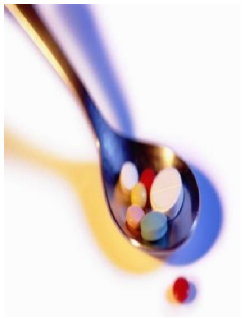

NewTherapiesSubgroup

Minutes

21st July 2015, 12:30 - 2:30 pm
Pharmacy Dept. CMFT

Greater Manchester Medicines Management Group

NHS

Present:

Elizabeth Adcock (formerly Craig) (EA) Medicines Information Pharmacist, PAHT
Jennifer Bartlett (JB) Senior Medicines Management Pharmacist – South Manchester CCG
Dr Peter Budden (PB) GP and Prescribing lead, Salford CCG (*Chair*)
Rachael Fallon (RF) Deputy Director of Pharmacy and Medicines Governance, CMFT
Makrand Goré (MG) Medicines Management Pharmacist, Bolton CCG
Keith Pearson (KP) Head of Medicines Management, Heywood Middleton and Rochdale CCG
Zoe Trumper (ZT) Medicines Management Pharmacist, Wigan Borough CCG

Support:
Andrew Martin (AM) Strategic Medicines Optimisation Pharmacist, GM CSU.
Bhavana Reddy (BR) Head of Prescribing Support, RDTC *(Professional Secretary)*

Apologies received: LA, HSo, RW and HS

Declarations of Interest
Two members of the meeting declared that they had attended an advisory board relating to Xultophy® which was on the agenda – they were excluded from decision making around the Xultophy® agenda item.
One member declared that they had attended two advisory boards relating to respiratory medicine, one for BI and one for TEVA - these were not product specific.
One member declared that they had attended a short advisory meeting on the use of aflibercept in DMO however no decisions on whether aflibercept should be used were due to be made however a DMO pathway had been tabled for comment.

1) Minutes of the meeting on May 2015.

The minutes were accepted as a true and accurate record.

ACTION: To be sent to GMMMG then to be published on website.

2a) Matters Arising:

The group were updated on the matters arising document.

2b) Matters arising – Xultophy® Re-review.

The group re-reviewed the data on Xultophy as summarized in the NICE evidence summary: new medicine document. The group noted that the summary looked at the main two phase III trials – DUAL I and DUAL II which the group had looked at previously. It was noted that there were still three completed phase III trials which had not yet been published. The group also reviewed the application received by a specialist from Bolton as well as previous comments received from other specialists. It was noted that most specialists were happy to use a combination of basal insulin and GLP-1 analogue rather than the Xultophy® combination product specifically.

The group further discussed the place in therapy of Xultophy® and agreed that prescribing a combination of basal insulin and a GLP1 may be useful for the patient group described, however they were unsure of the benefits (other than one injection) of a fixed dose combination product. It

was felt that use of a fixed-dose ratio of the combination product did not allow for the insulin and GLP-1 analogue doses to be titrated separately in order to optimise individual patient diabetes control. In addition NICE TA203 does not recommend the use of liraglutide 1.8 mg daily. For those patients requiring doses of insulin degludec of 34 units and above, they will receive higher than the NICE recommended dose of 1.2mg liraglutide when using Xultophy®. Furthermore, NICE guidance recommends that the use of insulin analogues in type 2 diabetes should only be considered if deemed clinically appropriate. i.e. failure to maintain glycaemic control overnight and in those patients in whom nocturnal hypoglycaemia is an issue despite optimisation of medication regimen or for those with an unpredictable lifestyle e.g. shift workers. The group agreed that other than administration of a single daily injection, additional clinical benefit over using separate basal insulin and GLP-1 analogue agents concomitantly has not been demonstrated.

It was also noted that two biosimiliar insulin glargine preparations will be available over the next month or so which will reduce the cost of insulin glargine prescribing.

The New Therapies Subgroup of the GMMMG considered the use of Insulin Degludec & Liraglutide (Xultophy®▼) for the management of adults with type 2 diabetes.

The group does not recommend the use of the combination product Xultophy® for the above indication.

The fixed-dose ratio of the combination product does not allow for the insulin and GLP-1 analogue doses to be titrated separately in order to optimise individual patient diabetes control. For patients receiving doses of insulin degludec of 34 units and up to 50 units the group noted that they will receive between 1.2 and 1.8mg of liraglutide. 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 reaching an HbA1c level of less than 7%.

As per NICE guidance Neutral Protamine Hagedorn (NPH) insulin is the preferred treatment option for type 2 patients who require insulin.

The use of long acting insulin analogues in type 2 diabetes should only be considered if deemed clinically appropriate. i.e. failure to maintain glycaemic control overnight and in whom nocturnal hypoglycaemia is an issue despite optimisation of medication regimen or those with an unpredictable lifestyle e.g. shift workers. If classed as appropriate the preferred long acting insulin analogue is **insulin glargine** as outlined within the GMMMG formulary. Insulin degludec is not routinely recommended.

Other than administration of a single daily injection, additional clinical benefit over using separate basal insulin and GLP-1 analogue agents concomitantly has not been demonstrated.

According to set criteria Xultophy® was deemed to be a low priority for funding

ACTION: BR to draft recommendation as above

2b) Update on previous recommendations.

It was noted that GMMMG opted not to publish the two recommendations on secukinumab and apremilast as NICE guidance was due to be issued shortly. A query was raised around the reviewing of recommendations due to be reviewed by NICE and whether NTS should be reviewing these in the first place however it was felt that it had been valuable to assess the two new drugs for psoriasis as there were rebate schemes in place which specialists wanted to take advantage of and these schemes were only available for a short period of time, prior to the NICE guidance being published. It was also noted that several IFR requests for these drugs had been received and publishing the recommendations may have been useful to reduce work load in dealing with these requests. It was felt at the time that it would have taken awhile to gain approval from AGG and by this point the NICE guidance would be available. The group agreed therefore that it would seem sensible to include a statement within their terms of reference to state that they would not review new drugs that would be reviewed by NICE within 6 months of launch.

It was agreed that in this particular case, as NTS was due to look at the biologic pathway in psoriasis it had been useful to review the individual drugs despite this.

ACTION: BR to add statement to terms of reference and send to the group for approval.

2c) Airsonett device – response from Specialists.

The group discussed the response received from the Specialists around the use of the Airsonett® device. It was noted that treatment success would be defined initially by an improvement in PAQLQ improvement scores; PAQLQ is a validated questionnaire and it is also what is used in the assessment of omalizumab after the 16 week trial. The group reviewed the preliminary information from the European data which is due for publication shortly, and shows a reduction in exacerbation frequency, however the data covered small patient numbers (n=30) and is not a randomised control trial so the information whilst encouraging needs to be taken with caution. The specialists were advocating use of Airsonett® in those patients (children) who cannot have omalizumab but who have severe allergic asthma and/severe allergic eczema with high IgE levels. If however a child was suitable and eligible for omalizumab this would remain the first line choice. The group noted that currently the company which provides Airsonett® had agreed to refund the first 3 months of treatment if treatment was not successful. It was felt that three months wasn't a long enough period of time to evaluate success and the group agreed that six months would be better. The group reviewed the device as per the NTS device classification and noted that the case for adoption would be partially supported based on the evidence available. After further discussion the group approved the use of Airsonett® as below:

The New Therapies Subgroup of the GMMMG considered the use of Airsonett® - a temperature controlled laminar airflow medical device, for use in children and adults, with poorly controlled persistent atopic asthma despite medium to high dose pharmacotherapy.

The group recommends the use of Airsonett® for those patients who are not eligible or suitable for treatment with omalizumab and have demonstrated symptom improvements (using the PACLQ questionnaire) following a six month trial of Airsonett®.

The group recommends that Airsonett® is initiated by a specialist in respiratory medicine, for those patients with atopic poorly controlled asthma at BTS step 4 and above who may be under consideration for long term oral steroids and who are not eligible or suitable for omalizumab therapy. A positive skin test/serology to at least 1 indoor perennial allergen and total serum IgE at least 70 IU/ml would also need to be demonstrated prior to initiation.

The current cost of Airsonett® is £208.80 per month; this includes all servicing, breakdown and consumables.

Please note that primary care funding will only be approved following a successful 6-month trial showing symptom improvements.

New Therapies Subgroup Device classification: Case for adoption is partially supported i.e. recommended for use in particular circumstances.

According to set criteria Airsonett® was deemed to be a medium priority for funding in the specific patient group identified.

ACTION: BR to draft recommendation as above.

2d) Biologics pathway (Psoriasis)

The group reviewed the proposed GMMMG psoriasis biologics pathway that had been written by Dr Warren and colleagues from Salford Royal. The group agreed with the approach contained within the document with one minor amendment, they proposed that biosimilar infliximab should be used in place of infliximab for new patients. The group also felt that an algorithm would be useful if this was possible.

ACTION: BR to update recommendation and feedback to RW then take to GMMMG for approval following amendment.

2e) Vitamin D deficiency and insufficiency in adults

The group noted that the above recommendation was now due for re-review however there had been no new evidence since the group last reviewed the document. It was agreed however that the

summary of the National osteoporosis society should be updated to include the now licensed products that are available.

ACTION: AM to update document and send to BR for publishing on website.

3) Vortioxetine for depression

The group reviewed the summary data within the review document. They noted that draft NICE guidance had now been published. An appraisal consultation document was published in June 2015 which indicates that the committee is *'minded not to recommend vortioxetine'*. Key reasons were the lack of robust comparisons to other antidepressants, the lack of data showing efficacy beyond 8 weeks use, and lack of generalisability to clinical practice.

In light of this the group opted not to produce a separate NTS recommendation but agreed that the data wasn't particularly compelling. The following points were raised:

- The clinical trial program for vortioxetine is extensive. Most trials were short (6-8 weeks) and used a placebo comparator. A meta-analysis of 12 of these short trials found that while vortioxetine was more effective than placebo for the treatment of major depressive episodes, the absolute difference was small and may not be clinically important.
- A network meta-analysis indirectly compared vortioxetine with other antidepressants including sertraline, escitalopram, venlafaxine and duloxetine, and found that all of the assessed drugs had comparable efficacy.
- Vortioxetine is commonly associated with gastrointestinal adverse effects such as nausea, as well as headache and dizziness. It appears to be slightly better tolerated than duloxetine or agomelatine, but comparative data are limited.
- Vortioxetine costs £360 per patient per year, which is the same as the current cost of duloxetine (Cymbalta®). However, generic preparations of duloxetine are now reaching the market, and the price may change accordingly.
- NICE guidance for treatment of depression specifies that, where an antidepressant is required, the first line choice should be a generic SSRI. Antidepressants of other classes should be considered after one or two SSRIs have failed.
- Vortioxetine has a limited safety history and clinical experience compared to other drugs currently available. Due to its novel mechanism of action, it may be useful for patients who have failed to respond to multiple other treatment options.
- Generic fluoxetine currently costs £14 per patient per year. Citalopram, sertraline, escitalopram, venlafaxine and mirtazapine all cost ≤ £20 per year.

4) Spiolto® Respimat® (tiotropium/olodaterol) combination inhaler for COPD.

The group noted that this was the fourth LAMA/LABA inhaler to be launched. The group noted the following points from the summary document:

- Spiolto is indicated as a maintenance bronchodilator treatment to relieve symptoms in adult patients with COPD.
- Two phase III, multicenter, 52 week clinical studies (TONADO 1 and 2) looked at over 5,000 patients with COPD.
- Results showed that lung function, as measured by trough forced expiratory volume in one second (FEV1), improved in patients receiving tiotropium + olodaterol (fixed dose combination product) delivered via the Respimat inhaler, and that St. George's Respiratory Questionnaire (SGRQ) total score was affected favourably compared to those receiving olodaterol or tiotropium alone.
- Data also showed that tiotropium + olodaterol Respimat® was well tolerated with a favourable safety profile that was similar to tiotropium or olodaterol alone.
- A network meta-analysis carried out by the manufacturer claims that Spiolto® has similar efficacy to that of other LAMA+LABA combination products.

- The 30-day cost of Spiolto® Respimat® is £32.50 which is cheaper than the cost of the constituent products but the same price as Anoro Ellipta® and Duaklir Genuair®.
- It was noted that as this product contains tiotropium as its LAMA it may be a useful option for the large numbers of patients currently being prescribed tiotropium, however it is important to note that this new combination is in the Respimat® device rather than the Handihaler® device.

The New Therapies Subgroup of the GMMMG considered the use of combination inhaler Spiolto® (tiotropium/olodaterol) to relieve symptoms in adult patients with COPD.

The group recommends the combination inhaler Spiolto® as an option only when the separate constituent LABA and LAMA inhalers would be prescribed.

Two phase III trials showed similar clinically relevant improvements as those reported in other LAMA/LABA combination trials.

Spiolto® combination inhaler costs £394 per patient per year which is the same price as Anoro®Ellipta® and Duaklir® Genuair® (other LAMA/LABA combination inhalers). This is cheaper than the cost of separate LAMA and LABA inhalers and may help with adherence for some patients.

According to set criteria for the above indication was deemed to be a medium priority for funding.

ACTION: BR to draft recommendation as above

5) COPD pathway

The group reviewed the COPD pathway that had been recently published in *Guidelines in Practice*. Professor Dave Singh had been involved in authoring the pathway and it covered a similar scenario to the pathway he had spoken to the group about when he attended a meeting last year. It was noted the pathway was based on GOLD guidance rather than NICE guidance, which are now thought to be out of date. The main changes are around using a LAMA/LABA combination earlier to reduce the use of high dose inhaled steroids. The group agreed that this pathway seemed useful and sensible and approved the content. It was agreed that this should be put into a GMMMG format and links to NTS recommendations and formulary choice of products should be included within the pathway. It was agreed that this should go to the formulary subgroup with a query around whether product choices could be rationalised; it was agreed, however that this would be difficult but a starting point would be to identify the most cost effective first line choices.

ACTION: BR to put pathway into GMMMG format and then send to FSG for further input.

6) DMO pathway

The group had been asked to review the DMO pathway from CMFT which had been sent to them from Central Manchester CCG. The group noted that the document was actually 'a guideline for use of aflibercept' rather than a full pathway for DMO. The group noted that there was currently a FAD from NICE which recommended use of aflibercept in DMO if the patient fulfilled certain criteria. It was therefore unclear as to why a guideline just for the use of aflibercept was being developed as use should be as per the NICE TA. The group agreed that the document was difficult to follow and didn't explain where in the pathway aflibercept would be used. It was recommended that a full DMO pathway would be more useful as there are now several options available for treatment of DMO and identifying which treatment would be used when within a pathway would be helpful. It was agreed that this would be fed back to the CCG and then followed up with the Eye Hospital. The group would be happy to work with specialists to get a pathway approved across GM, if they were able to draft an initial document.

ACTION: BR to feedback comments to Manchester CCG and then to contact specialists to discuss the development of a full pathway for DMO.

7) Current work plans & new submissions received since April & Horizon Scanning

The group discussed the current work plan and noted that they had agreed to look at the biosimilar insulin glargines, ivermectin cream and anal irrigation systems in September. The group asked if it was possible for a specialist nurse requesting anal irrigation systems could attend the meeting to give the group an idea of the kind of patients this is likely to be used in. It was noted that the healthcare professionals requesting use were variable and in one case a clinical psychologist had requested a GP to prescribe. BR agreed to contact the specialist incontinence nurse at CMFT to see if she was able to attend.

One member raised an issue around the pain clinic requesting GP's to prescribe gabapentin 10% gel. It was agreed that the group would look at the evidence for this in September if there was room on the agenda.

It was noted that edoxaban for DVT was to be looked at under a NICE TA so this could be removed from the work plan. It was noted that two PCSK9 inhibitors (alirocumab and evolocumab) were due to be launched soon and that these could be looked at in the November meeting.

ACTION: BR to update work plan as above.

8) Updates from other groups.

Formulary Subgroup
The group was updated on the last formulary subgroup meeting. It was noted that the group was currently undertaking an inhaler review. The group welcomed the review but asked that cost effectiveness be considered when first line choices were recommended. i.e. if two products contain the same ingredients and are contained within a easy to use device then the product with the lowest acquisition cost should be recommended.

GMMMG
The group was updated on the last GMMMG meeting. The group noted that the next GMMMG meeting had been cancelled and that the next meeting would be September.

Interface Subgroup
The group was updated on the interface subgroup meeting and noted the issues surrounding the use of low strength antipsychotics in dementia patients.

9) AOB
No other issues were raised under any other business.

10) *Date of Next Meeting: 15th September 2015, 12.30-2.30pm, CMFT*