GMMMG Greater Manchester Medicines Management Group NHS

FORMULARY AND MANAGED ENTRY SUBGROUP

July 25th 2017 Minutes
12:30 - 2:30 pm
Pharmacy Dept. CMFT

Present:

Name	Title	Organisation	Jan	Mar	May	July
Elizabeth Arkell (EA)	Medicines Management Lead	UHSM	✓	A	✓	✓
Liz Bailey (LB)	Medicines Optimisation Lead	Stockport CCG	A	✓	A	✓
Dr Pete Budden (PB)	GP Prescribing Lead	Salford CCG *(Chair)*	A	✓	✓	✓
Sarah Boulger (SB)	Senior Medicines Information Pharmacist	The Pennine Acute Hospitals NHS Trust	A	A	✓	✓
Dr Paul Chadwick (PC)	Consultant Microbiologist and Chair of Meds Management Committee	SRFT	✓	✓	A	✓
Aoidin Cooke (AC)	Medicines Management and Medicines Information Pharmacist	CMFT	✓	LH ✓	✓	✓
Claire Foster (CF)	Senior Medicines Optimisation Advisor	SM CCG	✓	A	✓	✓
Dr Anne Harrison (AH)	Gp Prescribing Lead	Trafford CCG	A	A	✓	A
Leigh Lord (LL)	Locality Lead Pharmacist	Trafford CCG	✓	A	✓	A
Keith Pearson (KP)	Head of Medicines Management	Heywood Middleton and Rochdale CCG	✓	✓	A	✓
Prof Peter Selby (PS)	Consultant Physician	CMFT	✓	✓	✓	A
Suzanne Schneider (SS)	MI Pharmacist	Bolton FT.	A	A	✓	✓
Lindsay Harper (LH)	Director of Pharmacy	SRFT	✓	✓	A	A
Jonathan Peacock (JP)	Deputy Chief Pharmacist	WWL	✓	✓	A	✓
Zoe Trumper (ZT)	Medicines Management	Pharmacist Wigan Borough CCG	✓	A	✓	✓
Andrew Martin (AM)	Strategic Medicines Optimisation Pharmacist	GM Shared Service.	✓	✓	✓	✓
Bhavana Reddy (BR)	Head of Prescribing Support	RDTC *(Professional Secretary)*	✓	A	✓	✓
Monica Mason (MM)	Principal Pharmacist Medicines Management	RDTC *(Professional Secretary)*	✓	✓	A	A

1. General Business

1.1 Apologies

Apologies had been received in advance as noted above.

1.2 Declarations of Interest:

No declarations of interest were received in advance or made at the meeting.

1.3 Draft minutes (June 2017)

The minutes were agreed as accurate record.

1.4 Matters Arising

Fiasp

The group noted the letter and feedback received from specialists relating to the decision of the committee on the use of Fiasp®. The following points were noted:

- The bulk of the slides shared, related to post prandial spikes in type 2 diabetes and not type 1's.
- The NICE guidance for type 1's was written in 2015 when all of the evidence quoted was available and was reviewed.
- The information shared on the relationship between CVD and post prandial glucose is not definitive and is not of the quality and standard required on which to base population decision making.

The group did however re-look at the information around the NovoRapid® patent and the likely-hood of any generics or biosimilars onto the market within the next year or so. This was noted to be several years away. It was also noted that Fiasp® was currently the same price as Novorapid®. However as Fiasp® is classed as a black triangle product this means it requires extra safety monitoring and therefore it should not be used over NovoRapid®. It was therefore suggested that Fiasp could be added to the grey list for use in pregnant patients and in type 1 patients with post prandial readings of >10mmol at 2 hours. The group agreed that specialists should monitor this post prandial use and report back to the group.

Action: BR to amend recommendation as above and bring to next meeting. BR to draft response to specialists and send to PB prior to sending.

2. New Drugs

2.1 QTERN (saxagliptin/dapagliflozin) combination product

The group discussed the application for the above drug that had been requested by specialists.

Qtern is indicated in adults aged 18 years and older with type 2 diabetes mellitus:

- to improve glycaemic control when metformin and/or sulphonylurea (SU) and one of the monocomponents of Qtern do not provide adequate glycaemic control,
- When already being treated with the free combination of dapagliflozin and saxagliptin.

The following points were noted from the review document:

- Qtern is a fixed dose combination of saxagliptin and dapagliflozin, licensed for use in patients with T2DM who are already using one or both of the constituent drugs. Both saxagliptin and dapagliflozin are recommended by NICE for management of T2DM, but the treatment pathway does not include their concomitant use.
- Three phase III trials assessed various combinations of saxagliptin, dapagliflozin and metformin in adults with T2DM. All three found that triple therapy led to greater reductions in HbA1c than dual therapy with metformin plus saxagliptin or dapagliflozin.

- Dapagliflozin appeared to have a greater contribution to the glucose-lowering effects of Qtern than saxagliptin. Some patients are likely to benefit from the combination of drugs, but it is not possible to identify these patients prior to treatment. Qtern should therefore not be used to step up directly from metformin monotherapy to triple therapy.
- The trials did not raise any new safety concerns. Adverse effects were in line with the known safety profiles of the constituent drugs (e.g. gastrointestinal effects with saxagliptin and UTI with dapagliflozin).
- Given the license for Qtern and current NICE guidance, the target patient group for this product is not clearly defined. Any decision to use these drugs together should involve a specialist in the management of T2DM.
- Qtern is less expensive than giving any combination of DPP-4 inhibitor + SGLT-2 inhibitor as separate treatments, but more expensive than using either drug alone.

The group discussed the place in therapy of QTERN and acknowledged that some patients may benefit from the combination however noted that the EMA assessment report stated that the addition of saxagliptin to dapagliflozin and metformin was of doubtful clinical significance. It was also noted that the effect of both drugs combined is less than the sum of the individual effects.

The group reviewed the GMMMG formulary choices and noted that saxagliptin is not the first line DDP-4 Inhibitor of choice in the formulary and approving this product would go against that stance. In addition empagliflozin now had CV outcome data. It was also agreed that several other combination products are likely to come to market and that this combination should not be approved just because it is the first product available. The group therefore agreed that QTERN would not be added to the formulary. It could be used for those patients who are already on dapagliflozin and require a DPP4-inhibitor as it is cheaper than the two components however this would be a minority of patients if prescribers are following the GMMMG formulary.

Action: BR to feedback to specialist. No change made to formulary section.

2.2 Sodium Oxybate for the treatment of narcolepsy with/without cataplexy review

The group had been asked to re-consider their previous new therapies recommendation on sodium oxybate which does not recommend use. NHS England commissions sodium oxybate for post pubescent children ≥40 kg and aged ≤18 years old, where attempts to control narcolepsy with cataplexy have failed. Details around criteria for use can be found in the NHS England Guidance. CCGs are the responsible commissioner for adult patients.

Narcolepsy is often diagnosed either in adolescence or in middle age. Narcolepsy with cataplexy is estimated to affect around 35 per 100,000 of the population.

There is currently no cure for narcolepsy and so treatment relies upon lifestyle changes and symptomatic treatments for the different elements of day time sleepiness, disturbed night time sleep and cataplexy. Cataplexy is an episode of muscular weakness triggered by strong emotions such as laughter, anger and surprise.

Although clinically effective against placebo, sodium oxybate was considered unlikely to be cost effective even if limited to the most severe patients.

There is limited new evidence since GMMMG last reviewed sodium oxybate. A meta-analysis and systematic review published in 2012 summarises all of the available randomised controlled trial evidence. All of the efficacy outcomes reported favoured sodium oxybate and all were statistically significant, with the exception of the proportion of REM sleep.

Narcolepsy is an orphan disease, and clinical studies included small numbers of people for a short duration of time.

The group agreed that where paediatric patients fulfilled the NHS England criteria and had been started on sodium oxybate and benefited from its use these may be continued into adulthood. However as there is limited new information available it is not recommended for

use in new adult patients. Use of sodium oxybate should be restricted to use by sleep specialist consultant with prior experience of use.

NHS England estimates that there are currently 10 children treated with sodium oxybate nationally, with a further 10 waiting for treatment. They also estimate that 10 children each year may be diagnosed with severe narcolepsy with cataplexy and qualify for sodium oxybate treatment.

Action: BR to amend Sodium Oxybate recommendation as above

3. RAG List

3.1 RAG Assessments:

3.1.1 Tolvaptan

FMESG had received an application from Wigan for Tolvaptan tablets to be made amber. They are currently red on the RAG list. Comments on this had been received by PS and these had been shared with the group. It was noted that tolvaptan in most cases is a short (10) day course and there is an NHS England policy around its use. The use described in the application by Wigan (longer term) would likely fall foul of this policy. It is PbR excluded so NHS England will pick up the costs if patients fall within their criteria for use. It was agreed that GP's would not be happy to pick up prescribing of this in patients due to the specialist nature of treatment; therefore no changes will be made to the RAG list. JP agreed to feed this back to the specialist.

3.1.2 Modafanil for Parkinson's Disease

The group discussed the RAG status of Modafanil for use in Parkinson's disease. It was noted that the licensed use in narcolepsy was amber however all unlicensed uses were classified as RED. The group felt this was appropriate due to the safety issues however this will be discussed further under agenda item 5.1 and assessment for the Grey list. No changes will be made to the RAG list currently and feedback from specialists should be sought.

Action: BR to ask for specialist feedback.

3.1.3 Octreotide

A proposed change to RAG status for octreotide for Intestinal secretion inhibition for palliative care use had been received following review of the palliative care guidelines. It was noted that use is likely to be at short notice and towards the end of life particularly in the management of GI obstruction syndromes. The group had requested further feedback from specialists on whether this is needed in an emergency and what would the duration of treatment be. The specialists indicated that often there is no one available within the palliative care team to provide the prescription. On further discussion the group agreed that use in the above manner was highly specialist and it did not fit the criteria for a GREEN medicine and shared care and an amber RAG status was still felt to be the most appropriate status. GPs would require specialist input and support to prescribe. It was therefore agreed that the RAG status would remain AMBER on the RAG list.

Action: AM to feedback above decision to specialist.

4. Formulary

4.1 Formulary amendments

It was agreed that the formulary will be updated in line with NICE TAs 444 – 45. Links to the MHRA safety guidance will also be included. It was agreed that Glucophage SR for its new indication should be added to the FMESG workplan.

Action: MM to update the formulary following GMMMG approval

4.2 Formulary Section Review

4.2.1 Drugs used in Diabetes:

The group discussed the section in the formulary related to drugs used in diabetes.

The following actions were agreed:

- **Rapid Acting Insulin Analogues** – remove the alternative box and leave all insulin products as equal choices as Novorapid is now the same price as apidra.
- **Biphasic Insulins -** Remove the section on biphasic insulins as these are not recommended by NICE guidance. There is historic prescribing however the formulary should be the gold standard and not based on historic use.
- It was agreed that a link to the Insulins cost comparison chart should be shared with the group.
- Remove any mention of **Lucozade** in treatment of hypoglycaemia as the new formulation now has a lower sugar concentration so it can't be used in this manner any longer.

4.2.2 Review of Insulin Pen Needles.

The group were informed that several applications had been received to update the insulin pen needle section of the formulary. The group reviewed the current formulary choices and agreed that if all other factors are the same there is no reason why the cheapest option cannot be used. However it was noted that some localities were recommending specific pen needles based on current GMMMG choices and were unlikely to change. The group also considered the fact that the cheapest option may change so wanted to 'future proof' the formulary section. It was therefore agreed that the formulary would recommend that a 4mm needle should be used as first choice as these reduce injection pain however only those needles that are less than £6 for pack of 100 will be recommended on the formulary. A link to the cost comparison chart will be included within the formulary. It was also suggested that the cost threshold should be reviewed in 6 months with a view to reducing this to £5.50. In addition all needles >£10 per pack of 100 should be assessed for the DNP list at the next meeting.

Action: BR to make changes as above and add expensive pen needles for assessment for DNP.

4.2.3 DDP-4 Inhibitors (Gliptins)

The group reviewed the gliptin entry in the formulary and noted that there are currently four products included. As there are no head to head trials there is limited information around whether there are any differences between the DDP-4 inhibitors however it is generally thought that they are similar in efficacy. Alogliptin as the cheapest option should remain as first choice and linagliptin had been included due to the fact that no dose reduction is required in renal impairment; however the reason for including both sitagliptin and saxagliptin is less clear. Alogliptin, Sitagliptin and Saxagliptin all have neutral CV outcome data. After further discussion the group agreed that sitagliptin should remain in the formulary due to the earlier patent expiry (~2022) and that saxagliptin should be removed from the formulary. The combination product with metformin should also be removed. The NTS recommendation on DPP-4 inhibitors refers to the NICE clinical guideline so can be superseded.

Action: BR to make changes as above.

4.2.4 SGLT2 Inhibitors

The group reviewed the NTS recommendation on SGLT2's and the corresponding formulary section. It was noted that all SGLT2 inhibitors need to be included in the GMMMG formulary as they all have NICE TA's. It was agreed that the NTS recommendation should be updated to include a link to the empagliflozin TA as this had not been available at the time of the recommendation. The group then moved onto discuss the cardiovascular outcome data that was available for empagliflozin in the EMPA-REG OUTCOME study. It was agreed that whilst all options should be available that empagliflozin should be the GMMMG SGLT2 preferred local

choice. There was some discussion around whether it was possible to have a preferred choice. AC and BR agreed to look into this.

Post meeting note: The NICE FAQ's around formulary inclusion address the above issue around local preferences: https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/Frequently-asked-questions-on-NICE-compliance.pdf

This states: *Providers or commissioners can suggest to healthcare professionals that a particular medicine is preferred locally. Reasons for this could include cost, if a medicine is cheaper than other options, to reflect local clinical expert opinion or to achieve optimal stock control. However this local recommendation must only be taken into account after a patient and prescriber have discussed all treatment options and only if they have no preference about which medicine they want to use.*

4.2.5 GLP-1 Receptor Mimetics

The group reviewed the GLP-1 entry in the GMMMG formulary. It was noted that the current choices were still suitable however current cost comparisons of treatments would have been useful. BR agreed to share this with the group following the meeting. No changes were proposed to this section of the formulary however the group then discussed the formulary application received for Xultophy.

Xultophy Review.

Xultophy is a combination of insulin degludec and liraglutide. The previous New Therapies Subgroup had reviewed this combination product in May 2015 and did not recommend use for the following reasons:

- The fixed dose ration of the combination does not allow separate titration of the two products
- Insulin Degludec is not the insulin analogue of choice in NICE or the GMMMG formulary
- The use of liraglutide in doses above 1.2mg is not recommended as results from a meta-analysis showed no significant difference between liraglutide 1.2mg and liraglutide 1.8mg in terms of patients achieving an HbA1c level of less than 7%.

An application to re-review the above statement had been received by a specialist from UHSM. He was requesting use in uncontrolled patients. It was noted that Xultophy now had approval from the SMC and All Wales. Both had accepted Xultophy for restricted use. The group agreed that the HbA1c results did look promising however further information on the types of patients this would be used in is required from the specialist. It was also agreed that the newer clinical data should be looked at. It was however noted that a new combination product – insulin glargine and lixisenatide was due to be launched shortly and that it may be sensible to look at both of these products together.

Action: BR to check patient group with specialist and look at new trial data for next meeting.

5 DNP and Grey Lists

5.1 Grey list assessment: Modafanil for PD and Narcolepsy

Due to time constraints the group agreed to discuss the above agenda item via email.

Post Meeting Note: the group agreed to add Modafanil to the Grey list for Parkinson's disease patients as per the NICE clinical guideline and for its licensed indication of narcolepsy with/without cataplexy. The RAG status for Parkinson's disease would be discussed at the meeting in September however the current RAG status of Amber for the narcolepsy indication was still appropriate. All other non-licensed indications are DNP.

Action: MM to update Grey list once item has been ratified by GMMMG.

5.2 DNP/Grey list assessment: Nefopam

The group reviewed the feedback received by specialists and agreed that nefopam should be added to the grey list for the following indication:

Patients with moderate to severe chronic liver disease who require analgesia stronger than paracetamol in whom NSAIDS and moderate strength opiates are contraindicated.

This would go to the next GMMMG meeting for approval.

Action: BR to take to GMMMG for ratification.

6 Horizon Scanning and Work-plan

Due to time constraints PB asked BR and AM to look through the work plan and horizon scanning documents and add any new items outside of the meeting.

The following items would be added to the work plan for the group:

- Proposal to DNP Atorvastatin 30 + 60mg as they are ten times the cost of 20-80mg.
- Cariprazine – new antipsychotic.
- Triple combination inhalers. The Chiesi product is likely to be launched first however others will follow.
- Spheroids – first in class. Likely to be PbR excluded.
- Grazax re-review.

7 Additional items

There was no other business discussed and the meeting concluded.

The next meeting will be held on 26th September 2017 at 12.30pm, CMFT.