NewTherapiesSubgroup

17th May 2016 Minutes

12:30 - 2:30 pm
Pharmacy Dept. CMFT

GMMMG Greater Manchester Medicines Management Group

NHS

Present:

Elizabeth Adcock (EA) Medicines Information Pharmacist, PAHT
Elizabeth Arkell (EAr) Medicines Management Lead, UHSM
Jennifer Bartlett (JB) Senior Medicines Management Pharmacist – South Manchester CCG
Dr Peter Budden (PB) GP and Prescribing lead, Salford CCG (*Chair*)
Makrand Goré (MG) Medicines Management Pharmacist, Bolton CCG
Rachael Fallon (RF) Deputy Director of Pharmacy and Medicines Governance, CMFT
Dr Peter Selby (PS) Consultant Physician and Honorary Clinical Professor of Metabolic Bone Disease, CMFT.
Dr Handrean Soran (HSo) Consultant Physician, Central Manchester University Hospitals Trust
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: HS, RF.

Declarations of Interest:
A declaration was made regarding the PCSK9 inhibitors however it was noted that no decisions were required on this agenda item and it was just an update.

1) Minutes of the meeting on March 2016.

The minutes were accepted as a true and accurate record.

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

2 Matters Arising:

The group were updated on the matters arising document. There was nothing new to report.

Review Dates on recommendations

ZT raised the issue of review dates again and requested that these be reinstated; the group discussed the merits of this. It was noted that Wigan CCG preferred to have review dates included however others did not feel as strongly. There were two viewpoints:

a) Reviewing every two years regardless of whether there is new data or not is time consuming and leads to a substantial workload for the support services with very few changes to the recommendations so some felt it was better to have no review date and just review as and when new data is available. This would be picked up via horizon scanning.
b) Others felt that having a two year review date ensures that the recommendation is up to date and that there could be confidence in the recommendation from prescribers.

It was however noted that most recommendations that do require updating are identified prior to the review date in most cases which then triggers an earlier review. It was noted that any recommendations superseded by NICE TA or National guidance would get removed from the site straightway and would be moved to the superseded section of the website. This would happen

within 90 days of issuing of the NICE TA. BR raised the issue that the NTS process needed better alignment with other GMMMG subgroups particularly as there had been occasions in the past when both subgroups had considered the same issue which had led to some duplication of workload. It had also been proposed that NTS recommendations once issued should be incorporated into the formulary and shouldn't be stand-alone documents as prescribers should be accessing all GMMMG advice via the formulary; this would negate the need for a separate review process just for NTS documents. The formulary already has a robust review process which includes some horizon scanning.

In addition the remit of the group was also raised with a view to highlighting that NTS should only consider new drugs (i.e. those drugs licensed within the last 18 months) as per the groups terms of reference and that if the group kept re-reviewing all old recommendations continuously it was impinging on the remit of the formulary subgroup. It was therefore proposed that all recommendations older than three years old should be superseded, after ensuring that the content had been incorporated into the DNP, Grey list or the formulary as applicable.

Post meeting note: *Following further discussions via email the majority of membership agreed that review dates should be removed from NTS recommendations and recommendations would remain valid. Recommendations would only be reviewed should substantial new data that may change the recommendation be highlighted via horizon scanning via the GMMMG Formulary Subgroup. In addition it could be raised by the RDTC, Specialists or the Industry. It was also agreed that recommendations older than 3 years old be archived. A separate archive section to the site would be developed so that these could be moved.*

ACTION: BR to liaise with professional secretary of Formulary Subgroup to ensure that horizon scanning processes will highlight any new data on existing recommendations to NTS and to ensure incorporating archived recommendations into the formulary where applicable.

2a) **PCSK-9 Inhibitors NICE FADs.**

The group noted that the NICE TAs for evolocumab and alirocumab were at the FAD stage. It was envisioned that the technology appraisal would be issued at the end of June. The group therefore agreed that it was not necessary to issue the NTS recommendation. It was however agreed that a pathway or protocol for use of these new drugs should be looked at so that the guidance can be clarified. It was felt that some guidance around the differences between the drugs may be useful as well as definitions for 'statin intolerance' and persistently high LDL. There was also some discussion around whether these drugs should be reserved for use by lipid specialists only. HS stated that specialists would be happy to work together to agree a protocol for use document. It was proposed that this should be raised at GMMMG for CCG medicines optimisation leads with the support of the shared service could work with specialists to develop a guideline.

ACTION: BR to raise at GMMMG on Thursday.

2b) Ulipristal

The group reviewed the ulipristal NTS recommendation which the group was happy with. It was agreed that it should be put into the new format. The specialist had forwarded a protocol for use which seemed to be based on a template from the pharmaceutical company. It was noted that the RDTC had seen a very similar template in the papers for York APC although the GM version had clearly been adapted to fit the pathways in GM. It was agreed that if the treatment protocol was to be used it should be put into a more generic GM format. PB also re-raised the issue of mirena coil. BR explained that the consultant had fed back that in most cases mirena coil cannot be used for the more severe patients in whom ulipristal would be used as they often have large fibroids and the coil would fall out. Whilst this was acknowledged it was however agreed that some reference to other options prior to the use of ulipristal within the flowchart would be useful.

ACTION: BR to put into GMMMG format, consult specialist and to add in further information as requested by the group.

2c) Idarucizumab (praxbind®)

This item was for information. The group noted that this final recommendation had already been signed off by GMMMG. The group had no further comments on the above.

2d) Etanercept Biosimilar (Benepali®)

The group approved the above recommendation.

ACTION: BR to send to GMMMG for sign off then publish on website

2e) Sufentanil® draft recommendation

The group approved the draft recommendation. Draft costings for sufentanil were available however these were not in the public domain so it wasn't clear whether they could be quoted within the recommendation. It was agreed that the recommendation could be updated once the product had been launched. The group were also informed that the AHSN had been involved in some clinical trial work for this and that CMFT and Pennine acute had been local evaluation sites. It was agreed that this should be looked into further however it would not impact on the current recommendation.

ACTION: BR to take to GMMMG for sign off.

2f) Rhinitis/Rhinoconjunctivitis pathway

The group reviewed the allergic rhinitis pathway that had been developed by the NW allergy group. It was noted that this had been developed to aid primary care in treatments prior to referral. The group liked the flow chart and pathway and felt it was very useful. They had a few comments and queries are some of the content:

- Under medical management, it was proposed that oral antihistamines should be a higher bullet point than the nasal corticosteroid.
- Notes section was slightly confusing and there was a query regarding Dymista® under note 2 and whether this should go under note 4 – add on treatment in special circumstances.
- There were also some queries around product choices in some cases:
    - Oral antihistamines are often used at higher than licensed doses rather than moving onto the next stage straight away so is this a safe option albeit unlicensed. E.g. 20mg cetirizine.
    - Nasal antihistamine sprays are not prescribed often in primary care and there was a query around whether there was any merit in using antihistamine nasally as opposed to oral use.
    - The group noted that the antihistamine eye drops proposed are not in line with the GMMMG formulary
    - For the section on nasal corticosteroids, it was noted that beclometasone nasal spray had not been included and the group noted that fluticasone furoate is preferred; this was cost effective however it would be useful to understand the rationale for choices made.

The group agreed that it was a useful document but felt that clarity on the above would be useful.

ACTION: BR to feedback above to specialists and put pathway on GMMMG website for consultation.

2g) i) Relvar® price reduction

The group reviewed the letter from GSK highlighting the reduction in price for Relvar® from £27.80 to £22.00 for COPD doses and £38.87 to £29.50 for asthma doses. This price reduction now brings it in line with other treatment options particularly for COPD. A query was raised regarding the safety of fluticasone furoate however the group had looked at this previously and agreed that although fluticasone furoate appears to be more potent this doesn't appear to increase the side effects (compared to propionate doses) however the long term use of high dose inhaled corticosteroids is still a concern. It was also noted that the Salford Lung study would soon report which may help with

regards place in therapy. The group agreed that due to the price reduction Relvar® should be included in the formulary and particularly as it was part of the COPD pathway.

ACTION: BR to feedback above to formulary subgroup.

2g)ii) Umeclidinium inhaler re-review

The group looked at the new data for umeclidinium which consisted of a randomised blinded study to evaluate the safety and efficacy of umeclidinium compared with tiotropium in patients with COPD. The group was pleased to note that there was now some comparison data for this LAMA. It was however noted that the trial was short (12 weeks) and that umeclidinium showed superiority for a disease orientated outcome when compared to tiotropium. Nonetheless it did add to the argument that it was at least as good as other LAMA's available. The group agreed therefore to update the previous recommendation and to draft a recommendation similar to other LAMA statements. It was felt that the COPD pathway would then define place in therapy of the various inhalers.

ACTION: BR to update recommendation as above and feedback to formulary subgroup.

3) Extended use of ticagrelor following an MI.

In February 2016 ticagrelor received a license extension for the long term prevention of atherothrombotic events in adult patients with a history of MI and a high risk of developing an atherothrombotic event. The dose for this indication is 60 mg twice daily; a new 60 mg tablet has been licensed to allow this.

Ticagrelor was previously licensed at a dose of 90 mg twice daily for prevention of atherothrombotic events in patients with acute coronary syndromes (ACS) (unstable angina, non ST elevation MI (NSTEMI) or ST elevation MI (STEMI), including patients managed medically, and those who are managed with percutaneous coronary intervention (PCI) or coronary artery by-pass grafting (CABG). Ticagrelor is licensed in this indication for up to 12 months.

The group reviewed the trial data from the PEGASUS-TIMI 54 trial and made the following points:

- The pivotal trial enrolled patients with a spontaneous myocardial infarction in the previous 1-3 years, plus an additional risk factor for cardiovascular disease.
- Exclusions included: patients taking other drugs that may alter bleeding risk and those with bleeding disorders or recent surgery, recent GI bleeding and those with a history of ischaemic stroke or intracranial vascular abnormalities.
- Ticagrelor at a dose of 60 mg or 90 mg twice daily reduced the risk of the composite outcome of cardiovascular death, MI or stroke compared to placebo. The reductions were small but statistically significant.
- Both doses of ticagrelor significantly increased the risk of major and minor bleeding. Ticagrelor was also associated with increased rates of dyspnoea and gout.
- The results of the pivotal trial suggest that for every cardiovascular death, MI or stroke prevented, ticagrelor 60 mg twice daily is likely to cause one major bleed, one bleed requiring a blood transfusion, three to four bleeds leading to discontinuation and seven new cases of dyspnoea.
- The NHS list price for ticagrelor is £54.60 for 56 tablets of either strength, equating to £710 per person per year. There were 147,000 acute myocardial infarctions recorded in England in 2013/14, equating to approximately 270 per 100,000 population. With a population of roughly 2.6 million Greater Manchester would expect to treat approximately 7,000 people with an incident MI each year. Treatment is licensed for up to an additional three years so treating all

eligible patients would cost approximately £5 million in year one, £10 million in year two and £15 million in year three.

The group agreed that the harms indicated above outweighed any benefits gained from extra treatment so did not recommend the use of ticagrelor for the above indication.

ACTION: BR to draft recommendation as above.

4) Lesinurad for the treatment of Gout.

Lesinurad is licensed for use in combination with a xanthine oxidase inhibitor (e.g. allopurinol or febuxostat) in adults for the adjunctive treatment if hyperuricaemia in gout patients (with or without tophi) who have not achieved target serum uric acid levels with an adequate dose of a xanthine oxidase inhibitor alone. Lesinurad works by removing uric acid from the body by blocking the protein 'uric acid transporter-1' (URAT-1) in the kidneys. URAT-1 normally allows some uric acid to return to the blood after the kidneys have filtered it out. Lesinurad was licensed by the EMA in February 2016 and it is expected to be launched shortly.

The group reviewed the data and noted that in three pivotal phase IIII randomised double blind placebo controlled trials in combination with a xanthine oxidase inhibitor lesinurad was shown to lower uric acid better than placebo. Adverse effects include upper respiratory tract infection, nasopharyngitis and back pain. In both studies the rate of gout flares was found not to be significantly different from placebo. All of the trials to date specifically excluded patients with unstable or severe cardiac disease. It should also be noted that none of the studies permitted the use of lesinurad monotherapy and there is currently no data available on the use of lesinurad in patients with hepatic impairment.

Adverse effects are reported as being more common for the combination of lesinurad with allopurinol or febuxostat, than with placebo plus allopurinol or febuxostat. The most commonly reported adverse effects reported when lesinurad was given in combination with allopurinol were upper respiratory tract infection, nasopharyngitis and back pain. The most commonly reported adverse effects reported when lesinurad was given in combination with febuxostat were arthralgia, hypertension, headache, nasopharyngitis and upper respiratory tract infections. It was also noted that lesinurad was associated with an increase in serum creatinine which was reversible. Cardiac adverse events were reported 5-7 times more frequently in lesinurad groups than in the placebo groups. This seems to suggest that there is an increased risk of severe cardiac events in patients with a prior history of cardiovascular events. However it should be noted that cardiovascular co-morbidities are common in patients with gout. As a result lesinurad is not recommended in patients with unstable angina, NYHA class III or IV heart failure, uncontrolled hypertension or history of myocardial infarction, stroke, or deep venous thrombosis within the last 12 months, due to insufficient data. For cardiovascular patients in a stable condition, the individual risks and benefits should be assessed on an ongoing basis. A post-marketing observational study to further assess cardiovascular risk in patients treated with lesinurad was a condition of the European product license being granted.

Due to concerns around the cardiovascular safety the group agreed that lesinurad should not be recommended for routine use however it may be prescribed by specialists for a niche group of patients who are symptomatic despite other therapies where the benefits outweigh any risks.

ACTION: BR to draft recommendation as above.

5) Brivaracetam for the adjunctive treatment of focal onset seizures.

The group reviewed the new drug evaluation as well as the consultant application for the above drug. The group noted that the pharmaceutical company had been active in promoting this drug. Brivaracetam was noted to be an analogue of the anti-epileptic drug levetiracetam (Keppra®). The group noted the following points from the clinical trial data and consultant application:

- Brivaracetam is indicated for adjunctive treatment of focal onset seizures in adults and adolescents.
- In short clinical trials most doses were more likely than placebo to reduce seizure frequency by ≥50%, although efficacy did not appear to increase substantially with higher doses.
- Trials found little difference in safety outcomes between brivaracetam and placebo.
- Brivaracetam is being marketed as being a high-affinity ligand for synaptic vesicle protein 2A (SV2A). SV2A is also the binding site for levetiracetam; however brivaracetam is known to interact with higher affinity.
- When data for all doses were pooled there was no difference in the overall rate of treatment-emergent AEs or serious AEs between brivaracetam and placebo. The rate of somnolence was higher with brivaracetam than placebo, as was fatigue.
- The published meta-analyses included trials of good quality, with low risk of bias. However, the longest trial only lasted 16 weeks whereas therapy for epilepsy is likely to be long term.
- There are no trials against active comparators.
- Brivaracetam tablets cost £1,685 per person per year. This is considerably more expensive than the first choice drugs for adjunctive therapy but comparable to newer second line choices such as eslicarbazepine, lacosamide or zonisamide.
- The group noted that a significant proportion of participants (n=412) had previously tried treatment with levetiracetam but discontinued due to lack of efficacy (n=278), adverse effects (AEs, n=77) or other reasons. A post-hoc analysis found brivaracetam to be less effective in this subgroup than in the trial population as a whole.
- There is little evidence that increasing the dose offers any additional benefit in terms of seizure reduction.

The group noted that Brivaracetam appears to reduce seizure frequency when used for adjunctive treatment in people with focal-onset seizures. However, evidence for safety and efficacy is limited by the short clinical trials and lack of any comparisons with drugs already in use. It was also noted that those that had already tried levetiracetam were less likely to respond. The group queried what extra benefit this drug would add. Further information on how specialists wanted to use this new drug was required before the group could make a definite decision.

ACTION: BR to contact specialists regarding place in therapy and advantages over levetiracetam.

6) Horizon Scanning and Work plan

The group discussed the horizon scanning document and noted that there wasn't much that needed to be added to the workplan. There had been some requests from CCGs for the group to review use of unlicensed indications for existing therapies that were being used in secondary care:

Pregabalin for chronic cough
And Colchicine in pericarditis pain

Both of the above drugs were added to the workplan. It was also agreed that the group would review birch bark extract and Sirolimus depending on the licensing process.

ACTION: BR to update work plan as above.

7) Update on other groups

Formulary Subgroup

The group was updated on the last formulary subgroup meeting.

GMMMG

The group was updated on the agenda for the next GMMMG meeting which is on Thursday.

Interface Subgroup

The group was updated on the interface subgroup meeting

9) AOB

No other issues were raised under any other business.

10) *Date of Next Meeting: 19th July 2016, 12.30-2.30pm, CMFT*