NCL Joint Formulary Committee (JFC) Meeting

Minutes from the meeting held on Thursday 25th April 2013
in the Board Room, Floor 3, UCLP Building, Tottenham Court Road

1. Present:	Prof L Smeeth	NCL JFC [Vice] Chair
	Ms W Spicer	RFH Chief Pharmacist
	Ms J Cope	GOSH Chief Pharmacist
	Mr A Dutt	NHS Islington, Head of Medicines Management
	Ms P Taylor	NHS Haringey, Head of Medicines Management
	Mr P Gouldstone	NHS Enfield, Head of Medicines Management
	Mr TF Chan	BCFH Chief Pharmacist
	Ms N Shah	NHS Camden, Head of Medicines Management
	Dr M Kelsey	WH DTC Chair
	Mr A Karr	NCL Procurement Chair
	Mr C Daff	NHS Barnet, Head of Medicines Management
	Dr R Urquhart	UCLH Chief Pharmacist
	Dr R Fox	RNOH DTC Chair
	Mr G Irvine	Lay Member
	Ms S Drayan	NMUH Chief Pharmacist
	Mr A Shah	RNOH Chief Pharmacist
	Dr A Tufail	MEH DTC Chair
	Mr T James	MEH Chief Pharmacist
	Dr A Jones	Consultant Oncologist, RFH/UCLH
	Ms L Reeves	C&I Mental Health Trust
	Dr T Sadhu	LMC GP Representative
	Dr C Stavrianakis	NHS Haringey, CCG
In Attendance:	Dr A Grosso	UCLP Pharmacist
	Mr K Thakrar	UCLH Formulary Pharmacist
	Ms K Chapman	MEH Formulary Pharmacist
	Mr P Bodalia	RNOH Deputy Chief Pharmacist
	Dr J Brazier	Consultant, Ophthalmology, UCLH
	Ms S Sanghvi	UCLH Pharmacist
	Ms R Holland	UCLH Pharmacist
	Ms A Coker	C&I Mental Health Trust
Apologies:	Prof R MacAllister	NCL JFC Chair
	Dr S Shaw	RFH DTC Chair
	Dr H Taylor	WH Chief Pharmacist
	Dr M Broadbent	BCFH DTC Chair
	Ms R Dallmeyer	Commissioning Support Unit
	Dr L Wagman	NHS Barnet, CCG

2. Minutes of the last meeting

Item 3.2: Clarity was requested with respect to the prescribing pathway for novel oral anticoagulants. Mr Dutt informed the Committee that the [draft] anticoagulation pathway is yet to be agreed by each CCG. It was agreed that an update on this issue should be presented at the next JFC meeting.

3. Matters arising

3.1 Rasburicase Feedback

Ms Spicer had informed the Committee that the RFH have reported a total cessation from the requirement for renal support since the introduction of rasburicase for patients at high risk of tumour lysis syndrome. Dr Grosso reported that subsequent site-specific feedback on this issue has not been forthcoming. It was agreed that further details regarding the cessation of renal support at the RFH should be presented to JFC before considering this issue again.

3.2 RA biologic pathway

Dr Grosso informed the Committee that this item was deferred at the April UMC meeting as Dr Leandro (UCLH Consultant Rheumatologist) was unable to attend, and that feedback on local discussions would be brought to the next JFC meeting. The rationale for developing this pathway, which deviates in part from NICE guidance, is based on either increased clinical effectiveness or potential cost saving arguments.

4. Members & applicants declarations of relevant conflicts of interests

None declared

5. Medicine Applications

5.1 Bromfenac (Bausch & Lomb) post cataract surgery

The Committee reviewed an application for topical bromfenac for two indications; (1) treatment of inflammation post cataract surgery in patients unable to tolerate topical corticosteroids and (2) prophylaxis of cystoid macular oedema (CMO) in high-risk patients.

The Committee was informed that topical diclofenac had previously been considered at the UCLH UMC for first line treatment of inflammation post cataract surgery several years ago where it was concluded that corticosteroids should remain the first line treatment but that there was a role for topical NSAIDs and requested clarification from the applicant on the population of patients in which NSAIDs would be used as treatment. An absence of a response had left no topical NSAID on the UCLH formulary.

The Committee agreed that use of an NSAID in patients contra-indicated, unable to tolerate, or unresponsive to, topical corticosteroids appeared reasonable, and focused the discussion on the differences and similarities between bromfenac and ketorolac (the least expensive topical NSAID). The Committee were informed that there are no direct comparison studies between bromfenac and ketorolac regarding efficacy or safety. The Committee reviewed studies by Walter et al and Waterbury et al reporting increased potency of bromfenac over ketorolac in terms of COX-II inhibition. However Bucci et al compared aqueous drug levels and prostaglandin E_2 levels in patients treated with ketorolac and bromfenac at trough dosing and found ketorolac to be superior for both endpoints.

With regards to extended use of bromfenac in diabetic patients for CMO prevention, as suggested by the applicant, the Committee discussed an open-label, randomised trial by Endo et al (n = 62) which investigated the efficacy of bromfenac in preventing CMO and inflammation after cataract surgery in patients with diabetes. However the Committee expressed concern regarding the extended use of bromfenac [6 weeks] beyond the licensed 2 week limit, for which there are a lack of safety assurance. In addition, the active comparator schedule included a low potency corticosteroid which would not be used in practice.

There were no direct comparative studies between ketorolac and bromfenac in terms of safety. The Committee reviewed safety results from a study by Donnenfeld et al (n = 527) which reported a higher incidence of ocular adverse events in the vehicle arm; including iritis (18% in placebo, 7% in bromfenac), eye irritation (4.7% in placebo, 2.5% in bromfenac), and photophobia (11% in placebo, 2% in bromfenac). The quantification of ocular irritation with ketorolac could not be elucidated. The Committee also noted that the bromfenac formulation contains 50% less benzalkonium chloride, a preservative known to cause ocular irritation, compared to ketorolac. The bromfenac formulation does however additionally contain sodium sulphite as an excipient, which can cause allergic-type reactions including anaphylactic symptoms and asthmatic episodes in susceptible patients.

In terms of convenience, the Committee acknowledged that bromfenac has a favourable dosing schedule for patients with twice daily dosing compared to thrice daily dosing for ketorolac however the significance of this advantage in the context of multiple-day steroid administrations [for prophylaxis of CMO] was questioned.

The Committee also specifically considered the use of topical NSAIDs for the prophylaxis of CMO, for which steroids are the current mainstay of treatment. A systematic review by the Cochrane Collaboration was commenced in 2011 to clarify the role of NSAIDs for prophylaxis but it is as yet unpublished. Dr Tufail noted that NSAIDs were not routinely used as prophylaxis at Moorfields except for patients with capsule rupture or development of CMO in the previously treated eye.

In summary, the Committee agreed that use of an NSAID in patients contra-indicated, unable to tolerate, or unresponsive to, topical corticosteroids should be supported and that there was insufficient evidence to conclude on the exact role of these agents to prevent CMO currently. It was therefore agreed that the criteria for use of NSAIDs should be determined by the individual specialist until further data are published.

The Committee discussed the formulary choice of NSAID at length and it was agreed that ketorolac should be recommended, as it less expensive, has additional safety assurances, is not restricted to a 2 week duration by its licence and would be consistent with the Formulary NSAID at Moorfields.

5.2 Travaprost (Alcon) for elevated intraocular pressure

The Committee reviewed an application for travaprost eye drops to treat elevated intraocular pressure in patients with ocular hypertension or open-angle glaucoma. The applicant had suggested inclusion of travaprost onto the formulary for patients requiring ocular hypotensive therapy for whom benzalkonium chloride exposure was inappropriate. These patients were normally treated with unpreserved timolol, but due to supply problems travaprost was suggested as an alternative. The Committee noted that Moorfields currently use a once daily preparation of timolol (Tiopex®) for patients with benzalkonium chloride sensitivity to overcome this intermittent supply problem. This was considered a more appropriate solution for patients requiring a topical beta-blocker without preservative. The Committee acknowledged that travaprost is currently on the Moorfields formulary as a third-line option after latanoprost and bimatoprost. Substitution to a second prostaglandin analogue for patients unable to tolerate latanoprost was considered reasonable. The Committee also noted that although bimatoprost may be slightly more efficacious, it is associated with a higher incidence of hyperaemia. The Committee supported use of travaprost as a third line option for elevated intraocular pressure pending a shared glaucoma algorithm clarifying the position of all glaucoma drug classes in the treatment pathway. To resolve supply issues with preservative free timolol, Mr Thakrar agreed to investigate use of Tiopex® as an alternative at UCLH.

5.3 Latanoprost preservative free (Spectrum-Thea) for elevated intraocular pressure

The Committee reviewed an application from Moorfields for latanoprost preservative free (Monopost) as a first line prostaglandin analogue for patients with elevated intraocular pressure who require a preservative free preparation due to preservative allergy, intolerance or severe dry eye. The Committee noted a study by Stewart et al, reporting a higher prevalence of dry eye in patients with ocular hypertension and primary open angle glaucoma than in a normal population, with approximately two thirds of patients reporting dry eyes, of which one third are considered severe. A study by Ishibashi et al reported that preserved drops specifically containing benzalkonium chloride cause toxicity, with more instability of the tear film and disruption of the corneal epithelium when compared to their non-preserved preparations. The improvement in the ocular surface has been shown to benefit patients in terms of tolerability and comfort.

The Committee reviewed a randomised study by Rouland et al of benzalkonium chloride preserved latanoprost versus Monopost over three-months, which reported treatment-related ocular adverse effects in 3.8% of patients in the Monopost group versus 5.3% of patients in the preserved latanoprost group. Conjunctival hyperaemia accounted for 21.4% of adverse events in the Monopost group and 29.1% in the preserved latanoprost group.

Monopost was also noted to be more cost effective compared to tafluprost, which was added to the Moorfields Formulary as the first preservative free prostaglandin available in the UK one year ago.

The Committee approved the Moorfields Eye Hospital glaucoma service prescribing guidelines for chronic open angle glaucoma and ocular hypertension focusing on prostaglandin analogues, which clarified the place in therapy for preservative free latanoprost. The Committee were satisfied that preservative free latanoprost was the most suitable first-line option for patients unable to use preserved prostaglandin analogues and that tafluprost should be removed from the formulary.

5.4 Bimatoprost preservative free (Allergan) for elevated intraocular pressure

The Committee reviewed bimatoprost preservative free (Lumigan UD) as a second line prostaglandin analogue for patients with elevated intraocular pressure which has not responded to latanoprost preservative free, and for patients previously controlled on preserved bimatoprost who develop a preservative allergy or intolerance.

The Committee reviewed a randomised controlled trial by Day et al (n = 597) which demonstrated a non-inferior efficacy profile for bimatoprost preservative free compared to preserved bimatoprost. In addition a small study by Gandolfi et al (n = 15) demonstrated that 13 out of 15 patients who were non-responders to latanoprost were successfully treated with bimatoprost, although these patients did experience a higher incidence of hyperemia.

The Committee noted that the Scottish Medicines Consortium approved the use of Lumigan UD within NHS Scotland for patients who have proven sensitivity to the preservative benzalkonium chloride.

In summary, the Committee approved the Moorfields Eye Hospital glaucoma service prescribing guidelines for chronic open angle glaucoma and ocular hypertension focusing on prostaglandin analogues, which clarified the place in therapy for preservative free bimatoprost. The Committee were satisfied that preservative free bimatoprost was the most suitable second-line preservative free prostaglandin analogue option. However it was agreed that an algorithm containing the role of all agents across all the drug classes for chronic open angle glaucoma and ocular hypertension should now be compiled to aid in the clarity of the overall pharmacological treatment paradigm.

6. Medicine review

6.1 Eptotermin alfa (Stryker) for tibia fusion and long bone fractures

The Committee considered eptotermin alfa (a bone morphogenic protein, BMP) for the treatment of long-bone (tibial, fibial, ulnar, radial, humoral, femoral and clavicular) fusion surgery at RNOH at the request of the local commissioners, NHS NCL. This treatment is currently on the RNOH Formulary and used in accordance with the East of England (EoE) Specialised Commissioning Group Policy on the use of BMP (2010).

The Limb Reconstruction Unit at RNOH is a tertiary level centre and therefore accept case referrals from other secondary care Trusts with the hope of providing one last chance in the correction of fractures which are regarded as either too complex to operate on, often with non-union having undergone one to two lines of standard interventions.

Conventional treatment options generally received by patients prior to referral to RNOH include immobilisation, external fixator, osteotomy / corticotomy, ultrasonic bone growth and autologous bone graft. The proposal remains unchanged from the above EoE policy i.e. use of eptotermin alfa in patients with non-union of long-bone (exceeding nine months) who have undergone conventional treatment including bone graft where appropriate.

Evidence from the most recently published meta-analysis (Cochrane Collaboration; eleven prospective randomised controlled trials; n=976) showed that eptotermin alfa is statistically more effective than autogenous bone graft, the considered gold standard, with regards to requirement for secondary procedures (RR 0.65, 95% CI 0.50 to 0.83). There were also fewer [statistically significant] hardware related failures in the group treated with eptotermin alfa compared with autogenous bone graft (RR 0.64, 95% CI 0.42 to 0.96). Although data [and marketing authorisation] relate predominantly to tibia bone, the Committee considered it reasonable to extrapolate the above data to all long-bone fractures as the healing ability and therefore impact of BMP on healing would likely be equivalent.

Despite uncertainty from the Cochrane review relating to the use of BMP in cases of previous non-union (RR 1.02, 95% CI 0.90 to 1.15), the Committee noted that a significant proportion of use in clinical practice (particularly overseas where BMP is considered a medical device) is off-label and unpublished. The Committee also noted that local use to date at RNOH (as per EoE policy above) has resulted in successful union of long-bone in nearly all cases.

With regards to safety, the Committee noted that a pooled analysis of published studies demonstrated a comparable rate of adverse events between surgeries which used BMP compared with those that did not. Furthermore, there is evidence to suggest that BMP use reduces osteomyelitis in non-union fractures compared with autograft as well as reduces the incidence of infections and pain in patients with severe fracture (Gustillo-Anderson type IIIA and IIIB).

With regards to cost-effectiveness, the Committee noted the conclusion of a Health Technology Assessment (2007) that treatment with BMP is more likely to be considered economically attractive, compared with the standard intervention, when used to treat patients with severe fractures (Gustilo-Anderson grades IIIB and IIIC; incremental cost per QALY gained is £13,616). The cost-effectiveness of using BMP is further enhanced when its impact on patient's quality of life is also considered alongside treatment effects and costs. The Committee considered the proposed indication to therefore aid its cost-effectiveness to that normally considered acceptable by the NHS.

In summary, despite limited published data reporting on the use of eptotermin alfa in previous cases of non-union, the Committee noted that this is a licensed indication and considered that use in this manner aids its cost-effectiveness as proposed by the HTA. The Committee therefore recommended its use for the above proposed indication i.e. non-union of any long-bone (tibial, fibial, ulnar, radial, humoral, femoral and clavicular) of at least 9 months duration. Finally, as BMP is a PbR-excluded drug, the Committee advised that centre's wishing to use this agent for the aforementioned indications will need to submit a business case to NHS NCL.

7. Local DTC recommendations

7.1 Exenatide for Parkinson's disease

Exenatide for Parkinson's disease was discussed at the UCLH DTC but deferred to next month pending further trial data from the applicant.

7.2 Tocilizumab for AA amyloidosis

The application for tocilizumab in AA amyloidosis was deferred by RFH DTC to next month.

7.3 Moxifloxacin for MDRTB, CAP & acute exacerbations of chronic bronchitis

Moxifloxacin for MDRTB, CAP & acute exacerbations of chronic bronchitis is due to be discussed at the next NMUH DTC meeting.

8. NCL-MMC minutes

These were included for information only.

9. Date of next meeting

23rd May 2013

10. Any other Business

It was agreed that once the JFC agenda has been drafted it should be forwarded to the CCG prescribing leads for information and financial implication analyses.