NCL Joint Formulary Committee (JFC) Meeting

Minutes from the meeting held on Thursday 21st March 2013
in the Board Room, Floor 3, UCLP Building, Tottenham Court Road

1. Present:	Prof R MacAllister*	NCL JFC Chair
	Ms W Spicer*	RFH Chief Pharmacist
	Dr H Taylor	WH 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 T James	MEH Chief Pharmacist
	Ms N Shah	NHS Camden, Head of Medicines Management
	Dr M Kelsey	WH DTC Chair
	Ms R Dallmeyer	Commissioning Support Unit
	Ms B Brese	Commissioning Support Unit
	Mr C Daff	NHS Barnet, Head of Medicines Management
	Dr R Fox	RNOH DTC Chair
	Mr A Shah	RNOH Chief Pharmacist
	Mr G Irvine	Lay Member
	Ms S Drayan	NMUH Chief Pharmacist
	Mr TF Chan	BCF Chief Pharmacist
In Attendance:	Mr P Bodalia	RNOH Deputy Chief Pharmacist
	Dr A Grosso	UCLP Pharmacist
	Ms S Sanghvi	UCLH Formulary Pharmacist
	Mr L Wilson	Consultant, Orthopaedic Surgeon, RNOH
	Dr Y Jayran-Nejad	Consultant, Pain Management, BCF
Apologies:	Ms L Reeves	C&I Mental Health Trust
	Dr E Boleti	RFH Consultant Oncologist
	Prof L Smeeth	NCL JFC Vice Chair
	Dr D Bavin	NHS Camden, CCG
	Dr L Wagman	NHS Barnet, CCG
	Dr R Urquhart	UCLH Chief Pharmacist
	Dr C Stavrianakis	NHS Haringey, CCG
	Dr W Zermansky	NHS Haringey, CCG
	Mr A Karr	NCL Procurement Chair
	Ms G Kuforiji	BEH Mental Health Trust

**Ms Spicer chaired the meeting for items 1,2,3.1,4 & 5.1. Prof MacAllister chaired the meeting for all other agenda items.*

2. Minutes of the last meeting

Item 6.1: The minutes stated that the Committee considered the rationale cited by Dr Leandro (UCLH Consultant Rheumatologist) to be able to use the subcutaneous formulation of abatacept [as a first-line biologic option in rheumatoid arthritis according to the NICE FAD as per the IV formulation] to appear reasonable. However the minutes did not state that further discussion was still required on this subject. It was noted that this was tabled to be discussed again under agenda 3.2 later during this meeting.

3. Matters arising

3.1 NOAC choice

The Committee were informed that the manufacturer of apixiban have no immediate plans to offer a discount on their product. As per discussion at previous meetings, the Committee agreed that rivaroxaban should be the preferred NOAC of choice for NCL.

3.2 RA biologic pathway

A response from Dr Leandro (UCLH Consultant Rheumatologist) was presented to the Committee outlining, in further detail, the rationale for the six proposed deviations from the NICE algorithm on rheumatoid arthritis. The first was a request to be able to prescribe the new subcutaneous formulation of abatacept as per the recent NICE FAD for the IV formulation. The Committee was informed that the subcutaneous formulation had not yet gained a UK Marketing Authorisation at the time the NICE review on abatacept commenced. The Committee was informed that a direct head-to-head randomized Phase IIIB study had compared both formulations in terms of clinical efficacy where non-inferiority was demonstrated. A pooled analysis of studies has also shown a comparable safety profile between the formulations on indirect analyses. These data were sufficient for the regulators to grant the subcutaneous formulation a UK Marketing Authorisation for the proposed use. Moreover, the Committee was informed that a recent randomized trial [only available in abstract form] had reported clinical non-inferiority between subcutaneous abatacept and subcutaneous adalimumab. The request from the UCLH rheumatologists was to be able to use subcutaneous abatacept as a biologic first-choice option. The Committee were informed that it is currently no more expensive than adalimumab and etanercept (anti-TNFs currently prescribed) and would be considerably less expensive for CCGs than using the IV formulation which would negate additional infusion-related tariffs. The proposal was to evaluate its use after 30 patients to ensure that clinical responses were as expected as a previous move to another less expensive [and NICE approved] option [certolizumab] proved disappointing in terms of response rates in actual clinical practice. However the Committee remained unsatisfied that the case as presented was sufficiently reassuring to support this proposed deviation from NICE. It was therefore agreed that discussions regarding the remaining deviations, which were significantly less straightforward, would likely be futile. It was therefore agreed to refer Dr Leandro and colleagues to discuss all the proposed deviations again locally (with the assistance of the UCLH Use of Medicines Committee) before being brought back to the JFC for consideration should any [or all] of these matters wish to be pursued any further.

3.3 Rasburicase

Ms Spicer 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. The Committee agreed to gain further site-specific feedback on this subject from other centres for discussion at the next meeting.

4. Members & applicants declarations of relevant conflicts of interests

Ms P Taylor has attended an advisory board for Grunenthal.

5. Medicine reviews

5.1 Dibotermin alfa (Wyeth Europa) for spinal fusion

The Committee considered dibotermin alfa (BMP-2) for the treatment of spinal surgery 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 Specialised Commissioning Group Policy on the use of Bone Morphogenic Protein [BMP] (2010).

The Spinal Surgery Unit at RNOH, as a tertiary level centre, therefore accept case referrals from other secondary care Trusts with the hope of providing one last chance in the correction of spinal fractures which are regarded as either too complex to operate on, often with non-union despite up to two lines of standard interventions. The patients referred to tertiary centres therefore represent a cohort with severe disease and exceptionality with no other viable treatment options available.

The first-line treatment option for patients with vertebrae instability is fusion with the use of autogenous bone graft (from the iliac crest). The proposal is for use of BMP (single- or multiple-level fusion at any site of the spine) for the following indications:

- Revision of spinal fusion surgery (CT-scan confirmed non-union following bone autograft)
- Primary spinal fusion surgery at high risk of pseudoarthrosis
    - Pars interarticularis
    - Repairs secondary to lytic spondylolisthesis
    - Osteoporotic bone
    - Metabolic bone disease
    - Scoliosis
- Sacro-iliac joint fusion

Evidence from a locally produced meta-analysis of ten prospective randomised controlled trials (update of the HTA report; n=1,152) showed that rhBMP-2 is more effective than autogenous bone graft, the considered gold standard, for radiographic fusion of primary spinal surgery in patients with single- or multiple-level degenerative disc disease [pooled odds ratio 2.26, 95% CI 1.66 to 3.08] as well as resulting in a significantly shorter duration of hospitalisation [mean difference -0.52 days, 95% CI -0.92 to -0.11]. The applicant informed the Committee that BMP is used second-line at RNOH, as autogenous bone graft is considered cost-effective.

The Committee noted that evidence for use in the other proposed indications (including revision of spinal surgery, and fusion surgery of the cervical spine, scoliosis and sacro-iliac joint; all of which are off-label) are generally limited to uncontrolled prospective studies or retrospective analyses, however, the excellent fusion rates (>95%) were noted.

The Committee reviewed the applicants presentation of local unpublished data which support the published literature [for primary spinal surgery] in the revision of spinal fusion surgery setting across the lumbar, thoracic and cervical spinal regions (single- and multiple-level) as well as for fusion of the sacro-iliac joint (successful fusion rate of >95%).

With regards to safety, the Committee noted that the SRS database demonstrated a comparable rate of complications between surgery which used BMP compared with those that did not (8.4% vs. 8.5%). A review of local audit data demonstrated that the use of a lower dose of BMP has served to maintain a high level of successful fusion whilst reducing the incidence of serious and clinically relevant adverse events.

With regards to cost-effectiveness, despite the higher cost of BMP when compared with autogenous bone graft, this becomes cost-neutral over a 24-month horizon (accounting for costs associated with operation time, revision surgery and secondary treatment costs) in the primary setting for uncomplicated cases.

In summary, despite an absence of prospective studies for the use of BMP outside of the primary setting, the Committee considered that there are sufficient data to recommend its use for the above proposed indications. This includes use (for single- and multiple-level fusion) in the revision of spinal fusion surgery setting as well as for primary fusion surgery in patients at high risk of pseudoarthrosis (such as pars interarticularis, repairs secondary to lytic spondylolisthesis, osteoporotic bone, metabolic bone disease, and scoliosis) and for fusion of the sacro-iliac joint. The Committee agreed that although the majority of use is within an off-label capacity, this stratification in the tertiary setting serves to facilitate the cost-effectiveness of BMP. Furthermore, although the licensed indication specifies use via the anterior route, in line with advances in surgical techniques it was accepted that is more practical and safer for access to the spine via the posterior route. Finally, as BMP is a PbR-excluded drug, the Committee advised that tertiary centres will still need to submit a business case to NHS NCL.

6. Medicine applications

6.1 Tapentadol (Grunenthal) for moderate to severe pain

The Committee reviewed an application for tapentadol, a centrally-acting analgesic with a dual mechanism of action. Tapentadol has been evaluated in three RCTs against placebo and oxycodone in patients with chronic osteoarthritis or lower back pain. There were no comparisons with tramadol, which has a similar dual mechanism of action. The Committee reviewed a meta-analysis of these studies which showed that tapentadol was non-inferior to oxycodone in terms of pain control. However, the Committee noted that the effect of these analgesics in this setting produced only a marginal improvement over placebo (about 0.5 points on an 11-point pain intensity scale). The Committee noted that the adverse event profile for tapentadol appears more favourable compared to

oxycodone for common opioid-related adverse events. The Committee also reviewed the evidence for tapentadol use in neuropathic pain. Again three trials were available [in patients with painful diabetic neuropathy] one was open-label and the other two were of an enriched patient design. Again, the magnitude of benefit appeared marginal above and beyond placebo [1.0-1.5 points on an 11-point pain intensity scale]. The Committee noted the large treatment effect seen in the open-label enrichment phase which then diminished considerably at the point of blinding and randomisation. The Committee was concerned that the enrichment design would also effectively remove the blinding as patients would likely notice absence of opioid effects and also possibily experience withdrawal symptoms. The Committee considered this important as the study endpoint was subjective and it was noted that no unblinding questionnaires were utilised in any of the studies. As oxycodone has recently lost market exclusivity in the UK, it would soon be available at lower cost. Given this, the marginal imporvements in tolerability compared to oxycodone, and the lack of comparisons with tramadol, the Committee did not see a clear place for tapentadol in the treatment of chronic pain. It was concluded that tapentadol should not be recommended for prescribing based on current evidence.

6.2 Probiotics for inflammatory bowel disease

The Committee reviewed several, relatively small and low quality studies, assessing the high-dose probiotic VSL#3. In essence, it was agreed that VSL#3 may be effective for maintenance of remission in ulcerative colitis (UC) in patients allergic or intolerant to 5-ASA however evidence is limited to a small single-arm study. Evidence for use in acute UC appeared more robust and the size of the treatment effect reported was substantial although concerns were raised about the high drop-out rates and potential for publication bias. It was therefore agreed that the potential for publication bias should be investigated further before any recommendations regarding endorsement of use in acute UC is made. Moreover, it was agreed that the ACBS should be contacted to enquire whether they have reviewed VSL#3 for use in UC. Paediatric studies of VSL#3 in UC allowing concomitant 5-ASA therapy provided conflicting evidence on efficacy with a significant number of patients in the single-arm study experiencing no change or even worsening of symptoms. For pouchitis, again limited data suggests potential efficacy in maintaining remission but it was noted that the ACBS has endorsed its use for pouchitis. It was therefore agreed to recommend the use of VSL#3 in the relatively small cohort of patients with pouchitis as its use may, importantly, reduce consumption of antibiotics.

7. Local DTC recommendations

7.1 Ingenol (Picato) gel for actinic keratoses

Ingenol (Picato) gel for actinic keratoses was discussed at the RFH DTC and it was recommended that there was insufficient evidence to support its inclusion on the formulary. The Committee agreed with this decision.

7.2 HPV (Gardasil) vaccine for recalcitrant warts

HPV (Gardasil) vaccine for recalcitrant warts was discussed at the RFH DTC and it was recommended for use in a small cohort of 5 patients under an evaluation. The Committee agreed with this decision.

7.3 TInzaparin for anti-coagulation of patients with renal failure/obesity

TInzaparin for anti-coagulation of patients with renal failure/obesity was discussed at the UCLH DTC and it was recommended that the risks of introducing a second LMWH on the formulary outweighed the [licensed] dosing advantages. The Committee agreed with this decision.

7.4 Lacosamide for refractory epilepsy

Lacosamide for refractory epilepsy was previously discussed at the UCLH DTC and it was recommended to support its inclusion on the formulary as a latter-line treatment option in refractory epilepsy. The Committee agreed with this decision.

8. Date of next meeting

25th April 2013.

9. Any other Business

There was no other business.