AREA PRESCRIBING COMMITTEE MEETING
Birmingham, Sandwell, Solihull and environs
Minutes of the meeting held on
Thursday 14th May 2015
Birmingham Medical Institute, 36 Harborne Rd, Birmingham, West Midlands B15 3AF.

PRESENT:

Dr Lisa Brownell	LB	Chair, BSMHFT
Alima Batchelor	AB	Birmingham South Central CCG
David Harris	DH	Birmingham Community Healthcare NHST
Prof Jamie Coleman	JC	UHB NHSFT
Dr John Wilkinson	JW	Solihull CCG
Prof Robin Ferner	RF	Sandwell & West Birmingham Hospitals NHST
Elizabeth Walker	EW	Sandwell and West Birmingham CCG
Inderjit Singh	IS	UHB NHS FT
Isabelle Hipkiss	IH	Midlands & Lancashire CSU
Jonathan Horgan	JH	Midlands & Lancashire CSU
Mark DasGupta	MD	Birmingham CrossCity CCG
Satnaam Singh Nandra	SSN	Birmingham CrossCity CCG
Tania Carruthers	TC	HEFT NHS FT
Dr Timothy Priest	TP	HEFT NHS FT
Tony Green	TG	Patient Representative
Brian Smith	BS	Royal Orthopaedic Hospital NHST

IN ATTENDANCE:

Kalvinder Bansal	KB	Minute taker, Midlands & Lancashire CSU
Mr Belal		UHB NHS FT for item 0515/11
Prof Hackett		HEFT NHS FT for item 0515/11
Dr Hanu-Cernat		UHB NHS FT for item 0515/12
Dr Blaney		UHB NHS FT for item 0515/12

No.	Item	Action

0515/01 Apologies for absence were received from:

- Dr Paul Dudley
- Alan Pollard
- Kate Arnold
- Mandy Matthews
- Maureen Milligan
- Nigel Barnes
- Patricia James

Digital recording of meetings

The Chair reminded the committee that the meetings were being digitally recorded for the purposes of drafting the minutes. A review has been carried out against the CSU Information Governance Policy and it was agreed that the APC Terms of Reference need to be amended to identify agreement to record the meeting, the reason for recording the meeting, where/who will have the only copy of the audio recording and when the recording will be destroyed.

It was agreed that written consent would be obtained by signing the attendance sheet.

Words have been added to the attendance sign in sheet to ensure all attendees are informed at each meeting. Presenters will also be informed.

It was agreed that the digital recording would be destroyed once the minutes were ratified by the Committee members, and before publication on the website.

0515/02 Items of business not on the agenda (for AOB)

- TC -Drugs that are approved by NICE and use of them in an indication that has not been approved by NICE.
- MD – Information about letter from Birmingham and Midland Eye Centre (BMEC) regarding changes to Bimatoprost eye drops.

0515/03 Declaration of Interest (DOI)

The Chair asked for any declarations of interests for any items on today's agenda and confirmation that DoI forms had been submitted.

No further declarations were raised.

0515/04 Welcome and introductions

The Chair welcomed the members and members introduced themselves.

0515/05 Minutes of the Meeting held on Thurs 9th April 2015

Page 6, under Chapter 4 CNS, 3rd line. IS requested an amendment to the sentence to read;

IS confirmed that it had been reviewed some time ago at UHB NHSFT but that the MMAG committee had not had the opportunity to consider the views of the CCG.

Subject to this amendment, the minutes were accepted as an accurate record.

Item: 0315/09 on page 2: Nalmefene. The Chair advised she was absent at the last APC meeting, and asked whether it was usual for the APC to publish the telephone number for services as had been done for the specialist service 'Reach Out Recovery' at the last meeting. It was confirmed that this was not usual practice for the Committee. This has been done because this is a new service and wide advertising is required to ensure that clinicians and patients are able to access it and to ensure that prescribing is managed through this service. It was confirmed that the APC will not routinely advertise contact details for commissioned services.

0515/06 Matters Arising. Action table

0415/02 APC away days **Closed**
IH confirmed no emails have been received.

LB requested that the topics for Away Days are circulated well in advance and that members consult internally on these and send appropriate representation to the event. She highlighted that there have been a couple of cases where members have queried decision after the Away day when these should have been raised at the time.

0415/07 – NICE Technology Appraisals
RICaD for rifaximin for overt encephalopathy. This is on the agenda today. **Closed**
RICaD for rivaroxaban in ACS. IH to liaise with KA. **Open**

0415/09 – Updated BNF chapters
IH to circulate Chapters 1, 2, 4 and 10 this week. **Open**
Chapters 6 and 7: there is work ongoing. MD requested that the finalised sections within these chapters be circulated to allow local formularies to be updated.

0415/10 – Respiratory Network
Following a request by IH, Jonathan North has replied to say that he can draft a RICaD for Grazax. Jonathan North (JN) wanted the APC to be aware of his declarations in relation to speaker fees, paid articles and other interests in relation to the pharmaceutical company. It was confirmed that Grazax had changed from Red to Amber status and Col. Wilson had requested supplementary information to ensure the safe use. It was agreed that IH would liaise with JN to draft the RICaD and JN would liaise with Col. Wilson to ensure the draft meets his requirement before approving through the APC. **Open**

0415/11 Abbreviated application for NRT
IH confirmed that a full application has been received and would be reviewed at the July meeting. **Closed**

0315/12 – Six drug applications for COPD **Closed**
IH circulated these on 21st April and they will be reviewed at the June Away Day.

0215/03 – Declaration of interest- Audit
IH has completed the DoI audit as requested by the members. 38 members are listed. Of these, 29 have completed DoIs: 20 had nothing to declare, 9 made declarations. With regards to the members who have not completed DoIs, these are deputies or those that don't attend. IH raised a question whether members need to declare individual pharmaceutical companies and amounts of money. It was confirmed that declarations are required for individual companies but the amount of fees if applicable are not required. MD highlighted that members will still need to make declarations at each meeting in relations to items on the agenda. **Closed**
JH suggested adding the pharmaceutical company next to drug names as a prompt.

0215/13 – APC membership to be published on the website
IH thanked the members for their comments on the membership list she had circulated, and advised that this would be uploaded to the website once Professor Jamie Coleman's title has been corrected. **Closed**

0215/13 - Website and Branding
IH has completed this. **Closed**

1214/03 LB to contact BCH
This is ongoing. **Open**

0515/07 NICE Technology Appraisal (TAs)

No new NICE TA's to discuss this month.

RICaD for rifaximin from Dr A. Holt

A number of minor amendments were suggested by JC, MD and RF for Isabelle to feedback to Dr Holt.

MD highlighted that the members had suggested 2 months' supply from the specialist before transferring prescribing to Primary Care.

RF highlighted his concerns about what to do if the blood tests are abnormal. IH to liaise with Dr Holt and consider a further revision.

Action: IH to make the proposed amendments and email document to JC and Dr Holt. A revised version to be brought back next month. **IH**

0515/08 Trust Chairs non Formulary approvals

No reports submitted this month.

0515/09 Feedback from Lancashire Medicines Management Group

This item was postponed to the next meeting.

0515/10 Insulin degludec (Tresiba®)– draft RICaD

Due to the shortness of time and heavy agenda, the Chair suggested that members sent their comments by email to the APC secretariat.

Action: members to send any comments/ amendments by email. **All**

IH to collate and recirculate revised document. **IH**

0515/11 BNF Section 7.4.2 and 7.4.5– Urology review

Guest speakers – Mr Belal (UHBFT) and Prof Hackett (HEFT)

The Chair welcomed Mr Belal and Prof Hackett to the meeting and the members introduced themselves. The Chair sought consent from the guest speakers to the digital recording for the purpose of the minutes.

The Chair reminded the members of the proposed questions;

- Is there justification for solifenacin to remain on the formulary given the cost and evidence base compared to other similar agents?
- Is there a difference between cost-effectiveness and lowest acquisition cost in terms of a second-line PDE-5 inhibitor?

<u>Mr Belal – Drugs for urinary frequency</u>

Mr Belal presented on this group of drugs. He confirmed that oxybutynin IR is a cost effective first line drug, and that tolterodine together with trospium were suitable alternatives. Mr Belal explained that there wasn't a significant difference between the second line anticholinergics in clinical practice compared to the differences in cost of the preparations. He understood that cost would be a key factor in formulary choice. He also queried the proposed entry for oxybutynin patches due to the high costs and main side effect being rash on application.

LB summarised the discussions from the Away day: is there evidence that solifenacin, or any other agent, would get a better response in individuals who do not respond to oxybutynin? In other words: do we need more than one anticholinergic on the formulary, or do we suggest that if an individual fails to respond to an anticholinergic, an alternative agent is used. The safety profile would also need to be considered, especially the effect on cognitive function.

Mr Belal stated that there is data to suggest that oxybutynin IR has a significant effect on cognitive function, whereas trospium and solifenacin have a better outcome in terms of cognitive function.

In regards to evidence that a second anticholinergic would be better if patient failed on one anticholinergic, the evidence is there but it is not high quality.

He advised that fesoterodine had been reviewed at UHB FT and had been turned down for the formulary. My Belal highlighted that we should ensure that formularies match across the area with local trusts. He also indicated very few practitioners use darifenacin, and therefore he had no objections
to both these drugs being removed from the formulary.

MD asked if there was a particular reason to keep solifenacin over tolterodine, given that solifenacin was twice the cost of branded generic versions of tolterodine MR. Mr Belal highlighted the STAR trial which resulted in some evidence of greater efficacy for solifenacin compared to tolterodine. Three quarters of the patients in the trial were on the 5mg doses, and a quarter of the patients were titrated to the 10mg dose. It was noted that this dose is significantly more expensive.

Mr Belal concluded that there was good quality evidence that solifenacin was better than tolterodine in respect of incontinence episodes and urge episodes. He also reminded the members that tolterodine has an association with longer QT interval.

Prof Hackett : Drugs for erectile dysfunction, PDE-5 inhibitors

Prof Hackett advised the APC members that in the treatment of erectile dysfunction, it was the patients or their partners that concluded if the treatment was effective or not. He acknowledged that since going off patent generic sildenafil was the cheapest agent in this group. He also clarified that the patients referred to his clinic were complex cases and that 90% patients of the patients he saw had already tried sildenafil and failed to respond or been intolerant. Patients may also present having been prescribed 4 tablets a month by their GP. He recommended that GPs are encouraged to give larger amounts (e.g. 8 tablets) to allow a better trial of sildenafil.

With regards to a second-line agent, tadalafil has a longer half-life (17.5 hours vs. 4 hours) than other PDE-5 Inhibitors which aids adherence. Many patients fail on short acting drugs because they can't get the timing right; also there is variability with sildenafil with food and alcohol interactions. In preference studies, 80% of patients preferred tadalafil as it has a longer duration of action.

Prof Hackett advised it was cheaper to use to 2x5mg tadalafil instead of 10mg and in younger men the dose can be reduced to 5mg.

He mentioned that the patent for tadalafil was due to expire in 18 months which would reduce the cost significantly.

In terms of other second line preparations they have been supply problems with caverject and some of the formulations (Virudal) have been difficult to adhere to for patients. Avanafil has a similar profile to sildenafil, and has no superiority and no experience in trials in dealing with sildenafil failures. The efficacy rate of avanafil in diabetes is 40%, whereas it is 48-50% with the other 2 PDE5- inhibitors.

With regards to co-morbidities, a significant group of patients seen in ED clinics have Benign Prostatic Hyperplasia (BPH). Sildenafil can cause hypotension which can be a problem in those patients on alpha blockers. Tadalafil has less of a blood pressure lowering effect which may be important in patients with BPH. Tadalafil is also licensed to treat BPH, so could be used as a single agent to treat ED and BPH in patients who cannot tolerate both drugs.

Evidence has been put forward to demonstrate a positive cardiovascular profile for PDE 5 inhibitors in type 2 diabetes. As yet this is unpublished so cannot be considered for this discussion.

The Chair invited questions for the presenters.

BS enquired on the place in therapy of mechanical interventions.
Prof Hackett's response was that vacuum devices are not very effective and are often discarded. The better vacuum devices are expensive.
With regards to MUSE, hardly any patients remain on this treatment 12 months after initiation.

Concerns about the restriction on the number of tablets for prescribing were discussed. It was noted that patients could be given twenty times the amount of sildenafil for the price of tadalafil. Prof Hackett agreed that increasing the amounts of sildenafil supplied by GPs would reduce referrals and improve effectiveness for patients. He highlighted however that GP wrote to him to advise of their restrictions.

HSC Policy guidance on the amount of PDE- 5 inhibitors prescribed for patient was noted. MD confirmed that the HSC guidance on 4 tablets a month still stands with regards to SLS requirements. IH commented that SLS criteria no longer applied to generic sildenafil.

The Chair thanked the consultants for their presentations and they left the meeting.

The committee discussed the presentations.

Drugs for urinary frequency and incontinence– members discussion

The members confirmed that the harmonised formulary should reflect the cost considerations. Whilst a robust case had not been made for keeping solifenacin on the formulary it was recognised that this product is widely prescribed. Concerns were raised that its removal from the formulary would lead to unnecessary escalation of patients to third line drug choices at even higher cost. It was agreed to keep this on the formulary as it would keep clinicians engaged with the formulary but flag up the costs to prescribers until it comes off patent.

The consensus reached was therefore:
Oxybutinin IR – green, first line
Oxybutynin MR- green £££
Oxybutynin patch- amber – if patients cannot tolerate oral agents

Mirabegron- green, for patients not tolerating / with contra indications to antimuscarinics, in line with NICE.
Duloxetine- red
Tolterodine – green
Tolterodine MR – green with £££
Solifenacin – amber with £££, and place it in a treatment pathway beyond agents that have effectiveness at lower costs.
Fesoterodine – to be removed and notify BWH to consider an application if required on the formulary. BWH were not represented at the meeting today.
Darifenacin - remove

DH pointed out that Oxybutynin 3mg was significantly more expensive than the 2.5mg and 5mg strengths– It was agreed that the 3mg strength be removed from the formulary due to being less cost effective. A note to be placed on the website to reflect the preferred strengths: 2.5mg and 5mg.

PDE-5 Inhibitors- members discussion

MD pointed out that the patent for tadalafil did not expire until November 2017, and not in Nov 2016 as suggested by Prof Hackett.

RF proposed that GPs should be encouraged to prescribe as much generic sildenafil as necessary to provide an adequate trial of treatment, and if that was still not sufficient, tadalafil would be a reasonable alternative. He suggested an amber RAG status. JC also supported an amber status as he was still unclear of the place in therapy compared to avanafil and vardenafil.

MD confirmed that the HSC guidance was based on an average 40 year old male, but recognised that the age of these patients ranged from 16 to 65+ years. He was also concerned about the substantial potential for diversion of these drugs.

BS and AB confirmed that SLS restrictions had been relaxed for generic sildenafil, but MD remarked that the HSC guidance on number of tablets had not changed for any of the PDE-5 inhibitors.

A comment was made that encouraging large numbers of sildenafil tablets would raise patients' expectations of similarly large quantities of other PDE 5 inhibitors. MD noted that the daily dose of tadalafil was more cost effective when more than 8 tablets per week were required. There was a lengthy discussion on the RAG status and whether supporting documentation was required (if amber). SSN enquired on the status of alprostadil injection, currently rated as amber. Does this need to be reconsidered in view of Prof Hackett's comments on availability? MD proposed removal of avanafil and vardenafil if tadalafil was to be considered.

A consensus was reached:

- sildenafil is GREEN 1st line, no restrictions on quantities to ensure adequate trial
- Tadalafil is GREEN with £££, on demand preparation only, quantities in line with HSC guidance (max 4 tablets per month),SLS criteria still apply
- Avanafil and vardenafil to be removed.
- Alprostadil injection-amber

0515/12 **Tapentadol SR**

Guest speakers – Dr Hanu-Cernat and Dr Blaney (UHBFT)

Both consented to the digital recording of their presentation.

Dr Hanu-Cernat advised that UHBFT was a tertiary referral centre and that patients that presented to them will have already been on a number of treatment options in primary care and secondary care before being referred to a specialist.

She outlined that they run a chronic pain clinic with a small group of patients who are managed on tapentadol SR approved through UHBFT. Prescribing is only done by a consultant and kept internal to the Trust. There is a strict protocol in place.

They must achieve 50% pain relief with no side effects. Once patients are stable then they would be referred to GPs to take over prescribing.

In 4 months they initiated 11 carefully selected patients on this drug in a clinic that sees around 2000 patients a year.

Types of patients that may be suitable for this agent;

- Intolerant to other opioid medication, but have opioid responsive pain.
- Increasingly high doses of opioids , and difficult to manage
- Benefit by reducing amount of opioid prescribing

Of the 11 patients recruited, 50% dropped out.

The chair invited questions for the presenters.

TP asked what the place in therapy for tapentadol is. Would it be second line to morphine, third line to oxycodone then fentanyl patches?
The application suggests this is an alternative to morphine MR. Dr Blaney suggested third line or beyond. These patients would have tried a range of other opioids or similar drugs. Patients would have to have shown some response to the other drugs before being commenced on tapentadol.

A discussion ensued on equi-analgesic effect and equivalent doses.

RF recognised the difficulty in managing pain for some patients. He also noted the difficulty with ensuring and controlling appropriate prescribing. He highlighted that there have been several newer drugs where prescribing volumes have grown and concerns have been raised about the quality of prescribing and demand for these drugs, e.g. buprenorphine patches, oxycodone, tramadol.

The benefits may be outweighed by the risks with such widespread prescribing. On this basis RF did not accept that adding another new drug to primary care would lead to appropriate prescribing for this drug. He also raised concerns about the pharmacological profile (combination of opioid agonist effect with noradrenaline reuptake inhibition) and the lack of comparative trials with morphine or tramadol.

Dr Hanu-Cernat confirms that the noradrenaline reuptake inhibition may have a protective effect against illicit drug use. The other advantage over tramadol is in patients on SSRI antidepressant drugs, as she sees a significant number of patients with clinical depression. There is a danger in combining tramadol with amitriptyline or SSRIs. She advised that they get requests for this drug from knowledgeable patients and felt under pressure to prescribe or offer further options for treatment.

Dr Blaney advised that he would be happy if this was Consultant managed and controlled by this route as opposed to widely available in primary care. It was agreed that the position of tapentadol needs to be restricted to ensure high quality prescribing.

BS asked for confirmation that tapentadol would be placed after morphine, oxycodone, buprenorphine and fentanyl, as any earlier treatment with tapentadol would restrict future options due to its effect on receptors. Dr Blaney confirmed this.

The Chair thanked the consultants for their presentations and they left the meeting.

The committee discussed the presentations.

TP advised that as a pain consultant he has never prescribed tapentadol and doesn't initiate these types of potent opioids in the 2000 patients he sees. He avoids multiple prescriptions for opioids by using psychology and behaviour and using drugs with an alternative pharmacology. However in a team of 5 pain consultants, 3 would appreciate the availability of tapentadol in certain circumstances. TP advised that UHBFT does not have a specialist status as a tertiary centre.

RF advised that his view was that this drug should remain under the remit of specialists wherever this was, and to leave the drug out of the formulary, but available in individual trusts through the DTC Chair's action.

JW – advised that GPs are not expert in the use of this drug or in those patients that may be required to use this in the pathway.
TP highlighted that pain services are not commissioned in a way to provide ongoing prescribing for patients in secondary care.

MD recognised that Birmingham CrossCity CCG had supported the application with very restricted use when it was discussed at MMAG, but acknowledged that he heard a different viewpoint at today's meeting.

The Chair guided the members through the decision support tool to reach a decision:

Patient safety: high potential for abuse, toxicity and significant drug interactions, as with all opiates. No serotonin reuptake inhibition so less chance of serotonin syndrome with concomitant SSRIs than with tramadol. Tapentadol inhibits NA reuptake, as does amitriptyline.

Clinical effectiveness: Uncertain. Small number of patients seem to benefit (only 11 patients recruited in 3 months, 50% drop out)

Strength of evidence: limited, only tried against oxycodone.

Cost effectiveness: equivalent to oxycodone MR (if used in line with SMC restrictions, however branded generic version of oxycodone MR is cheaper) but more costly than other oral opiate analgesics and fentanyl patches.

Place of therapy relative to available treatments: last (4th line)

National guidance: accepted by SMC with restrictions (severe chronic pain, not responsive to morphine, with close monitoring)

Local health priorities: CCG views- despite original concerns about increased use, prescribing trend has remained fairly flat in BCC CCG, considering it was approved at UHBFT 12 months ago.

Equity of access – N/A
Stakeholder views: N/A
Implementation requirements: ESCA was submitted as part of the application, on the assumption it would be accepted as AMBER.

Decision summary:
The members agreed on RED RAG rating with the understanding that individual Trusts can chose not to put it on their formulary.
Rationale: concerns about escalating use in primary care, awareness of complexity of this group of patients and need for close monitoring.
An application may be made for review in light of additional experience but the APC wouldn't expect to see this within 12 months.

Action: IH to inform Dr Hanu-Cernat and Dr Blaney of decision **IH**

0515/13 Any Other Business

- MD- Bimatoprost eye drops:
  MD recalls alerting the committee that Allergan was discontinuing the 0.03% multidose presentation of bimatoprost eye drops as of 1st July 2015. He circulated a letter from Sandwell and West Birmingham Hospitals NHST to the GPs in the Birmingham area confirming this and recommending GPs prescribe bimatoprost 100 micrograms/ml (0.01%) eye drops once daily, administered in the evening as an alternative. Correspondence from Lucy Titcomb at the Birmingham and Midlands Eye Centre (BMEC) confirmed that in general bimatoprost was not used first line, but in patients with low intraocular pressure targets, and did not

support going back to latanoprost as most of these patients will have already tried it. MD considered this was a formulary level decision and therefore brought it to this committee to be ratified before sending the letter out. JC asked about the reason for discontinuation if it was not patent expiry. The company has told MD that this was following concerns over side effects of higher strength, and reducing the strength offered a more rational product range. The letter was approved.

- TC- NICE approved drugs for non- NICE indications
  TC used certolizumab as an example: it is approved by NICE for use in rheumatoid arthritis. It is also licensed for use in psoriatic arthritis and ankylosing spondylitis. It is a cost effective treatment for these indications. NICE has no plans to review this drug soon. The evidence is all non-inferior to other anti-TNFs, and the adverse reaction profile is similar. TC asked if the members supported the use of certolizumab for psoriatic arthritis and ankylosing spondylitis. MD commented that as the safety and efficacy were equal to other anti-TNFs, the lower cost was a reasonable factor to support its use for this condition. The members agreed.

LB thanked the members for their input today. The meeting closed at 16.40pm

Date of next meeting
Thursday 11th June 2015. 14:00-16:00
Birmingham Medical Institute,
36, Harborne Road, Edgbaston, Birmingham B15 3AF
Solomon Wand Room, 1st Floor