NewTherapiesSubgroup

20th September 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
Sue Banfield (SB) Pharmacist - Manchester Community Services, CMFT
Dr Peter Budden (PB) GP and Prescribing lead, Salford CCG (*Chair*)
Dr Handrean Soran (HS) Consultant Physician, Central Manchester University Hospitals Trust
Susan McKernan (SM) Senior Medicines Optimisation Advisor, North Manchester 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 Shared Service.
Bhavana Reddy (BR) Head of Prescribing Support, RDTC *(Professional Secretary)*

Apologies received: MG, RF,DoR,PS

In attendance for agenda item 3: Dr Richard Warren, NIHR Senior Clinical Lecturer and Consultant Dermatologist, SRFT.

Declarations of Interest:
Declarations were made regarding the attendance of an advisory board for the following agenda items by two members:

- Ixekizumab
- Safinamide and Opicapone

It was noted that the procedure for declarations of interest would be changing in line with the newly updated GMMMG policy. This policy had been updated and was based on the NHS England updated recommendations. It was noted that in future those that had a direct financial interest (e.g. attendance at advisory boards) would need to leave the room and for voting members they would not be involved in decision making. This was to remove any possible perceived conflict of interests. BR would email the updated policy to group members.

1) Minutes of the meeting on July 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.

2a) Safinamide for the management of mid-late Parkinson's disease

The group discussed the draft recommendation and approved it with no changes.

ACTION: BR to take to next GMMMG meeting for sign off.

2b) Gabapentin/Pregabalin for the treatment of chronic cough

The group reviewed the recommendation on the unlicensed use of gabapentin/pregabalin for chronic cough. It was agreed that generic pregabalin could be trialed only if patients cannot tolerate gabapentin after an adequate trial. It was felt that a statement around reviewing effectiveness and stopping treatment if not affective should also be included. The group approved the recommendation with changes outlined above.

ACTION: BR to take to next GMMMG meeting for sign off.

2c) Colchicine for the treatment of pericarditis pain (unlicensed)

The group discussed the draft NTS recommendation for colchicine for the above unlicensed indication. It was noted that there are European Guidelines on the use of colchicine. The group approved the draft recommendation and asked that it be sent for GMMMG approval.

ACTION: BR to take to next GMMMG meeting for sign off.

3) Ixekizumab for the treatment of plaque psoriasis

RW attended the meeting to support this agenda item and gave the group a brief background in the treatment of plaque psoriasis.

Ixekizumab is licensed for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy. Biological therapies for psoriasis are third line treatment options. Ixekizumab is the second of treatments available which block IL-17A (a key effector cytokine that mediates inflammation in psoriasis), the other being secukinumab. Other treatments for psoriasis are the anti-TNF's (adalimumab, etanercept and infliximab) and anti-IL-12/IL-23 (ustekinumab).

The efficacy and safety of ixekizumab has been assessed in three pivotal phase III studies: UNCOVER-1, UNCOVER-2 and UNCOVER-3. These were multicentre, randomised, double-blind, placebo-controlled studies. UNCOVER-2 and UNCOVER-3 also included etanercept as an active comparator.

All of the UNCOVER studies met their co-primary end points, demonstrating that ixekizumab was statistically significantly superior to placebo and etanercept in terms of the proportion of patients achieving PASI 75 and sPGA 0/1 at week 12. The pooled proportion of patients reaching PASI 75 was 89% and 82% for ixekizumab 80 mg Q2W and ixekizumab 80 mg Q4W, respectively, compared to 4% for placebo and 48% for etanercept. Ixekizumab was similarly superior with respect to secondary outcomes. By week 12, response rates of around 40% were observed for the more stringent outcomes PASI 100 and sPGA 0 (i.e. complete clearance of symptoms) for ixekizumab 80 mg Q2W, compared to 5-7% for etanercept and practically none for placebo. For most outcomes, the response rates were about 4-7% higher for the 80 mg Q2W vs the Q4W induction dose regimen.

Ixekizumab was also associated with a fast onset of action. The main limitation of the UNCOVER studies was the duration. Efficacy and safety data are currently available for up to 60 weeks of treatment. The results of long-term studies are required to fully clarify the long-term efficacy and safety profile of ixekizumab. Most of the study population was white (>90%) which may limit the generalizability of the study findings to populations of other ethnic groups. There were very few patients above the age of 75 years (~1%) included in the studies and patients with severe renal and hepatic impairment were excluded. The biologic etanercept is considered an acceptable comparator but not the gold standard as its efficacy in plaque psoriasis is generally considered to be lower compared to other biologics used for this indication.

In general, reported adverse events with ixekizumab are consistent with what would be expected for similar biological products. The most commonly reported TEAEs occurring at higher rates than placebo were nasopharyngitis, upper respiratory tract infection, injection site reactions and headache with higher rates than the placebo group. Injection site reactions particularly were very common and significantly more frequent than placebo (but similar to etanercept); although most were mild or moderate in severity and did not lead to treatment discontinuation. About 1% of patients had confirmed neutralising antibodies (Nabs) which was associated with low drug

concentrations and a reduced clinical response. Eli Lilly are required to follow up the presence of Nabs and in the extension phases of the phase III studies to characterise their consequences.

The group noted that ixekizumab is higher in cost than most other biologic treatments used for plaque psoriasis. A year's treatment at the recommended dose currently costs £20,250.

They also noted that secukinumab is currently available with a NICE approved patient access scheme. Place in therapy for ixekizumab will therefore depend on if there are any discounts available to the NHS. A NICE TA on ixekizumab is not due until April 2017 however it was noted that local clinicians were keen to include ixekizumab within the biologics pathway for psoriasis.
The group queried whether ixekizumab should be used for secukinumab failures, RW agreed that this would be reasonable but also felt that it may be useful for specific patient groups. The group noted that this would be agreeing a third biologic within the sequential biologics treatment pathway which was currently only available via IFR. It was noted that failure to respond to one biologic doesn't predict treatment response to another so there isn't any rationale to restrict numbers of biologics prescribed as long as they are all similar costs. It was therefore agreed that the current NTS recommendation titled: 'The sequential use of biologic agents in the treatment of Chronic or Plaque Psoriasis, for those patients, fulfilling NICE criteria for a biologic' should be updated to include ixekizumab rather than drafting a new recommendation.

The group asked if RW could update the accompanying pathway. RW indicated that he would be able to do this as he had a registrar working with him who would be able to take on this work.

ACTION: BR to email RW with current recommendation for updating.
Once updated to be brought back to a future meeting.

4) Ferric Maltol (Feraccru®)

The group reviewed the LMEN review on ferric maltol and made the following points:

- Ferric Maltol (Feraccru®) is a new oral iron product indicated for the treatment of iron deficiency anaemia in patients with inflammatory bowel disease.

- It was noted that there is an unmet need for effective and well tolerated treatments for IDA in IBD that are easy and safe to administer. This can affect compliance and reduce the likelihood of desired treatment outcomes (raised serum iron levels) being achieved. It is thought that oral ferric maltol will be better tolerated than other iron salts such as ferrous sulphate and unlike IV iron; it can be safely self-administered by the patient at home.

- The manufacturer has proposed that Feraccru® should be considered to be second-line to currently available oral iron products and an alternative option in patients with mild to moderate IDA with either CD or UC who have reported intolerance to oral ferrous salts due to adverse effects. In these patients, it should be considered as an alternative to IV iron if there is no urgent need to raise Hb levels (e.g. prior to surgery).

- The pivotal phase III trial programme of Feraccru® consisted of two identical prospective randomised, double blind, placebo-controlled, multicentre trials; AEGIS-1 and AEGIS-2 which involved 128 patients with mild to moderate IDA associated with (stable) IBD. After 12 weeks, Feraccru® led to a statistically significant improvement in Hb of 2.25g/dL from baseline to week 12 compared to placebo ($p<0.0001$) with the median time to normalisation of Hb levels being 57 days. Ferritin and transferrin saturation also improved over 12 weeks compared to placebo. Hb levels continued to increase to an average maximum of 14g/dL at 48 weeks in the open label extension study with continued use of Feraccru®.

- The group noted however that the AEGIS studies were relatively small, of short duration and only compared Feraccru® with placebo. They included only patients with mild to moderate

IDA at baseline so it is not clear how these results would apply to patients with more severe IDA.

- A direct comparison study of Feraccru® vs. Ferinject® (n=240) is currently in progress and aims to report data in 2017.

- Data from the AEGIS studies suggest that Feraccru® may be well tolerated in many patients with previous intolerance of oral ferrous salts. The most commonly reported adverse effects were arthralgia and mild to moderate gastrointestinal effects - abdominal pain, reflux, flatulence, rectal haemorrhage, abdominal distension and constipation. The EMA notes in the EPAR for Feraccru® that it did not exacerbate IBD during the AEGIS studies or during the open label extension study.

- The estimated budget impact per 100,000 population based on the manufacturers model is -£12,740 i.e. a cost saving using ferric maltol. This would therefore be a cost saving of -£348,166 for the Greater Manchester region due to a reduction in outpatient appointments and nurse time associated with the administration of IV iron.

The group was minded to approve the use of Feraccru® provided that there had been an adequate trial of at least two ferrous salts and if initiated or recommended by an IBD specialist. PB agreed to contact specialists for comments on proposed recommendation.

ACTION: BR to draft recommendation as above
PB to contact specialists for comments.

5) FreeStyle Libre Glucose Monitoring System

FreeStyle Libre whilst currently not available on FP10 is undergoing the process with the BSA so it can be available to prescribe. It was noted that there had been several IFRs for the device. The group therefore agreed to review FreeStyle Libre.

The FreeStyle Libre is a flash glucose monitoring system which allows people to monitor their glucose levels and trends without performing capillary (finger prick) testing. It lies somewhere between a traditional blood glucose meter and a continuous glucose monitoring (CGM) system. CGM sensors measure the glucose levels in interstitial fluid rather than in the bloodstream, with measurements every few minutes, thereby enabling patients to monitor hyper and hypo- glycaemia.

The FreeStyle Libre system consists of sensor worn on the upper arm that measures interstitial glucose every minute and a reader device that is scanned over the sensor to get a result. The FreeStyle Libre system is indicated for measuring interstitial fluid glucose levels in people (age 4 and older) with diabetes mellitus. The indication for children (age 4 - 17) is limited to those who are supervised by a caregiver who is at least 18 years of age. A caregiver at least 18 years old needs to be responsible for supervising, managing, and assisting the child in using the FreeStyle Libre system and interpreting its readings.

Monitoring of interstitial glucose is the same method of measuring sugar levels as that used by conventional continuous glucose meters. Patients are still advised to monitor blood glucose via capillary testing during periods of rapidly changing levels of interstitial glucose when interstitial glucose levels may not accurately reflect blood glucose levels, if hypoglycaemia or impending hypoglycaemia is reported, or the patient's symptoms do not match the system readings. Patient's will also still need to do finger prick blood tests prior to and during driving to meet DVLA requirements.

The product is classified as a device and received European CE mark certification in August 2014.

Trial data for the equipment comes from company sponsored trials which indicate accuracy being marginally superior to existing continuous glucose monitoring systems. The majority of the trial data is only available in conference abstracts. The device may offer some advantages in terms of

patient acceptability and quality of life but good quality clinical trial data to support long-term clinical effectiveness and cost-effectiveness is lacking.

The products are available to buy online (incl. VAT):

FreeStyle Libre Reader + 2 x Sensors: £159.95; FreeStyle Libre Reader: £57.95 (has a 3 year lifespan before requiring a service); FreeStyle Libre Single sensor: £57.95 (each sensor as a life-span of 14 days).

In comparison the cost of continuous glucose monitoring varies according to which system is used. Starter kits which include the transmitter and the receiver cost approximately £1000, or if the system is integrated into an insulin pump the cost is around £500 for the transmitter. Sensors last for between 3 days and 7 days depending on which system is used and cost approximately £40-£60 each. Traditional glucose monitoring test strips cost around £9-£10 for 50 strips with additional lancet costs of around £3 for 100.

The group discussed use in those patients who may be suitable for continuous glucose monitoring however they noted that FreeStyle Libre doesn't have an alarm to indicate hypo or hyperglycaemic episodes so may not be as useful. The group were therefore unsure around where the device would fit; as compared to traditional glucose monitoring test strips FreeStyle Libre is more expensive. It was agreed that further information on use from specialists was required before a definite recommendation could be made.

HS agreed to contact a specialist at CMFT to get further opinion on the use of this device.

ACTION: HS to contact specialist for further feedback and to discuss at next meeting or via email.

6) Opicapone for mid-late stage Parkinson's disease (PD).

The group discussed the evidence review on the new medicine for mid- late stage PD. This had been identified through horizon scanning.

Opicapone is a once-daily catechol-O-methyltransferase (COMT) inhibitor indicated as adjunctive therapy to preparations of levodopa/DOPA decarboxylase inhibitors (DDCIs) in adult patients with Parkinson's disease and end-of-dose motor fluctuations who cannot be stabilised on those combinations.

The efficacy of opicapone has been evaluated in two randomised, controlled, double-blind, multinational phase III studies (BIPARK-I and BIPARK II) of 14 to 15 weeks duration and one open-label extension with a duration of up to one-year. In the two phase 3 trials opicapone 50 mg/day reduced motor fluctuations to a significantly greater extent than placebo, and demonstrated non-inferiority to the adjunctive entacapone. Maintenance of treatment effect was demonstrated for up to 1-year in open-label extensions of these studies. Comparison of opicapone to entacapone in the BIPARK I (per-protocol population) showed that the reduction in absolute OFF-time was greater in the opicapone 50 mg group than in the entacapone group. Opicapone 50 mg was shown to be non-inferior to entacapone; however, superiority to entacapone was not demonstrated. The majority of adverse events were comparable to other COMT inhibitors with the most common treatment emergent adverse events being dyskinesia, constipation, insomnia and dry mouth.

The group noted that levodopa in combination with a dopa-decarboxylase inhibitors benserazide or carbidopa is the mainstay of treatment for patients with late-stage PD. However, the majority of patients develop levodopa-related motor complications and dyskinesias within several years of starting levodopa. Fluctuations in response become increasingly common and severe with switches from normal movement during 'ON' periods to weakness and restricted mobility during 'OFF' periods. Whilst these fluctuations can initially be managed with dose modifications most people will eventually require adjuvant therapy. NICE guidelines on the diagnosis and management of PD (CG35, 2006) states It is not possible to identify a universal first-choice adjuvant drug therapy for people with later PD. The guidance recommends that when choosing treatment clinical and lifestyle preferences and patient preference, after informing the patient of the short- and long-term benefits and drawbacks of drug classes, should be taken into account. Recommended first-choice adjuvant

therapy options for later PD are dopamine agonists, monoamine oxidase B inhibitor (MAO-B), and COMT inhibitors. In view of problems with reduced compliance, people with later PD taking entacapone should be offered a triple combination preparation of levodopa, carbidopa and entacapone. Tolcapone should only be used after entacapone has failed in people with later PD due to lack of efficacy or side effects however it was noted that in practice this is very rarely used due to adverse effects.

The group noted the prices of the three COMPT inhibitors as below:

Entacapone	600-2000 mg	£15.04 - £50.12	£196 - £652
Tolcapone	300 mg	£79.97	£1040
Opicapone	**50 mg**	**£87.64**	**£1142**

The group considered the use of opicapone for entacapone failures however they agreed that further information was required before a definite decision could be made. The group asked that BR contact specialists for further information on proposed place in therapy. SB agreed to share contact details of Consultants from CMFT that could be contacted.

ACTION: SB to forward specialist contact details to BR.
BR to ask for feedback from specialists as above.

7) Horizon Scanning and Work plan

The group discussed the horizon scanning document and noted that most items were already on the workplan. It was agreed that the group would review the following in the November meeting, bearing in mind that this may be the first meeting of the joint formulary/new therapies subgroup:

- DUAVIVE
- Eluxadoline for IBS

7) Update on other groups

Formulary Subgroup

The group was updated on the last formulary subgroup meeting. It was noted that most current work was around pathway development.

GMMMG

It was noted that GMMMG had approved the terms of reference for the formation of the new GMMMG subgroups as follows:

- Formulary and Managed Entry Sub Group
- Pathways and Guidelines Development Subgroup
- High Cost Drugs Subgroup

A letter would be sent out by the GMMMG chairs to all Trust Medical Directors and CCG Clinical Chairs asking for nominations for the above groups. Where possible it would be useful to have some continuity so current members were encouraged to put their names forward to their clinical chairs or medical directors. However GMMMG were also keen to ensure a good mix of secondary and primary care membership. It is expected that the new groups will be formed over November so this would be the last meeting of the current new therapies subgroup.
BR stated that she would keep members informed once nominations had come in mid-October as to when meetings would take place.

Interface Subgroup

The group was updated on the interface subgroup meeting

9) AOB

No other business was raised and the meeting concluded. The first meeting of the Formulary and Managed Entry Subgroup is likely to be in November however this would be confirmed via email.