NewTherapiesSubgroup

Minutes

17th November 2015, 12:30 - 2:30 pm
Pharmacy Dept. CMFT

Present:

Elizabeth Adcock (EA) Medicines Information Pharmacist, PAHT
Jennifer Bartlett (JB) Senior Medicines Management Pharmacist – South Manchester CCG
Rachael Fallon (RF) Deputy Director of Pharmacy and Medicines Governance, CMFT
Makrand Goré (MG) Medicines Management Pharmacist, Bolton CCG
Keith Pearson (KP) (Chair) Head of Medicines Management, Heywood Middleton and Rochdale CCG
Zoe Trumper (ZT) Medicines Management Pharmacist, Wigan Borough CCG
Dr Hina Siddiqi (HSa) General Practitioner, Trafford CCG
Dr Handrean Soran (HS) Consultant Physician, Central Manchester University Hospitals Foundation Trust

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

In attendance:
Suzanne Ryder (SR) – Pelvic Floor Specialist Nurse, CMFT.

Apologies received: PB, LA and RW.

Declarations of Interest:
One member declared an interest, regarding a non-personal involvement in the Odyssey long term clinical trial for alirocumab within her previous organisation.

Another member declared an interest as they had attended an advisory board on alirocumab – it was noted that as he was non-voting member he wouldn't be involved in the decision around use of alirocumab.

As the clinician requesting use HS would be excluded from decision making regarding agenda items 5 and 6.

As PB had sent apologies KP chaired this meeting.

1) Minutes of the meeting on September 2015.

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. The formulary review for GLP1 receptor agonists was on the agenda. The group noted that GMMMG were to tackle the outstanding issues around wAMD so this would be removed from the NTS matters arising document.

2a) **Anal Irrigation Systems**

SR gave the group a brief introduction to the various types of systems available and to the types of patients that would be suitable for anal irrigation systems. It was noted that faecal incontinence affected predominantly women (70% compared to 30% men).

As discussed at the previous meeting it was noted that anal irrigation systems are recommended for use as per NICE CG49 for the management of faecal incontinence in adults.

SR outlined the following patient groups who may be suitable for use of anal irrigation systems:

- Low anterior resection syndromes (e.g. rectal removal following cancer) who have frequency (>20 x day)
- The functional patient; aged 22-55 who have had 4-5 procedures.
- Those with a medical issue such as opiate dependent patients who are re-admitted within 30 days despite treatments with other therapies.

SR stated that once the patient had been referred into the service she would normally carry out a thorough review and establish what had been tried first. Biofeedback treatment is always first line and patients are referred for a dietetic review. In addition a referral is made (where available) for access CBT and counselling. A personal management plan is developed and the patient reviewed regularly. Anal irrigation has improved the quality of life in appropriate patients however it's important to note that it isn't suitable for everyone so patient selection is key. The group queried whether a specific product was recommended over any of the others however SR stated that it would be dependent on which product the patient could manage but that Peristeen® was the product used most.

The New Therapies Subgroup of the GMMMG considered the use of anal irrigation systems for neurogenic bowel dysfunction, chronic constipation and chronic faecal incontinence.

The group recommends use for patients with long-standing ineffective bowel emptying, slow-transit constipation or neurogenic bowel dysfunction where all other methods have failed or proved ineffective (i.e biofeedback, digital stimulation, and providing there is a robust specialist treatment pathway in place which includes referral to a dietician and allows the patient access to CBT and counselling if required.

The group noted that anal irrigation systems may improve quality of life for a small minority of patients who have failed on other treatment options and who are under the care of a specialist service. Some types of patient (e.g. may require additional supervision or monitoring, until it is clear that irrigation is not producing any problems.

The choice of product should be made in conjunction with the patient and the product that the patient finds easiest to use should be chosen, however the cost of the product must be borne in mind when making recommendations.

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

According to set criteria use of anal irrigation systems as outlined above were deemed to be a medium priority for funding in the specific patient group identified.

ACTION: BR to draft recommendation as above

2b) Insulin Glargine high strength and biosimilar draft recommendations

The group discussed the above two items separately.

The draft recommendation for insulin glargine biosimilar was approved and the group agreed that this should be taken to the next GMMMG meeting for approval.

The draft recommendation for Toujeo® was approved however the group asked if a sentence relating to 'the reduction of numbers of injections required for those patients on high doses' could be included.

Post meeting note: it was noted in the SPC for Toujeo® states that 'the Toujeo® SoloStar pre-filled pen can provide a dose of 1 to 80 units in one injection, in steps of 1 unit.' Therefore use of Toujeo® would not reduce the number of injections required in patients who require high doses of insulin glargine however a smaller volume could be injected which is less painful for patients. It was agreed that the recommendation should be updated to reflect this.

ACTION: BR to update as above and take to GMMMG for sign off.

2c) GLP-1 formulary choice

The group discussed the choice of preparations for the GMMMG formulary. An NTS recommendation regarding GLP-1 products has already been drafted and approved by GMMMG and is on the website. The formulary choice wasn't reviewed at the time as the group was awaiting the launch of albiglutide (a newer product) however it was noted that this product wasn't due to be launched anytime soon. In addition there has been a price reduction for dulaglutide which brings it in line with other treatment options. Following this price reduction diabetologists had been in touch with the group to ask if dulaglutide could be considered for inclusion in the formulary.

The group noted that exenatide once weekly and liraglutide have NICE TA's so these two products need to remain as an option within the formulary.

Having reviewed the data the group agreed that

- Lixisenatide should be the first line daily as the most cost effective option (costing £57.93 per 28 days) and the clinical data showed a tendency towards a lower number of GI side effects and hypoglycaemia (compared to exenatide bd).
- Dulaglutide should be the once weekly product of choice. Dulaglutide is the same price as liraglutide (once daily) and exenatide (once weekly) however the clinical data showed that dulaglutide is superior to exenatide twice a day but non inferior to liraglutide but is a weekly preparation.

The group agreed that the above proposal should be sent to the formulary subgroup for inclusion as per the agreement for NTS to review drugs for inclusion in the formulary.

ACTION: BR to feedback to formulary subgroup.

2d) Draft Airsonett® Recommendation

The group reviewed the draft NTS Airsonett® recommendation again as feedback had been received to state that the manufacturer would only be willing to provide 3 months use free of charge. It was noted that 3 months was sufficient time to review use for children, however it was unclear why adults required 6 months use before the effect could be reviewed. The group agreed that as the specialist requesting use was a paediatrician and there had been no requests for use in adults the recommendation should apply to in children only. It was noted that the specialist had indicated that it would only be suitable for around 10 children across the NW.
The group then approved recommendation.

ACTION: BR to update recommendation as above and take to GMMMG for sign off.

3) Tapentadol Re-review.

The group had been asked to re-review the original tapentadol recommendation by various specialists as well as the manufacturer. It was noted that the original recommendation does not preclude use but places it after other more established treatments which would be standard for a new drug. It was however noted that there has been some confusion from pain specialists regarding the criteria for inclusion within the GMMMG formulary which only highlights first and second line options. Tapentadol is however on the grey list which defines its place as *"Use of this agent should be restricted to those patients requiring treatment of severe chronic pain which CANNNOT be managed with more established opioid therapies".*

The group re-reviewed the data supplied by the specialist and noted that they had reviewed the majority of this information at the time of the previous review. Some data included summary from poster presentations or abstracts and these were not reviewed for decision making as per the groups terms of reference as only published peer reviewed data can be used.
The group noted the following:

- There is no clear evidence that any particular opioid analgesic is better than any other in terms of efficacy therefore the most cost effective options should be trialled first.
- A large number of published trials have assessed the efficacy of tapentadol for relief of a number of types of pain. Tapentadol immediate and prolonged-release formulations generally had comparable analgesic efficacy to oxycodone immediate- and controlled-release preparations.
- The Scottish Medicines Consortium (SMC) published a summary of a health economic analysis as part of their review of prolonged-release tapentadol. The analysis found that in a subgroup of patients with severe pain and prior opioid use, tapentadol resulted in savings of £77 and a gain of 0.0045 quality adjusted life years (QALYs) when compared to oxycodone. Similarly, savings of £201 and a QALY gain of 0.00379 were achieved compared to transdermal fentanyl. However it should be noted that a key driver in these outcomes was a more favourable adverse effect profile and not better efficacy.
- While tapentadol appears well tolerated there is a lack of long-term safety data.
- The annual cost of tapentadol treatment is approximately £970; higher than the cost of morphine or fentanyl but less costly than oxycodone, although the price of oxycodone is currently falling.

The group agreed that recommendation should be updated as below:

The New Therapies Subgroup of the GMMMG considered the use of tapentadol prolonged and immediate release tablets for the treatment of acute and severe chronic pain in adult patients who can be adequately managed only with opioid therapy.

The group recommends the restricted use of tapentadol as a third or fourth line option in those patients who are have failed other therapies and are intolerant to oxycodone.

Other more established therapies should be trialled first and morphine sulphate remain the 1st line treatment options for all patients who require therapy with opioid analgesics.

Tapentadol should only be prescribed or initiated under the advice of a specialist in pain management.

It should be noted that while tapentadol appears to be well-tolerated, there is a lack of longer term safety data and there are no direct comparative data against transdermal fentanyl. Tapentadol PR is currently more costly than transdermal fentanyl.

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

ACTION: BR to draft as above and take to GMMMG for approval.

4) Capsaicin 8% (Qutenza®) patch

The group had received an application for the use of the above patch from a Dr Krishnamoorthy from Wigan Trust. The group reviewed the data and noted the following:

- Evidence for the use of capsaicin patches in the treatment of PHN comes from five randomised, double-blind, controlled studies which shared a similar design: two large phase III studies and three supporting phase II/III studies.
- In all studies, patients aged between 18 and 90 had a diagnosis of post herpetic neuralgia (PHN).
- While the two main phase III studies met their pre-defined primary efficacy endpoint, the results from some of the supporting studies did not meet this same endpoint, reducing the confidence in the overall evidence of efficacy. The supporting studies however, were powered to detect a larger difference between the groups, a difference not realised in any of the studies. The negative studies may have had insufficient sample sizes to detect the true difference in response.
- Although the two main phase III studies indicated a statistically significant difference between capsaicin patch and control (low-strength capsaicin control patch) in terms of NPRS score reductions, the clinical significance of the effect size was questioned by the EMA. An integrated analysis of all studies using capsaicin patches for 60 minutes for PHN was prepared, using the reduction of NPRS scores from baseline to weeks 2 to 12. This satisfied the licensing authority, and they acknowledged that the small effect size could be due in part to the use of the low concentration patch as the control in all the studies. The large effect exhibited by the control patch was also highlighted by the SMC.
- The evidence for repeated application of capsaicin patches in PHN is limited.
- All patients were pre-treated with a topical local anaesthetic cream, lidocaine 4%, for one hour before application of the patch.
- Qutenza® is associated with a high frequency of adverse effects although the majority are transient administration site reactions of mild to moderate severity. Treatment-related serious adverse reactions are rare. Qutenza® is typically associated with a short-term transient (one or two days) modest increase in pain before its beneficial effects become apparent. It is also associated with temporary increases in blood pressure and therefore blood pressure monitoring may be recommended during treatment application.
- Qutenza® patches present a potential hazard to healthcare staff and must be handled with appropriate precautions.
- Due to the nature of administration and cost of therapy, Qutenza® would probably be reserved for severe treatment-refractory cases and for specialist use only.

The New Therapies Subgroup of the GMMMG considered the use of capsaicin patches (Qutenza®) for the treatment of peripheral neuropathic pain in non-diabetic adults alone or in combination with other medicinal products for pain.

The group recommends the restricted use of capsaicin patches for the treatment of adults with post-herpetic neuralgia (PHN) who have not achieved adequate pain relief from, or who have not tolerated, conventional first and second-line treatments.

Treatment must be initiated prescribed by a specialist in pain management. Prescribing of

capsaicin patches is not recommended in primary care.

Clinical data available relates mainly to use in post herpetic neuralgia only. Capsaicin patch reduced pain scores compared to low concentration control patches in three phase III clinical studies.

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

ACTION: BR to draft recommendation as above.

5) and 6) Alirocumab and Evolocumab.

The group discussed the above two PCSK 9 inhibitors together, although separate clinical data was available for both drugs. The group noted the following from the clinical trials:

Evolocumab:

Evolocumab is licensed for the treatment of adults aged 18 and over with primary hypercholesterolemia (heterozygous familial or non-familial) or mixed dyslipidaemia, as an adjunct to diet:

- in combination with a statin or statin with other lipid-lowering therapies in patients unable to reach LDL-C goals with the maximum tolerated dose of the statin or,
- Alone or in combination with other lipid-lowering therapies in patients who are statin-intolerant, or for whom a statin is contraindicated.

It acts by reducing circulating levels of low-density lipoprotein cholesterol (LDL-C). Treatment for homozygous FH is commissioned by NHS England, and was therefore not discussed.

Clinical trial data summary:

Five published trials assess the efficacy of evolocumab for the reduction of LDL-C in various populations. Evolocumab produced greater reductions in LDL-C than either placebo or ezetimibe in all trials. Reductions were around 55-60% at the end of 12 weeks treatment, compared to typical reductions of 15-20% in the groups assigned to ezetimibe. LDL-C reductions in the 52 week DESCARTES trial were slightly lower than in the 12 weeks studies at 45-50%. The efficacy in the two weekly and monthly dosing groups was comparable at 12 weeks. Significant reductions in other lipid parameters were also observed. Whilst there are no head to head trials, evolocumab appears to result in slightly greater LDL-C reductions than alirocumab, but variances in the underlying populations studied may explain these relatively small differences. The effect of evolocumab on cardiovascular morbidity and mortality has not been established. Rates appear to be lower than in control groups, but the number of events collected in published trials was low. A 5 year cardiovascular outcomes trial is currently underway.

The safety profile of evolocumab was comparable to the comparators. The most common AEs were nasopharyngitis, upper respiratory tract infection, headache and back pain. Rates of serious AEs and AEs leading to discontinuation were low. However the long-term safety of evolocumab remains to be established.

Alirocumab:

Alirocumab is licensed for the treatment of primary hypercholesterolaemia (familial and non-familial) and mixed dyslipidaemia in adults as an adjunct to diet:

- In combination with a statin or statin with other LMTs in patients unable to reach LDL-C goals with the maximum tolerated dose of a statin or,
- Alone or in combination with other LMTs in patients who are statin-intolerant, or for whom a statin is contraindicated.

It acts by reducing circulating levels of low-density lipoprotein cholesterol (LDL-C).

Clinical trial data summary:

Across ten phase 3 trials evaluating patients with HeFH and non-FH at high and moderate CV risk, alirocumab demonstrated a substantial reduction in the primary endpoint of LDL-C reduction after 24 weeks. On top of standard care (maximally tolerated statin +/- other lipid modifying treatments), a reduction of 39% to 62% compared to placebo was observed. Compared with ezetimibe, a reduction of 30% was found on top of standard care, 24% to 36% on less than maximal statins, and 30% to 32% without statin background therapy. The primary endpoint analyses were supported by consistent changes in the secondary lipid profile endpoints across all studies. The effect of alirocumab on cardiovascular morbidity and mortality has not been established. None of the trials completed to date had mortality associated with CV events as a pre-specified primary outcome although a trial is under way.

The safety profile of alirocumab was comparable to that of the control groups (placebo or ezetimibe). The most common treatment-emergent adverse events were nasopharyngitis, injection site reaction, upper respiratory tract infection, influenza, headache, myalgia, and arthralgia. The number of patients discontinuing treatment or experiencing serious adverse events was low. None of the safety concerns commonly associated with other LMTs, such as liver disorders, renal disorders, diabetes and musculoskeletal disorders, was evident with alirocumab treatment. However, the long-term safety of alirocumab remains to be established.

The group then discussed the specialist application. HS gave the group an update on the patient type he was requesting use in. It would be specifically for those patients with Heterozygous Familial Hypercholesterolaemia (HeFH) patients with progressive, symptomatic coronary heart disease, and persistently high non-HDL-C >5.0 mmol/L (equivalent to LDL-C >4.0 mmol/L) despite maximal tolerated lipid lowering therapy for secondary prevention i.e. meeting the NICE guideline current criteria for apheresis. It was noted that there would be around 20-30 of these patients across GM currently who were currently receiving apheresis at a cost of around £30,000 per annum each. The PCSK9 inhibitors cost approximately £4300 - £6,100 per patient per annum. The group is aware that a patient access scheme is available for both of these drugs which may reduce these costs. It was agreed that the most cost effective drug (taking into account any cost reductions) should be used first line.

The group queried whether patients may require both treatment with the drug but may then need to go on to have apheresis again, however HS explained that would only happen if the LDL reduction seen in clinical trials was not borne out in practice, in which case the drug would be stopped as soon as possible. It was noted that once treated with the drug the patients LDL should reduce (by ~30%) which would then mean they no longer hit the criteria for apheresis.

The group agreed that in this high risk group of patients it would be suitable to recommend use however use for all other patient groups was not recommended at this time. The group would await the NICE guidance on these patient groups and in particular would await the debate around LDL –C measurements and whether they are a suitable proxy-marker for event reduction.

The New Therapies Subgroup of the GMMMG considered the use of the two monoclonal antibodies that inactivate proprotein convertase subtilisin–kexin type 9 (PCSK-9 inhibitors): alirocumab and evolocumab for the treatment of primary hypercholesterolaemia and mixed dyslipidaemia.

The group approved restricted use of alirocumab or evolocumab in those patients with Heterozygous Familial Hypercholesterolaemia (HeFH) who meet the current criteria for apheresis i.e. those with progressive, symptomatic coronary heart disease and persistently high LDL-C >4.0mmol/l despite maximal tolerated lipid lowering therapy for secondary prevention. Use in any other patient group is not recommended.

Initiation of either alirocumab or evolocumab (and ongoing prescribing) is restricted to a lipidologist and the patient must remain under the care of a lipid clinic so efficacy can be evaluated.

Alirocumab and evolocumab produced greater reductions in LDL-C than either placebo or ezetimibe in all trials. Whilst there are no head to head trials, evolocumab appears to result in slightly greater LDL-C reductions than alirocumab, but variances in the underlying populations studied may explain these relatively small differences. The group therefore agreed that the choice of drug should therefore be based on cost to the health economy and the cheapest option should

be used first line (taking into account any local discounts offered).

Safety profiles of both drugs were comparable to the comparators and both drugs appear to be well tolerated however long term safety data is not available. It should be noted that there is currently no data showing effects on cardiovascular morbidity and mortality although trials are currently underway.

According to set criteria use of the PCSK-9 inhibitors is a high priority for funding in the specific patient group described above only.

ACTION: BR to draft recommendation as above.

7) Horizon Scanning and Work plan

The group reviewed the monthly horizon scanning document and agreed the following should be added to the work plan:

- Idarucizumab (reversal agent for dabigatran)

It was noted that there were already several topics on the agenda for January:

- Sacubitril/valsartan however a NICE TA was underway.
- Guanfacine for ADHD

The group had also received several requests for re-review:

- Ulipristal (expanded indication)
- Dymista® (new data)

ACTION: BR to update work plan as above.

8) 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 January 2016 12.30-2.30pm, CMFT*