated and potentially life-threatening influenza A or B virus infection

The Committee considered a proposal to replace compassionate-access IV zanamivir with licensed IV zanamivir. The proposed place in therapy is consistent with both the product license and current use of the compassionate-access product i.e. the treatment of complicated and potentially life-threatening influenza A or B virus infection in adult and paediatric patients (aged ≥6 months) where other anti-viral medicinal products for treatment of influenza, including inhaled zanamivir, are not suitable.

There are no placebo-controlled studies to unequivocally establish the efficacy of IV zanamivir. One Phase III active-comparator study failed to demonstrate superiority of IV zanamivir over oral oseltamivir for hospitalised patients (>16 years of age) with complicated influenza. The usefulness of the study is further limited as it did not recruit patients with oseltamivir resistance, which is specified in the product license and its intended use in NCL. The EMA however granted a license due to comparable effects to oseltamivir, evidence of adequate exposure at the infection target tissues compared to inhaled zanamvir (which has proven efficacy to uncomplicated influenza), extrapolation of efficacy of other neuraminidase inhibitors conducted in patients with uncomplicated influenza to that of the complicated setting and a generally favourable safety profile of neuraminidase inhibitors.

The Committee heard that unlicensed IV zanamivir is already available at UCLH, NMUH, RFL, WH and GOSH. Based on usage over the last 12 months, the annual budget impact for moving to licensed stock is estimated to be £30,500 per annum (30 patients).

The Committee considered the limited clinical evidence in support of IV zanamivir however noted it was already standard-of-care for the proposed cohort and that there were no alternatives available to treat these individuals who would typically be on a ventilator on the ITU with very poor outcomes. The Committee agreed to add IV zanamivir to the NCL Joint Formulary for the proposed indication.

Decision: Approved for patient's whose influenza virus is known or suspected to be resistant to anti-influenza medicinal products other than zanamivir, and/or other anti-viral medicinal products for treatment of influenza, including inhaled zanamivir, are not suitable for the individual patient.
Prescribing Secondary care, restricted to virology approval only
Tariff status: In tariff
Funding: Trust
Fact sheet or shared care required: No

11. Rufinamide Shared Care Guideline (update)

The rufinamide shared care was deferred to the next meeting as an outstanding action had not been resolved.

12. Ciclosporin eye preparations factsheet (update)

The ciclosporin eye preparations fact sheet was presented for approval. The update reflects the addition of Verkazia®. The Committee approved the ciclosporin fact sheet.

13. Psoriatic arthritis pathway (for information)

The pathway is fully compliant with NICE TA recommendations therefore does not require clinical approval at JFC. The pathway permits one line of therapy per mechanism of action and will be discussed at the Heads of Medicines Management meeting for funding approval before being published on the NCL MON website.

14. Next meeting

Monday 21st October 2019

15. Any other business

Nil