Northern Treatment Advisory Group

Minutes of meeting 3rd June 2014, 9-12am,

Ramside Hall, Durham, DH1 1TD.

Present:

- David Campbell, Clinical Director for Medicines Optimisation, Northumbria Healthcare NHS Foundation Trust
- Joe Corrigan, Chief Finance Officer, Newcastle & Gateshead Alliance CCGs
- Ian Davidson, Director of Quality and Safety, North Durham CCG & chair of N-TAG
- Tim Donaldson, Chief Pharmacist, Northumberland, Tyne & Wear NHS Foundation Trust
- Jackie Gillespie, Prescribing Lead, Sunderland CCG
- Janet Hattle, Head of Pharmacy, Gateshead Healthcare NHS Foundation Trust
- Andrea Loudon, Clinical Pharmacy Lead, Cumbria CCG.
- Mike Lavender, Consultant in Public Health Medicine, Durham County Council
- Susanna Mills, Public Health Speciality Registrar, Durham County Council
- Nick Quinn, Consultant Physician, South Tees Hospitals NHS Trust
- Bhavana Reddy, Head of Prescribing Support, RDTC (professional secretary)
- Geoff Stephenson, Medical Director, Sunderland CCG
- Neil Watson, Director of Pharmacy, Newcastle upon Tyne NHS Foundation Trust
- Roger Wheeler, General Medical Practitioner, Middlesbrough
- Ali Wilson, Chief Officer, Hartlepool & Stockton-On-Tees CCG

Apologies were received in advance from: Geoff Crackett, Toks Sangowawa, Hilary Wynne, Simon Thomas, Keith Godfrey, Andrew Berrington, Craig Steele, Sue Hunter, & Alison Thompson.

Introductions were made by all parties present at the request of the chair. The chair welcomed everyone to the second meeting of NTAG.

The chair invited declarations of interest relating to the agenda. None were made.

1) Draft Minutes February Meeting

The group approved the February minutes. A suggestion was made that all decisions or actions within the minutes should be highlighted. This was approved.

ACTION: Secretary to ensure all actions and decisions are highlighted within future minutes.

2) Matters Arising

a) Terms of reference

Discussion ensued regarding the terms of reference for the group. It was noted that the ToR was based largely on those of NETAG and as such some aspects required further amendment. It was agreed that further clarification around remit was necessary to ensure that duplication of workload with local APC's was kept to a minimum. As a starter the group approved the inclusion of the following to further narrow the remit of NTAG:

- Drugs which are likely to have significant commissioning issues (very expensive or require a full pathway review)
- Tariff excluded drugs where home share issues or regional procurement may require consideration.
- High to moderate cost drugs provided via a tertiary centre.

Further discussion took place around including a financial or prevalence threshold for referral to NTAG as had been included previously. However it was agreed that the thresholds and the old NETAG Ethical Framework should be reviewed at the next meeting prior to making a definite decision.

ACTIONS: Secretary to update ToR with bullet points above and to table the Ethical Framework and other documents for discussion at the September meeting.

b) Patient involvement

Discussions took place around patient involvement into NTAG. It was noted that there are several ways engagement could take place i.e by contacting specific expert patient groups when a disease area is to be discussed, by sending draft recommendations to CCG patient forums or by membership of the group. It was acknowledged that the latter option may be time intensive as substantial support would be required to explain the commissioning landscape as well as clinical trial information.

A suggestion was put forward that the appraisal documents should include a half to one page summary in plain English so that patients would be able to read this summary and pick up the key points. The group agreed to feedback on this section of the report so this could be modified prior to publication if required. Another suggestion was put forward that the group should seek out an existing patient rep from one of the CCG groups as they may be more informed and understand the current NHS landscape.

The group agreed the best option was to get a patient representative to the meetings and the secretary would follow this up by contacting Health Watch Newcastle as well as discussing this with local CCG patient engagement leads.

ACTIONS: Secretary to ensure that future appraisal reports include a plain English summary and to contact Health Watch Newcastle. CCG members to seek out interested patients from existing groups within their local CCGs.

c) Decision Making Tools.

The secretary fed back that various tools had been reviewed and there were two main types: prioritisation tools or a structured summary of a recommendation. It was noted that the prioritisation tools were of more relevance for CCG formulary groups where comparisons with existing therapies or drugs could be made and drugs were prioritised. Other structured summaries available were mostly similar to the decision summary used by NTAG however some included a separate section on *safety* and *patient factors* as well as cost and efficacy. It was agreed that inclusion of a safety and patient perspective section within the current decision summary would be useful.

Whilst it was agreed a new tool wasn't necessary the group requested that a checklist of criteria for review be developed to ensure that all key aspects of the data had been discussed.

ACTIONS: Secretary to add a section on safety and patient perspective onto the current NTAG decision summary and to develop *criteria for review* checklist for use at next meeting.

d) NTAG website

The secretary updated the group on the NTAG website and that this was still in progress. Approval for the web address from NHS Connecting for Health had taken longer than expected which had resulted in an unforeseeable delay. The group asked if a temporary page could be developed so the existing recommendations could be accessed easily. It was agreed that access would be via the RDTC website.

ACTION: RDTC to include link to temporary NTAG page from home page of their website.

e) NICE Accreditation

The group discussed whether they should apply for NICE accreditation however it was felt that robust communication processes, patient involvement and paperwork would need to be in place prior to this taking place. It was therefore felt that this should be put on hold until further notice.

f) NTAG decision summaries: Nalmefene and sequential pharmacological management of MO secondary to RVO.

The group approved both NTAG recommendations and asked that these be available on the temporary web page. It was agreed that in future all draft decision summaries would be issued to the group within 10 working days of the NTAG meeting and then distributed wider prior to the next meeting. The secretary informed the group about a pilot project with nalmefene that the manufacturer was keen to set up in conjunction with a local GP practice. It was agreed however that approval or not of this kind of project was not within the remit of NTAG.

ACTION Secretary to ensure that draft recommendations are distributed to membership within 10 working days of the NTAG meeting. It was also agreed that the majority of communication would be via the website so the recommendations should be on the website within 20 working days of the meeting.

g) Previous NETAG recommendations

The group reviewed the table containing old NETAG recommendations which had been updated to show if they had been superseded by NICE guidance, who the responsible commissioner was and whether there was any new data since the drug was last reviewed.

Clarification was requested on those entries marked *'NHS England Commissioned; no longer remit of NTAG'*. It was agreed that this should state that *NHS England was the responsible commissioner and now no longer the remit of NTAG* so that readers didn't mistakenly assume that the drugs were now commissioned. The secretary agreed to update this prior to the document being published on the website.

The group agreed that only those recommendations that had substantial new evidence should be reviewed. Of those listed this applied to the following recommendations:

- Agomelatine – new advice from the MHRA regarding hepatotoxicity.
- Paliperidone depot injection – new data that has now been published.
- Ulipristal – due to EMA review in women over 75kg.

Further discussions took place around the urgency of review required for the ulipristal recommendation. Whilst the group recognised the urgency it was felt that NTAG was not funded to respond to urgent requests and therefore if a decision was required prior to the September meeting then this should be carried out locally.

Discussions also took place around how the old recommendations should be included on the website. It was agreed that they should be kept in a separate section of the website to the current recommendations as most of old recommendations are $\geq$ two years old. For future recommendations it was agreed that a re-review would be triggered automatically after two years and searches for new evidence would be performed. If no new data was available then the decision would stand however clinicians would be encouraged to appeal if they had access to any further real world data that could also be considered. All recommendations greater than 2 years old would be highlighted on the website.

ACTION: Secretary to update the summary table with responsible commissioner as discussed above and to ensure that old NETAG recommendations are kept separate to current recommendations on the website.

An automatic recommendation review of 2 years to be included within the ToR and re-reviews of Agomelatine, Paliperidone and Ulipristal to be added to the September agenda.

3) Work Plan

The group discussed the draft work plan and comments that had been received. The group agreed that regional procurement issues (e.g. regional insulin pumps) weren't within the remit of NTAG and that the CCG forum had already tasked the regional diabetes network to look at this so this was not included within the work plan.

It was also agreed that respiratory and diabetes drugs should be removed from the work plan as these were more appropriate for local discussion.

It was suggested that aripiprazole long acting injection be discussed at the September meeting as well as the re-reviews of the above drugs and this was approved.

Discussions took place around whether NTAG should look at pathway review (psoriasis and phototherapy) and it was agreed that this was outside the remit of the group and that this should be CCG led.

The group felt that the work plan should be clinician led and they therefore requested that clinicians have an opportunity to comment on the drugs proposed prior to the review as part of the authoring process of the appraisals. It was noted that clinicians had been contacted for the three reviews today but very few comments had been received.

ACTION: Secretary to add aripiprazole to agenda for the September meeting and to update the work plan as above.

Clinician feedback to be sought via clinical networks if possible.

4) NTAG draft Appeals Policy

The group discussed the draft appeals policy. It was noted that this document was largely based on the old NETAG appeals policy. The following changes were agreed:

- To include a broad statement around geography i.e covering the areas covered by NTAG. It was agreed that explanation of the geography should be within the terms of reference and not here.
- Inclusion of an initial step where all appeals would be sent to NTAG officers first and they would then triage them and forward any process appeals to the CCG forum. This was to ensure that only appropriate appeals would be sent to the forum.
- Include a statement that all process appeals must be made within one month of the meeting taking place.
- To include a statement around the new process that the group will automatically horizon scan for new data at 24 months following the recommendation issue date.

ACTION Secretary to update policy with above changes and re-distribute prior to September meeting.

5) NTAG Declaration of Interest Policy

The group reviewed the draft NTAG declaration of interests' policy. This draft policy was based on the NICE declaration of interests' policy. This policy was approved with no amendments and this will be available on the website once developed.

ACTION Secretary to publish policy on NTAG website.

6) Appraisal: Rivaroxaban for ACS.

The appraisal report concerning rivaroxaban in the management of acute coronary syndromes was introduced by the secretary. The group was interested to know of the reduced primary composite outcome of cardiovascular death, non-fatal MI or stroke compared to placebo. However they also noted the increased risk of bleeding; with major bleeding, bleeding requiring medical attention and intracranial haemorrhage all increased by rivaroxaban, but there was no difference in the incidence of fatal bleeding. The NNT for two years to prevent one primary event outcome was 63. The NNH for two years to cause one additional major bleed was 84, and the NNH for two years to cause one bleed requiring medical attention was 19.

The group noted that at the end of the clinical trial, information on vital status was missing for 8.4% of trial participants. The FDA had declined approval of rivaroxaban for this indication on three occasions due to the missing data, as well as use of the mITT analysis, polypharmacy and bleeding risk.

There were also other factors that may limit the applicability of the trial to UK clinical practice:

- Due to the trial exclusion criteria, patients were likely to be at a lower risk of bleeding than is typical in the UK.
- The mean age of participants was 62 years and approximately one third were over 65, contrasting to a mean age of 71 for patients with acute MI in England.
- There are no trial data available on combining rivaroxaban with other drugs used in ACS such as ticagrelor or prasugrel.
- The licensed indication includes the use of rivaroxaban and aspirin without a thienopyridine, a combination used by only 7% of participants in the pivotal trial. Rivaroxaban tended to be more effective than placebo in these patients, but the difference was not significant (HR 0.69, 95% CI 0.45 - 1.05). There were insufficient patients in this group to determine whether there was any difference in bleeding risk.

The group considered the cost of treatment, the safety concerns and the issues with the applicability of the clinical trial data and voted unanimously not to recommend rivaroxaban for ACS.

7) Appraisal: Dapoxetine for Premature Ejaculation

The appraisal report concerning dapoxetine for premature ejaculation was introduced by the secretary. The group were informed that dapoxetine is a short acting SSRI which is licensed for on-demand treatment of persistent premature ejaculation associated with marked personal distress or interpersonal difficulty. There are no universally accepted definitions of PE and there are no reliable estimates of the prevalence of persistent PE in the UK. Clinical trials have demonstrated that dapoxetine prolongs the time from penetration to ejaculation by between one and two minutes more than placebo. A minimum clinically important difference for IELT has not been established. It was also noted that the longest duration of clinical trial data evaluating efficacy and adverse effects of dapoxetine was 24 weeks. Adverse events reported were consistent with the established adverse effect profile of SSRIs but there are concerns about an increased risk of syncope, especially at the higher dose and as with all new drugs there are very limited data on longer-term efficacy and safety.

A number of limitations to the studies were noted:

- No active comparators were used.
- Just over half of those enrolled completed one study (NCT00229073) with 21% in the dapoxetine group and 31% in the placebo group discontinuing by choice.
- Although the majority of results with dapoxetine were significantly better than placebo there were still some placebo effects as can been seen by the improvements in IELT times and with regards the subjective secondary end-points. A quarter of men taking placebo in the integrated analysis still perceived that they had slightly better/better/much better improvements in PE.
- SSRIs have been used for many years 'off label' and there is a large body of evidence for their efficacy. Current data suggests that dapoxetine provides a roughly 3-fold increase in IELT compared to paroxetine which produces an 8-fold increase when taken regularly.

No cost effectiveness data for use of dapoxetine for PE is currently available however the cost of dapoxetine used 3-6 times per month is significantly more expensive than off label SSRIs with dapoxetine treatment costing more than ten times the cost of paroxetine and fluoxetine. It has been suggested that fewer than 2% of men (18-64) may have severe PE and of these 25% will seek treatment and 70% of these will be suitable for dapoxetine.

Based on these figures it can be estimated that 200 men per 100,000 populations may be eligible for treatment with dapoxetine. It is estimated therefore that treatment costs for dapoxetine could be approximately £50,000 per 100,000 populations.

However potential costs would also need to include the costs of referral into an appropriate specialist outpatient clinic as the license requirement to carry out a detailed evaluation of PE and establish an IELT of less than two minutes will be challenging in primary care.

Due to concerns around lack of any cost effectiveness and long term safety data, a lack of consistency in diagnosis and the lack of any published active comparator trials, the group voted unanimously not to recommend Dapoxetine for PE.

8) Appraisal: High Dose Vitamin and Mineral supplements for prevention of progression of AMD.

The appraisal report concerning the review of multivitamin products for AMD was introduced by the secretary. The evidence for the use of high-dose vitamin and mineral supplements in the treatment of AMD is based primarily on the two large randomised controlled trials. In the AREDS study, a specific combination of antioxidant vitamin and mineral supplements (AREDS formulation) demonstrated a modest reduction in the progression to advanced AMD compared to placebo. Supplementation was most beneficial for people who had intermediate or advanced AMD. However the wide confidence interval suggests that there may be some uncertainty in the result and that the observed effect may not be clinically important. (OR = 0.73 (99% CI 0.52-0.99). In AREDS2, the addition of lutein plus zeaxanthin or omega-3 to the AREDS formulation did not provide additional benefit. There is no data to support the use of vitamins and minerals in the prevention of AMD i.e. in currently healthy patients with increased risk factors for AMD.

Nutritional supplements claiming to improve eye health are unlicensed and generally have not undergone the rigorous testing (including safety testing) required of licensed products. These products contain significantly higher than recommended daily allowances and their long-term safety is unknown. Hospitalisation for genitor-urinary problems was more common in people taking zinc supplements and yellowing of the skin was more frequent in people taking antioxidants. The original AREDS supplements contain beta-carotene and people who smoke or are recent ex-smokers should not take them. An AREDS 2 formula without beta-carotene is now available. In view of recent findings of possible harm from high doses of vitamins C and E, the benefits and risks of supplementation in patients with pre-existing diabetes, heart or vascular conditions will also need to be taken into consideration.

Treatment costs are difficult to estimate due to the increasing burden of disease. Based on RNIB projections, it is estimated that in the UK by 2015, the prevalence of early AMD and geographic atrophy in people aged 50 years and over will be 8.0%. Using this prevalence estimation and if treatment was restricted to those with intermediate or advanced AMD then treatment costs would be £147,825 (AREDS formula) or £208,053 (AREDS 2 formula) per 100,000 patients aged 50 years or over.

Due to concerns around the quality of the clinical evidence (wide confidence interval) and the lack of any long term safety data with high dose supplementation, the group voted unanimously not to recommend high dose vitamins and minerals for the prevention of progression of AMD.

9) AOB

No other business was raised and the meeting thus concluded.
The date of the next meeting was noted to be 9th September 2014.

Minutes produced by B Reddy, Professional Secretary to NTAG, 12th June 2014.