

JOINT FORMULARY COMMITTEE (JFC) – MINUTES

Minutes from the meeting held on Monday 15 March 2018
G12 Council Room, South Wing, UCL, Gower Street, London WC1E 6BT

Present:	Dr R MacAllister	NCL JFC Chair	(Chair)
	Dr R Sofat	UCLH, DTC Chair	
	Dr R Urquhart	UCLH, Chief Pharmacist	
	Ms K Delargy	BEH, Deputy Chief Pharmacist	
	Mr P Gouldstone	Enfield CCG, Head of Medicines Management	
	Dr M Kelsey	WH, Chair DTC	
	Mr T Dean	Patient Partner	
	Ms A Fakoya	NEL CSU, Senior Prescribing Advisor	
	M S Semple	MEH, Interim Chief Pharmacist	
	Ms P Taylor	Haringey CCG, Head of Medicines Management	
	Dr A Sell	RNOH, DTC Chair	
	Mr A Dutt	Islington CCG, Head of Medicines Management	
	Dr M Dhavale	Enfield CCG, GP Clinical Lead Medicines Management	
	Mr S Richardson	WH, Chief Pharmacist	
	Ms W Spicer	RFL, Chief Pharmacist	
	Dr S Ishaq	WH, Consultant Anaesthetist	
	Dr D Hughes	RFL, Consultant Haematologist	
	Ms R Clark	Camden CCG, Head of Medicines Management	
	Dr A Stuart	Camden CCG, GP Clinical Lead Medicines Management	
In attendance:	Mr A Barron	NCL JFC, Support Pharmacist	
	Mr J Minshull	NCL JFC, Support Pharmacist	
	Mr P Bodalia	UCLH, Principal Pharmacist	
	Ms M Bhogal	NMUH, Formulary Pharmacist	
	Ms M Kassam	MEH, Formulary Pharmacist	
	Ms I Samuel	RFL, Formulary Pharmacist	
	Ms S Sanghvi	UCLH, Formulary Pharmacist	
	Dr Z Zair	UCLH, SpR Clinical Pharmacology	
	Mr A Fakokunde	NMUH, Consultant Gynaecologist	
	Ms E Gortari	UCLH, RNTNE and Eastman Dental Hospital Pharmacist	
Apologies:	Mr G Kotey	NMUH, Chief Pharmacist	
	Dr F Gishen	RFL, Palliative Care Consultant	
	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	
	Ms K Davies	NEL CSU, Deputy Director Medicines Management	
	Ms L Reeves	C&I, Chief Pharmacist	
	Ms E Nassuna	Enfield Community Nurse, Bone Health	
	Dr R Woolfson	RFL, DTC Chair	
	Mr C Daff	NHS Barnet, Head of Medicines Management	
	Dr A Mian	NMUH, Clinical Director for Specialty Medicine	

2. **Meeting observers**

Dr Zair (UCLH, SpR Clinical Pharmacology) was welcomed as an observer to the meeting.

3. **Minutes of the last meeting**

The minutes were corrected to record Dr Kelsey was in attendance and Dr Ishaq sent apologies to the February 2018 meeting. The minutes were otherwise accepted as an accurate reflection of the February meeting.

The abbreviated minutes were not reviewed; these would be reviewed and approved at the next meeting.

4. **Matters arising**

4.1 **Sirolimus for ‘arteriovenous malformation – low flow’**

The Committee heard there are four major categories of vascular malformations based on their flow characteristics: slow-flow (capillary malformations, venous malformations, lymphatic malformations) and fast-flow (arteriovenous malformations-AVMs). Consequentially it was queried whether references to ‘arteriovenous malformations – low flow’ in the RFL DTC December 2017 minutes and JFC February 2018 minutes should be changed to ‘low-flow vascular malformations’.

UCLH DTC evaluated bleomycin as first line therapy for low-flow vascular malformations of the head and neck in February 2018, restricted to named consultant neuroradiologists. The Committee therefore asked for clarification on the specific indication and position in therapy of sirolimus relative to bleomycin sclerotherapy so that pathways can be aligned across NCL.

Action: Ms Samuel to liaise with Dr J Brookes (RFL) and UCLH (Ms S Sanghvi and Dr A Rennie) to resolve this query.

5. **Declarations of relevant conflicts of interest**

There were no declarations of interest.

6. **Local DTC recommendations / minutes**

6.1 **Approved**

DTC site	Month	Drug	Indication	JFC outcome
RFL	Jan-18	Tocilizumab (compassionate access)	Diffused cutaneous systemic sclerosis	Decision: Approved for RFL only Prescribing: Secondary care only Tariff status: Included Funding: FOC Fact sheet or shared care required: No
RFL	Jan-18	Nivolumab (EAMS scheme)	Metastatic inoperable gastric or gastro-oesophageal cancer following first and second line treatment	Decision: Added to the NCL Joint Formulary Prescribing: Secondary care only Tariff status: Included Funding: FOC Fact sheet or shared care required: No
UCLH	Jan-18	Papaverine	Used topically intraoperatively for vasospasm during microvascular anastomosis in patients who may be undergoing free flap surgery (mandibulectomy, major glossectomy or laryngectomy)	Decision: Added to the NCL Joint Formulary Prescribing: Secondary care only Tariff status: Included Funding: Trust Fact sheet or shared care required: No
UCLH	Jan-18	Rucaparib (compassionate use)	Homologous recombination deficiency (HRD) associated gynaecological cancers	Decision: Approved for UCLH only Prescribing: Secondary care only Tariff status: Included Funding: FOC Fact sheet or shared care required: No

UCLH	Jan-18	Propranolol	Adjunct or alternative for the third and subsequent line of treatment of angiosarcoma and haemangioendothelioma either in combination with chemotherapy or as a single agent as maintenance treatment	Decision: Approved for UCLH only Prescribing: Secondary care only Tariff status: Included Funding: Trust Fact sheet or shared care required: No
UCLH	Feb-18	Bleomycin sclerotherapy	Low Flow Vascular Malformations of the Head and Neck	Decision: Added to the NCL Joint Formulary Prescribing: Secondary care only Tariff status: Included Funding: Trust Fact sheet or shared care required: No

6.2 Approved under evaluation

DTC site	Month	Drug	Indication	JFC outcome
RFL	Jan-18	Floseal	Epistaxis whereby conservative measures or chemical cautery have failed to cease bleeding	Decision: Under evaluation at RFL-Barnet site only Prescribing: Secondary care only Tariff status: Included Funding: To be confirmed [†] Fact sheet or shared care required: No

[†] RFL are exploring with Commissioners whether this intervention which is designed to reduce A&E re-attendance can be funded.

7. New Medicine Reviews

7.1 Utrogestan® (progesterone) vaginal capsules for luteal phase supplementation during assisted reproductive technology cycles (Applicant: Ms M Davies, Mr V Talaulikar, UCLH)

The Committee considered an application to use Utrogestan® (micronized progesterone) vaginal capsules to supplement luteal phase during Assisted Reproductive Technology (ART) cycles. The Committee heard that women are offered progesterone as luteal support following IVF in line with NICE CG 156; this is currently provided by progesterone pessaries. The applicant identified that some patients find progesterone pessaries inconvenient due to their texture, therefore having progesterone vaginal capsules available would allow an alternative option for these patients.

The Committee noted that there are no head-to-head trials comparing progesterone pessaries to progesterone vaginal capsules, therefore they were unable to make an assessment on the relative convenience of these two formulations.

The Committee considered the findings of a large systematic review and meta-analysis (van der Linden *et al* 2015, 94 RCTs, n=26,198 women) that compared relative safety and efficacy between different types of luteal phase support in ART. None of the studies compared progesterone pessaries to progesterone vaginal capsules. Of the analyses presented by the authors that included Utrogestan® in one of the arms, there seemed to be little difference in terms of “clinical pregnancy” between it and its comparator (OR 0.98 [95% CI 0.87 to 1.09]). This finding was confirmed by the Scottish Medicines Consortium, who acknowledged that different vaginally administered progesterone formulations are equivalent in efficacy.

The Committee noted that use of progesterone vaginal capsules is associated with a cost impact of approximately £12k per annum when compared to progesterone pessaries. Based on the information provided, the Committee did not consider this additional cost to be justified.

In summary, the Committee could not see evidence of additional benefit from Utrogestan® (progesterone) vaginal capsules compared to Cyclogest® (progesterone) pessaries that are currently used for this indication, therefore did not agree to add them to the formulary.

Decision: Not approved

7.2 **Cilodex (ciprofloxacin and dexamethasone) ear drops for ear infection/inflammation if perforated/damaged tympanic membrane (Applicant: Dr J Lavy, UCLH)**

The Committee considered an application to use Cilodex (ciprofloxacin/dexamethasone ear drops) for patients with an ear infection/inflammation with perforated/damaged tympanic membrane.

There are three potential comparators for Cilodex for this indication; off-label use of antibiotic eye drops in the ear, combination antibiotic/steroid ear drops (Sofradex, Gentisone HC, Otomize; all of which contain aminoglycosides) and off-label use of antibiotic eye drops in the ear used in combination with betamethasone ear drops.

Sofradex and Otomize are both contraindicated where a perforated tympanic membrane has been diagnosed or is suspected or where a tympanostomy tube (grommet) is in situ. The SPC for Gentisone HC warns "irreversible toxic effects may result from direct contact of gentamicin with the middle and inner ear. The benefits of gentamicin therapy should be considered against the risk of infection itself causing hearing loss". The Committee heard there is a paucity of evidence to quantify the ototoxicity risk with topical aminoglycoside used in patients with perforated/damaged tympanic membrane however the general advice is that short-term therapy (≤ 14 days) with topical aminoglycoside appears not to affect hearing however, severe hearing loss has been attributed to excessive, prolonged use of these medications.

The Committee heard evidence from one low-quality randomised controlled trial comparing Cilodex to ciprofloxacin drops in children with microbiologically confirmed acute otitis media with tympanostomy tubes. Mean time to cessation of otorrhea was significantly shorter in the Cilodex group than with ciprofloxacin (4.22 days vs 5.31 days respectively; $p=0.04$) however there were no significant differences in the clinical response or the microbial eradication rate on day 14. Significant limitations in the study were noted. Dr Kelsey noted the application did not specify whether Cilodex was being proposed for patients with otitis media or otitis externa however otitis externa was the most logical indication. JFC Support agreed to review the available literature for otitis externa and come back to the Committee if any concerns were identified for this indication.

When comparing Cilodex with off-label use of antibiotic eye drops in the ear, the Committee heard off-label uses of eye drops in the ear can be confusing for patients, GPs and community pharmacies. The Committee also heard from Ms Gortari that FP10 prescriptions mistakenly written for antimicrobial 'ear drops' risk community pharmacies billing for specials to be manufactured at significant expense. The Committee heard patient confusion could potentially be mitigated with Patient Information Leaflets (PIL) however the risk of unlicensed specials being manufactured could not be resolved. The Committee agreed the use Cilodex, a licensed product with an appropriate PIL was preferable to off-label use of antibiotic eye drops in the ear.

When comparing Cilodex with combination antibiotic/steroid ear drops (Sofradex, Gentisone HC, Otomize), Cilodex was the preferred agent for patients with a perforated/damaged tympanic membrane as Cilodex is not contraindicated in this cohort and is less costly. Dr Kelsey advised that topical use of antimicrobial increase the risk of antimicrobial resistance therefore if choosing between Gentisone HC (containing gentamicin) and Cilodex (containing ciprofloxacin), Cilodex is the preferred choice.

In summary; the Committee agreed to add Cilodex to the NCL Joint Formulary for the treatment of otitis externa with perforated/damaged tympanic membrane. The Committee also recommended Gentisone HC be removed from the NCL Joint Formulary as it is more costly and offers no advantage over Sofradex and Otomize.

Post meeting note: A second RCT (Roland 2004) was reviewed by JFC Support Pharmacists which supported a claim of at least non-inferiority between Cilodex and topical neomycin/polymyxin B/hydrocortisone for otitis media.

Decision: Approved

Prescribing: Primary and secondary care

Tariff status: In tariff

Funding: Primary and secondary care

Fact sheet or shared care required: No

7.3 **Levosert® (levonorgestrel) intrauterine system for heavy menstrual bleed (Applicant: Mr A Fakokunde, NMUH)**

The Committee considered an application to use Levosert® levonorgestrel intrauterine system (LNG-IUS) in the treatment of heavy menstrual bleeding as a first-line alternative to Mirena®.

The Committee heard how Levosert® LNG-IUS delivers 20 micrograms/day levonorgestrel directly into the uterus, which is the same as with the Mirena® LNG-IUS.

The Committee considered the findings of one multicentre, randomised, single-blind, controlled, one-year equivalence study that compared the reduction in menstrual blood loss (MBL) between Levosert® and Mirena® LNG-IUS in non-menopausal women who were experiencing heavy menstrual bleeding. It was noted that the equivalence limit of ± 20 mL was generous considering heavy menstrual bleeding was considered to be >80 mL/cycle, however the mean baseline loss was 180 mL/cycle, therefore the equivalence interval was only 11%. This study met its primary efficacy end-point, demonstrating that the two devices are equivalent in terms of reduction in mean blood loss between baseline and the end of the study.

It was noted that Levosert® has a lower list price (£66+VAT) than Mirena (£88+VAT), but that the manufacturer is offering secondary care a confidential discount that provides a considerable saving per device inserted compared to Mirena®. Unfortunately, this discount is not available in primary care.

The Committee discussed how long these devices would be kept in situ as the trial provided data on HMB only for 1 year, yet the licensing authorities allow the device to remain in place for up to 4 years. Mr Fakokunde explained to the Committee that if patients don't have the device removed within the first six months, they tend to keep it in situ for the full four years. The average age of insertion is approximately 42 years, therefore they would go on to receive a second device after four years to take them through to menopause. Mr Fakokunde explained that this is the same as practice with Mirena®.

The Committee asked whether Levosert® device could be used as contraceptive as well as to prevent heavy menstrual bleeding. Mr Fakokunde explained that he does explain to his cohort of patients that the device will also prevent pregnancy, but this is not the primary purpose he uses it for. It was noted that Levosert® is indicated for contraception.

In summary, the Committee thought that Levosert® offered an equally effective, less expensive option to reduce heavy menstrual bleeding compared to Mirena® and agreed this should be added to the formulary as an additional option. The Committee agreed it would be appropriate to recommend this product as a contraceptive if it is found to have a similar PEARL score to Mirena®.

Post-meeting notes: The cumulative pregnancy rate for Levosert® calculated as the Pearl Index in a large clinical trial (women aged 16 years to 35 years inclusive) is 0.15 (95% CI 0.02 to 0.55) at the end of year one, and 0.21 (95% CI 0.09 to 0.41) at the end of year four. By comparison, the Pearl index for Mirena® (studied in five clinical studies) is approximately 0.2% at end of year one and 0.7% at end of year five, demonstrating that Levosert® is likely to be equally efficacious to Mirena® at avoiding pregnancy.

The Royal Free Hospital wish to switch from Mirena® to Levosert® for both heavy menstrual bleeding and contraception in the family planning clinic.

Decision: Approved

Prescribing: Primary and secondary care

Tariff status: In tariff

Funding: Primary and secondary care

Fact sheet or shared care required: No

8. **Eastman Dental Hospital formulary – discussion to agree a pragmatic plan for the review of routinely prescribed but non-formulary (and some cases unlicensed) medicines for oral mucosal inflammatory disease**

The committee heard that the UCLH Use of Medicines Committee is undertaking a review of off-label uses of medicines across the Trust. Many of these are from inherited services or are historical uses of drugs, some of which predate the current formulary processes. The purpose is to assess risk, update the formulary and consider whether transfer of prescribing to primary care is appropriate. A prioritisation process and pragmatic approach is required to address the large number of medicines within this review. The first pathway that is being considered, and which will help inform the process for future work within this review is from the Eastman Dental Hospital (EDH; part of UCLH).

EDH developed a treatment pathway for the management of oral mucosal inflammatory disease for consideration at JFC. The pathway included 24 individual medicines; 10 were non-formulary at UCLH and of these 9 were considered established practice and 1 was a new request. Oral mucosal ulcerative inflammatory disease is an umbrella term comprising 7 distinct conditions (Pemphigus vulgaris [PV], Mucous membrane pemphigoid [MMP], Recurrent aphthous stomatitis [RAS], Oral lichen planus [OLP], Oral Crohn's disease [OCD], Linear IgA disease and Oral ulceration in Behcet's disease). A total of 10 non-formulary medicines indicated for 7 distinct conditions creates an impractical workload therefore JFC Support asked the Committee to agree a pragmatic approach to dealing with these applications.

JFC Support Pharmacists presented a paper outlining a pragmatic approach to processing the applications. The Committee agreed to the following approach:

- Accepting the EDH's proposal to extrapolate evidence from one oral mucosal ulcerative and inflammatory disease to the others
- Assigning a risk rating to each drug
- Accepting that where already on the hospital formulary, prescribing can be in primary or secondary care (except thalidomide), utilising the DMARD monitoring quick reference where applicable
- Working with SEL JFC / SEL APC in developing a dental formulary

The following definitions were agreed:

- Low risk: established therapy; the product is licensed for an oral mucosal disease, or is an off-label use of a licensed topical medicine
- High risk: high risk medicine or not established therapy
- Intermediate risk: established therapy; systemic treatment with long term monitoring requirements or an unclear safety profile

The following actions were agreed:

- Low: adopt onto the NCL Joint Formulary without additional review (secondary/tertiary care initiation, GP continuation)
- High: requires review at JFC/UMC, do not prescribe until JFC/UMC have approved
- Intermediate: continue to use however requires review at JFC/UMC within next 12 months to ensure appropriateness (secondary/tertiary care initiation, GP continuation)

There was a request that DMARDs not already included on the DMARD fact sheet underwent a full evaluation because it had implications for GP enhanced service payments and workload. The Committee acknowledged that additional monitoring will have an impact in primary care, though it was noted that GPs are already undertaking prescribing for some of these patients, therefore an estimate of patient numbers should be provided alongside details of monitoring requirements to inform budget impact calculations.

The Committee agreed with the pragmatic approach (including definitions and actions) presented. It was therefore agreed to add the following established therapies to the NCL Joint Formulary:

Betamethasone 500mcg soluble tablets	Decision: Added to the NCL Joint Formulary for oral mucosal inflammatory disease Prescribing: Secondary care initiation, continuation in primary care Tariff status: In tariff Funding: Primary and secondary care Fact sheet or shared care required: No
Fluticasone propionate nasules or nasal spray	
Mometasone 0.1% ointment	
Clobetasol 0.05% ointment	
Tacrolimus 0.1% ointment	
Prednisolone	
Mycophenolate mofetil	Decision: Added to the NCL Joint Formulary for oral mucosal inflammatory disease Prescribing: Secondary care initiation, continuation in primary care Tariff status: In tariff Funding: Primary and secondary care Fact sheet or shared care required: Incorporate into DMARD monitoring guideline
Azathioprine	

Triamcinolone acetonide injected underneath the ulcerated area	Decision: Added to the NCL Joint Formulary for oral mucosal inflammatory disease Prescribing: Secondary care only Tariff status: In tariff
Thalidomide	Funding: Secondary care Fact sheet or shared care required: No

The Committee requested full applications to be heard at JFC/UCLH DTC within the next 12 months to ensure appropriateness (secondary/tertiary care initiation, GP continuation) although EDH could continue to prescribe in the interim period:

- Colchicine
- Dapsone
- Pentoxifylline
- Hydroxychloroquine
- Azithromycin
- Pilocarpine for salivary stimulation (symptomatic relief)

Rituximab should not be prescribed for this indication until approved by JFC/UCLH DTC.

9. **Lidocaine Plasters: Comparison between JFC and NHS England positions**

Lidocaine plasters were reviewed at JFC in November 2012 for neuropathic pain (including post-herpetic neuralgia) and the Committee recommended against their use. The Committee have not received applications for off-label uses therefore lidocaine plasters are de facto non-formulary for these indications also. In September 2017, JFC approved a position statement recommending against the use of lidocaine plasters for any indications.

In December 2017, NHSE recommended that lidocaine plasters should not be initiated for any patient (with consideration for de-prescribing) except for patients treated in line with NICE CG173 'Neuropathic pain in adults: pharmacological management in non-specialist settings' but are still experiencing post-herpetic neuralgia.

The Committee considered the difference between the JFC and NHSE recommendation. It was noted there was no statutory requirement for JFC to adhere to the NHSE recommendation (as is true for NICE CG/NGs and unlike for NICE TAs) and clinicians in NCL had not appealed the JFC position statement therefore there was no automatic requirement for the Committee to re-review. The Committee however compared the evaluations written by SPS (on behalf of NHSE) and JFC; there were no new studies published since 2012 (date of original JFC review) and both evaluations reviewed the 3 main double-blind RCTs. The JFC review did not include two very short term studies (Galer 2002 and Rowbotham 1996) however the Committee agreed the studies were too short in duration to reliably inform decision making. Multiple open-label, short duration, single-arm studies were also not included (all of which were excluded by NICE, Cochrane and PresQIPP). Recently published SLRs by Cochrane and Lancet were unable to meta-analyse the results from the key trials due to heterogeneity therefore did not raise the level of evidence.

The Committee heard the majority of lidocaine use was for off-label indications, including palliative care and rib-fractures. The Committee asked that Formulary pharmacists requests users of lidocaine patches to put forward application to the Committee could review the appropriateness of this use.

In summary, the Committee agreed there were no new trials to justify JFC reconsidering the evidence base of lidocaine plasters for post-herpetic neuralgia. JFC and NHSE reviewed the same evidence base and came to different conclusions; JFC does not have a statutory responsibility to adhere to NHSE recommendations therefore the JFC recommendation is upheld and the position statement remains appropriate.

Action: JFC Support to write to Dr Gishen to request a full application for lidocaine plasters in the palliative setting. Formulary pharmacists to decline request for off-label indications and instead ask the requestor to write a full application for review at JFC.

10. **Evaluation update: Dermatronics Once Heel balm**

The Committee noted the findings of a twelve month evaluation into Dermatronics Once Heel balm (25% urea) that had been undertaken by the podiatry clinic at Whittington Hospital. The service collected data on 120 patients presenting to their service. 23% (n=27) were lost to follow up and 35% (n=42) patients either did not collect their prescription or did not get this prescribed by their GP following recommendation by Podiatry. 95% of patients (n=49) with skin scale 3 or 4 at baseline had dropped to

skin scale 1 or 2 following daily application of Dermatronics®. The Podiatry Service was unable to collect accurate data on time to re-attend at the Podiatry Clinic due to staffing changes.

The Committee noted that Dermatronics Once Heelbalm is of an equivalent price to other urea containing preparations available, including less potent 10% urea cream, therefore its introduction would not result in additional expense to prescribing budgets.

In summary, the Committee supported approval of Dermatronics Once Heelbalm for prescribing in primary and secondary care for treatment of anhidrotic, fissured, calloused and hard foot skin in diabetic patients at high risk of ulceration.

Decision: Approved

Prescribing: Primary and secondary care

Tariff status: In tariff

Funding: Primary and secondary care

Fact sheet or shared care required: No

11. **Guidelines for approval: ADHD Shared care**

The Committee approved this shared care guideline.

12. **Guidelines for approval: Antiplatelets**

The Committee acknowledged that this guideline was very useful to support general practitioners to understand treatment durations for different antiplatelets. There was discussion about the need to incorporate perioperative management of antiplatelets into this guidance, however the Committee acknowledged that was outside the remit of this particular piece of work and would require a separate guideline to be developed.

The Committee approved this guideline.

13. **Guidelines for approval: Antipsychotics Monitoring Fact Sheet**

The Committee approved this fact sheet.

14. **Melatonin dosing – for fact sheet**

Mr Minshull reminded the Committee that when melatonin was approved for use in the management of insomnia in children (>2 years) with neurological and developmental disorders, the Committee had asked whether there was any correlation between endogenous melatonin levels and effect on sleep. Mr Minshull explained that he had been unable to find any information relevant to this. Additionally, a communication from Prof Gringras (Children's Sleep Medicine) had highlighted that there was no correlation between endogenous melatonin levels and effect of exogenous dose.

Mr Minshull noted that he had proposed a dose escalation strategy for this indication that was similar to the MENDS study; this would include a review of the maximum titrated dose to ensure children were being treated with the minimum effective dose. The Fact Sheet will be developed to reflect this.

15. **JFC Work plan**

This item was included for information only. Any questions should be directed to Mr Barron.

16. **Next meeting**

Monday 16 April 2018, G12 Council Room, South Wing, UCL, Gower St. WC1E 6BT

17. **Any other business**

Nil