Northern Treatment Advisory Group

Minutes of meeting 9th September, 9-12am,

River Green Centre, Durham, DH1 5TS.

Present:

- Joe Corrigan (JC) Chief Finance & Operating Officer, Newcastle & Gateshead Alliance CCGs
- Ian Davidson (ID) Director of Quality and Safety, North Durham CCG & chair of N-TAG
- Tim Donaldson (TD) Chief Pharmacist, Northumberland, Tyne & Wear NHS Foundation Trust
- Andrea Loudon (AL) Clinical Pharmacy Lead, Cumbria CCG.
- Mike Lavender (ML) Consultant in Public Health Medicine, Durham County Council
- Frank McAuley (FM) Associate Medical Director, Gateshead Healthcare NHS Foundation Trust
- Mark McGivern (MM) Public Health Speciality Registrar, Durham County Council
- Bhavana Reddy (BR) Head of Prescribing Support, RDTC (professional secretary)
- Simon Thomas (ST) Consultant Physician, Newcastle upon Tyne NHS Foundation Trust
- Alison Thompson (AT) Chief Finance Officer, North Tyneside CCG
- Roger Wheeler (RW) General Medical Practitioner, Middlesbrough
- Ali Wilson (AW) Chief Officer, Hartlepool & Stockton-On-Tees CCG

Apologies were received in advance from: Geoff Stephenson, Nicholas Quinn & David Campbell.

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

1) Draft Minutes June Meeting

The group approved the June minutes with no changes.

ACTION: Secretary to publish June minutes on the NTAG website.

2) Matters Arising

a) Ethical Framework.

Discussion ensued regarding the draft Ethical Framework for the newly reformed group. It was noted that the framework presented was based on the previous NETAG Ethical Framework with a few minor updates. The group agreed that the Framework was a useful document and approved the document with some adjustments as below:

- The wording under the purpose of the ethical framework to be updated to state: *'Promote good practice with respect to patient safety of healthcare interventions and cost effectiveness'* it was also agreed that the sentence around the NHS constitution should be further clarified.

- The group agreed to update the wording under the treatment efficacy section to read '*Individual patient or clinician **preference** will not be taken as evidence of clinical effectiveness'*

ACTION: Secretary to update the Ethical Framework document as above and then publish on the NTAG website.

b) Review Criteria for Area Prescribing Committees.

The group discussed the previous NETAG document entitled '*what treatments will NETAG consider'*; this document included a flow chart around whether a drug/treatment should be referred to NTAG for discussion.

Detailed discussions took place around including a financial or prevalence threshold for referral to NTAG. It was agreed that the previous financial threshold of £5,000 per patient per annum should remain and that an additional option of a cost per 100,000 populations be included to cover medium cost therapies that may affect a large population. This would ensure consistency of decision making and a reduction in variation if these were also discussed at NTAG. It was agreed that the flow chart could be streamlined and suggestions were put forward as to how this could be done. It was agreed that the document should be brought back to the next meeting once changes had been made.

ACTIONS: Secretary to update document as outlined above and table for approval at the November meeting.

c) Decision Making Tools

The secretary presented a 'checklist of criteria for review' that had been requested at the previous meeting. Membership felt this was useful to make sure the covered the key aspects of the data when treatments were discussed.

The checklist was approved and will be available on the NTAG website.

d) Patient involvement

The Secretary fed back that Health Watch Newcastle had been contacted with a view to filling the patient rep role on NTAG. Whilst Health Watch Newcastle had stated that they couldn't attend local meetings themselves they had put forward a volunteer. The Chair and Secretary will meet with the volunteer to discuss the patient role with the intention that he attends the November NTAG meeting.

ACTIONS: Chair and secretary to meet with the Volunteer and discuss the patient representative role on NTAG.

e) NTAG website

The secretary gave a demonstration of the new NTAG website which had been launched the previous week. Members fed back that they found the website easy to use and that they liked the design. An email had been sent out to Trust and CCG distribution lists and the website was the top link when 'northern treatment advisory group' is put into a Google search.

3) Updated Appraisal: Sequential pharmacological therapies in the management of macular oedema secondary to retinal vein occlusion (RVO)

A RVO treatment pathway from the North East Retina Group (NERG) had been received. The group discussed the treatment pathway and noted that it does highlight when patients could be considered for a switch to another therapy e.g. no response, allergy or toxic response. The group noted that the current recommendation stated that '*the group may be minded to support sequential treatment for the reasons related to specific adverse effects and reactions pending receipt of a suitable treatment protocol from the relevant clinical group'* The clinical evidence was as discussed in the February meeting i.e. there is no robust clinical evidence to support a sequential treatment strategy. However the group was of the opinion that certain aspects of the protocol, such as those relating to adverse effects and tolerability, although not supported by clinical evidence were empirically rational. As an updated treatment protocol had now been received, the group agreed to update their previous recommendation and approve the use of sequential pharmacological therapies in the management of macular oedema secondary to RVO for the NICE approved medicines (Intravitreal Ranibizumab, Aflibercept or Dexamethasone implant)

ACTION Secretary to update previous decision summary with updated position as above

4) Appraisal: Ulipristal Emergency Contraception and BMI review.

The updated appraisal report concerning the *efficacy of emergency contraception in women over 75kg* was introduced by the secretary. The group were informed that manufacturer initiated changes to the summaries of product characteristics of levonorgestrel emergency contraception (EC) products marketed in Sweden and Ireland had prompted an EU-wide review of the available evidence on the effect of bodyweight on efficacy of all oral EC products.

The EMA considered data on the relationship between bodyweight and EC efficacy from three meta-analyses of studies of levonorgestrel, ulipristal or both. The EMA completed this review in July 2014 and concluded that "*the data available are too limited and not robust enough to conclude with certainty that contraceptive effect is reduced with increased body weight and recommended that statements on the impact of bodyweight should be deleted from product information*".

The group were also informed that the UK Faculty of Sexual and Reproductive Health recommended that *irrespective of body weight, all women requesting emergency contraception should be informed that the copper intra-uterine device is the most effective method of EC with an estimated failure rate of considerably less than 1%.*

The group discussed the data presented and a number of limitations to the studies were noted:

- No studies were set up to investigate the effect of body weight on efficacy and body weight was not measured as part of the clinical trials.
- The body weights used within the data were self-reported by women so therefore may not be reliable.
- One of the studies (Creinin et al. 2006) compared the efficacy of two doses of levonorgestrel 0.75mg taken 12 hours apart to a single dose of 50mg Ulipristal plus placebo 12 hours later. Neither of these doses are currently available in the UK. All levonorgestrel products provide 1.5mg as a single dose. The ulipristal product Ellaone® provides 30mg as a single dose.
- The second study (Glasier et al. 2010) included women given levonorgestrel 72-120 hours post unprotected sex for which it is not licensed or used.

The group also noted that the three World Health Organisation studies which were also evaluated by the EMA showed no reduction in efficacy for those patients with an increased body weight or BMI.

Data on the relationship between bodyweight and EC efficacy are conflicting and some of the data presented in the meta-analyses may not be reliable. As a result the group welcomed the EMA decision and agreed that no changes to the current Ulipristal recommendation should be made however it should be updated to make a note that a further review of the clinical data had taken place.

ACTION Secretary to update previous decision summary with updated information as above

5) Appraisal: Aripiprazole Long Acting Injection (LAI) for Schizophrenia

The appraisal report concerning the use of aripiprazole long acting injection was introduced by the secretary. Aripiprazole is licensed for the maintenance treatment of schizophrenia in adult patients stabilised with oral aripiprazole.

A summary of the pivotal phase III (n=662) trial data was discussed. This clinical data found that aripiprazole LAI was non-inferior to oral aripiprazole for the primary outcome of impending relapse after 26 weeks treatment. A second trial showed that it was superior to placebo.

Pooled safety data published by the EMA did not identify any new safety concerns associated with the aripiprazole depot compared to existing formulations, other than injection site pain. The incidence of extrapyramidal symptoms was higher than with oral aripiprazole

(18.4% vs. 11.7%), and a post-authorisation study has been requested to investigate this. Clinically-significant weight gain was comparable between the depot and oral formulations, but weight loss was more common with the depot.

Three other second generation antipsychotics are currently available in depot form: olanzapine, risperidone and paliperidone. The licensed populations for the four depots do not substantially overlap, due to differing requirements for patients to be stable on oral medicines.

The group noted that NICE guidance recommends that a depot or long-acting injectable (LAI) antipsychotic medication should be offered to people with schizophrenia who would prefer such treatment after an acute episode, or where avoiding covert non-adherence (either intentional or unintentional) to antipsychotic medication is a clinical priority within the treatment plan.

Aripiprazole LAI has a lower drug acquisition cost compared to other available second generation antipsychotic depots, with the exception of the lowest dose of risperidone. None of the available depots can be self-administered, and administration costs will vary with setting. Aripiprazole is administered monthly, as is paliperidone. Administration costs will be lower for these than preparations which must be administered 2-weekly (risperidone, some olanzapine doses). It should also be noted that aripiprazole LAI does not require refrigeration.

TD summarised the position of the Mental Health Trusts regarding aripiprazole and that the clinicians would be keen to use the drug in appropriate patients as there were practical and cost advantages compared to risperidone LAI.

Both the Scottish Medicines Consortium (SMC) and the All Wales Medicines Subgroup (AWMSG) have approved aripiprazole for use within Scotland and Wales respectively. The group also noted that the patent of risperidone LAI is due to potentially run out over the next few years, however due to the complexity of the technology it is uncertain as to whether a lower cost generic product would become available. A summary of cost-effectiveness published by the SMC found that, taking into account administration costs, aripiprazole LAI was cheaper than both risperidone and paliperidone during both the initiation and maintenance phases. (£5946 total per annum compared to £7265 and £7981)

The group also noted that aripiprazole tablets are due to come off patent so this may encourage more prescribing which may then increase the population in whom the aripiprazole LAI could be used which in turn would increase costs substantially. The group therefore agreed that the decision should be deferred until further information could be presented.

Due to concerns around cost and affordability the group agreed to defer the decision on aripiprazole LAI until a treatment protocol or pathway had been received from the Mental Health Trusts across the region outlining place in therapy.

6) Appraisal: Paliperidone Long Acting Injection (LAI) for Schizophrenia

The appraisal report concerning the re-review of paliperidone long acting injection was introduced by the secretary.

Paliperidone LAI is licensed for the maintenance treatment of adult patients with schizophrenia stabilised with risperidone or paliperidone. In selected adult patients with schizophrenia and previous responsiveness to oral paliperidone or risperidone, paliperidone may be used without prior stabilisation with oral treatment if psychotic symptoms are mild to moderate and a long-acting injectable treatment is needed.

The group discussed the new clinical data that had now been published which wasn't available at the previous re-review and noted that there were now two short term phase III clinical studies which showed non-inferiority against risperidone LAI. In another 33 week study, paliperidone LAI significantly delayed time to relapse compared with placebo.
The overall safety profile of paliperidone LAI appears comparable to the established safety profile of its related compounds, paliperidone and risperidone. There were no new safety signals from either short or long term phase III studies

The group noted that whilst overall net drug expenditure would increase in-line with the small increase in drug acquisition costs, overall savings in healthcare costs may result from the practical advantages of paliperidone LAI compared to risperidone LAI, such as a less frequent dosing schedule, no requirement for reconstitution, and no need for refrigeration and therefore a reduction in wastage and finally no requirement for oral antipsychotic supplementation. Some of these savings may however be difficult to realise in practice and may not translate in direct financial savings to the NHS commissioning organisation.

An interim result of an observational study also shows a tendency that paliperidone may reduce hospital admissions however this data will need to be fully published before any definite conclusions can be drawn.

It was also noted that Paliperidone LAI has been approved for use in Wales by the AWMSG and in Scotland by the SMC based upon clinical and economic evaluation vs. risperidone LAI.

As per the previous the discussions the group agreed that the decision should be deferred until further information could be presented.

Due to concerns around cost and affordability the group agreed to defer the decision on paliperidone LAI until a treatment protocol or pathway had been received from the Mental Health Trusts across the region outlining place in therapy.

7) Appraisal: Bevacizumab (Avastin®) in the management of neovascular age-related macular degeneration (AMD)

The appraisal report containing the updated clinical data relating the use of unlicensed bevacizumab for AMD was introduced by the author. It was noted that the NETAG had undertaken work on this previously and issued a positive recommendation in 2011 recommending *bevacizumab (Avastin®) 1.25mg intravitreal injection as a cost effective treatment option for AMD.* Subsequent to this, the full clinical trial data from both the CATT and IVAN trials has now been published and provides the most informative contemporary clinical evidence. Bevacizumab was found to be non-inferior when compared to ranibizumab in terms of efficacy on visual acuity. With regards safety there is no difference between the two drugs in deaths or thrombotic events at 2 years, however inconsistent results were seen on other serious events, with a risk being identified in the CATT trial but no significant difference from the IVAN trial.

The group noted the cost analysis which showed a potential cost saving of £49, 211,130 over 5 years if bevacizumab were used instead of ranibizumab. The group again highlighted the licensing issues however whilst mindful of the problems it was felt that this was for commissioners to address and out with the remit of NTAG. It was noted that a separate paper outlining these issues would be brought to the attention of CCGs.

The group agreed that the previous recommendation should be updated but that the recommendation should remain as previously i.e. that bevacizumab was a treatment option for AMD. For those patients who fulfil NICE criteria should also be offered the choice of ranibizumab or aflibercept.

ACTION Secretary to update previous decision summary with updated information as above

8) Work Plan

The group discussed the work plan and agreed that this would need to be updated to include the price per patient and or cost per 100,000 so that the newly approved criteria could be applied.

The group agreed to add the following to the November agenda:

- Biologics in the management of ulcerative colitis (to avoid colectomy) – whilst this had been identified through IFR it was noted that a specialist from Northumbria had requested that it be discussed.
- Sativex for pain (non-licensed indication) which had been a CCG request.
- Verteporfin with photodynamic therapy for chronic central serous retinopathy. This had been requested for re-review by the specialists at the RVI.
- Evaluation of Ranibizumab Cost Models

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

9) AOB

No other business was raised and the meeting thus concluded.

The date of the next meeting was noted to be 25th November 2014, Meeting Room 4, The Durham Centre.

Minutes produced by B Reddy, Professional Secretary to NTAG, 19th September 2014.