Northern Treatment Advisory Group

Minutes of meeting held on the 9th April 2015, 9-12am,

Meeting Room 4, The Durham Centre

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, Chief Pharmacist, Northumberland, Tyne & Wear NHS Foundation Trust
- Mike Lavender (ML) Consultant in Public Health Medicine, Durham County Council
- Bhavana Reddy (BR) Head of Prescribing Support, RDTC (professional secretary)
- Janette Stephenson (JS) Head of Medicines Optimisation, North East Commissioning Support Unit
- Neil Watson, Director of Pharmacy, Newcastle upon Tyne NHS Foundation Trust
- Roger Wheeler, General Medical Practitioner, Middlesbrough
- Ali Wilson (AW) Chief Officer, Hartlepool & Stockton-On-Tees CCG

Apologies were received in advance from: Geoff Stephenson, Nicholas Quinn, Frank McAuley, Craig Steele, Simon Thomas, David Campbell and Bill Glendinning.

The group noted that the meeting wasn't quorate (nine voting members needed to be present for quoracy) and therefore agreement on decisions made would need to be sought with the full membership via email before they could be published.

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

1) Draft Minutes November Meeting

Following a minor update, the group approved the November minutes with no changes. Actions within the minutes were verified.

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

2) Matters Arising

a) Membership update

The Secretary fed back that Gateshead Foundation Trust had indicated via email that they would be happy for CD&D Trust to represent district generals at NTAG as they were struggling to provide representation on a regular basis following internal changes within the Trust. They were keen however to remain on the distribution lists (as deputy) so they could input into discussions as necessary. After discussion with the Chair it was agreed that CD&D should be contacted and offered the vacant position.

Discussions regarding the patient role took place again. No response had been received from the previous patient representatives. The group agreed that more than one representative would be useful if they could be identified. NW fed back that several patient

representatives took part in the Academic Health Science Network (AHSN) work streams. It was suggested that an initial approach to the AHSN to support NTAG in securing patient representation may be another way forward.

ACTION: NW to follow this up with his contacts at the AHSN.

b) Quoracy

Following the cancelled NTAG meeting in February, the Chair raised the issue of quoracy and NTAG membership. The current terms of reference, membership list and attendance were tabled to aid this discussion. Members agreed that the work of NTAG was important and valued by its member organisations however it was noted that some organisations had not attended one meeting since NTAG reformed. It was agreed that those organisations that were '*serial non-attenders'* i.e. hadn't attended the last three meetings should be contacted to enquire whether they still wanted to retain membership of NTAG as other organisations not represented may wish to take their place. The group also discussed the role of the deputy and agreed that deputy arrangements should be strengthened and that early identification of non-attendance by the primary member should be made so deputies were able to attend in their place. If named deputies are not able to attend the group discussed the possibility of organisations sending another deputy on their behalf; it was agreed that this would be preferable to sending apologies. However the group agreed that if someone other than the named deputy was sent then they would need to have the skills required to enable them to be actively involved in decisions. As NTAG only meets four times a year, with meetings planned a year in advance, the group felt that this should not be difficult to implement. It was also agreed that it was not unreasonable to expect that the primary member correspond with the deputy in order to ensure that their organisation was represented if they weren't able to make the meeting and that this should not be the responsibility of the secretary or other NTAG members to chase up.

Finally the issue of quoracy was discussed. The group agreed that current quoracy arrangements (9 members out of 14 members including public health and a patient rep) were difficult to meet. It was agreed that this should be reduced to 7, with at least 4 (out of the 6 CCG representatives) present and 3 (out of the 6 provider representatives) to be present, with one of these a mental health representative where a mental health drug is being discussed. The group agreed that this should be updated within the terms of reference and proposed that a letter should be sent to all members to remind them of the need for a strong deputy arrangement and to consider whether they wanted to retain membership of NTAG for the *'serial non –attenders'.*

ACTION: Secretary to update terms of reference around quoracy as above
Chair to write to membership as above.

c) NICE TAs and NTAG website.

The Secretary asked the group for clarity around how they wanted superseded guidance to be displayed on the website as several recommendations had now been superseded by NICE; previously they had been removed from the website. The group agreed that it would

be useful to retain these recommendations on the website so the appraisal document and associated recommendation are still accessible to CCGs but proposed that the recommendation include a watermark that states that it is *'superseded by a NICE TA'* and a comment be included under the recommended section with a link to the NICE guidance.

ACTIONS: Secretary to update documents as above and publish on website.

3) Appraisal: Aripiprazole and Paliperidone Long Acting Injections and North of England Guidance.

TD presented the guidance paper on the *'Use of Antipsychotic Long-acting Injections in the North of England'.* It was noted that as per NTAG's request following the September meeting, the three Mental Health Trusts across the region had produced a guidance paper outlining when the second generation long-acting antipsychotic injections (LAI's) should be used. The document proposed that aripiprazole and paliperidone LAI's should be used second line where first line options are not effective or not tolerated and as per their individual licensed indications. It was noted that a request form will need to be completed and sent to pharmacy for approval prior to the injection being prescribed. This was to ensure that all requests are in line with the proposed pathway. This will contain costs but also allow use for appropriate patients. The group was pleased to note that the guidance was comprehensive and well written and that it covered all the points that had been raised by NTAG. The group noted that the guidance document assumes a secondary care pathway, however after discussions it was agreed that if appropriate prescribing could be continued in primary care under a shared care agreement, however this would need to be determined locally.

After reviewing the document and the previous appraisal reports the group approved the use of both aripiprazole and paliperidone LAI's as per their licensed indications and as outlined in the *'Guidance on the Use of Antipsychotic Long-acting Injections in the North of England'*

ACTION Secretary to draft decision summaries with updated position as above

4) Appraisal: Lurasidone for schizophrenia in adults.

The appraisal report concerning the use of the new antipsychotic: lurasidone for the treatment of schizophrenia in adult patients was introduced by the secretary.
It was noted that this request had come from TEWV mental health trust who had received an application for use.

Lurasidone (Latuda®) is a new addition to the list of antipsychotics already available for the treatment of patients with schizophrenia. It is licensed for the treatment of schizophrenia in adults aged 18 years and over. It was launched in the UK in August 2014.

The recommended stating dose is 37mg daily with food; the maximum dose is 148mg daily. Doses marketed in the UK are expressed as the amount of active moiety, as opposed to

lurasidone hydrochloride. Licensed doses therefore appear to differ slightly from those cited in clinical trials.

Five pivotal double-blind randomised controlled trials have evaluated the efficacy of lurasidone. However, only four of the trials were evaluated, as the fifth trial has not been fully published and is only available in abstract form.

The efficacy of lurasidone compared prolonged release quetiapine was evaluated in a phase III double-blind randomised controlled trial lasting 12 months, whilst its efficacy against placebo has been demonstrated in several 6-week studies. In addition the long-term safety and tolerability of lurasidone was assessed in a 12 month long double blind study of 629 adult patients, who had remained clinically stable for at least 8 weeks prior to baseline assessments, compared to risperidone. Lurasidone appeared to produce fewer metabolic-related adverse effects (including lipid profile, glucose, HbA1c, insulin and prolactin) compared to risperidone (11.7% vs 20.8%, NNH -11). However it should be noted that there was a high dropout rate in the lurasidone group (17%) compared to the risperidone group (11%) and that the secondary outcome of non-inferiority to risperidone was not demonstrated in this study.

The limited available data suggest that it may have some advantages over other antipsychotics for patients where weight gain or other metabolic disturbances are likely to have significant adverse consequences, although other adverse effects- including akathisia- may be more troublesome with lurasidone. Data on longer term efficacy and safety are limited and it has not yet been adequately compared to other existing alternatives.

Rating scales such as PANSS (as used in the clinical studies) are considered suitable surrogate markers for improvement in symptoms, but patient-orientated outcomes such as relapse rates may be a more desirable method of assessing efficacy. It remains unclear whether the statistically significant improvements in the rating scales used to assess treatment response in the trials are also clinically significant in the management of schizophrenia.

Lurasidone costs fall within the existing price range of licensed antipsychotics and it is currently less expensive than branded alternatives such as aripiprazole (Abilify®) and paliperidone (Invega®). But it is significantly more expensive than most other oral antipsychotics. The cost of 28 days treatment with lurasidone at a dose of 37-148mg daily is £90.72 to £181.14. The patent for aripiprazole has now expired and the NHS price of generic aripiprazole is falling.

It was noted that lurasidone had been approved by both the SMC and AWMSG.

The group felt that as there is limited comparative data against established therapies, a place in therapy for lurasidone is difficult to ascertain. The group agreed that lurasidone is likely to compete with aripiprazole for use in patients in whom it is important to avoid weight gain and metabolic adverse effects, however further data showing advantages over aripiprazole are required before it can be routinely recommended for use.

ACTION Secretary to draft decision summary as above

5) Appraisal: Rituximab for the treatment of immune (idiopathic) thrombocytopenic purpura (ITP)

The appraisal report concerning the use of off label rituximab for the treatment of immune (idiopathic) thrombocytopenic purpura (ITP) was introduced by the secretary. This appraisal was referred to NTAG from Cumbria who had received several individual funding requests for this. It was noted that rituximab for the above indication had already been approved for use in the North of Tyne region by the APC.
Immune (idiopathic) thrombocytopenic purpura (ITP) is an acquired autoimmune disorder most commonly resulting from auto-antibody mediated peripheral platelet destruction and, in many cases, impaired platelet production. The condition is characterised by isolated thrombocytopenia (platelet count <100 x 10^9/L) in the absence of any obvious underlying cause, and an increased risk of bleeding and bruising.

ITP occurs in both adults and children. In adults ITP generally follows a chronic course, while in children it is typically acute in nature (<six months). Most children with acute ITP do not require treatment, and the condition generally resolves spontaneously. In the majority of adults, treatment is indicated only in those with very low platelet counts (<30 x 10^9/L), or significant bleeding. The goal of treatment is to achieve a platelet count associated with adequate haemostasis, rather than restoring the platelet count to normal levels. For adults with chronic ITP who require treatment, first-line options include: corticosteroids (dexamethasone, methylprednisolone and prednisolone), intravenous immunoglobulin and in a few instances intravenous anti-D immunoglobulin. Response to these agents is usually transient, and over two thirds of patients' will either become refractory or experience intolerable long term side effects.
Second-line therapy is individualised to according to patient and clinician preference and individual tolerability. Second-line options include: immunosuppressive agents (azathioprine, ciclosporin, danazol, dapsone, and mycophenolate), cytotoxic agents (cyclophosphamide and vinca alkaloids), rituximab and thromboprotein receptor agonists (romiplostim and eltrombopag). Most patients will require continuous treatment, with some experiencing intermittent relapses that can be managed with rescue treatment. Only a minority of patients will experience a sustained off-treatment response. A splenectomy is a viable second-line treatment choice, but is rarely performed before 12 months from diagnosis in the UK. Although around two thirds of splenectomised patients achieve a normal platelet count, there is an increased risk of infection and mortality from post-splenectomy sepsis. In children with ITP, treatment should be considered by specialists on a case by case basis in those with moderate to severe bleeding symptoms, or those at increased risk of bleeding. Treatment options are comparable to those in adults.
Rituximab (MabThera®) is a monoclonal antibody that targets the CD20 antigen expressed on the surface of B-lymphocytes. Rituximab is not licensed for the treatment of ITP, and it is not currently under regulatory review for this indication. The majority of evidence for the use of rituximab in ITP therefore, is derived from observational studies, with no comparator arm. Only a few randomised controlled studies have been performed. Overall, the results of studies are inconsistent, and the efficacy of rituximab compared to other established treatments for ITP could not be determined. The limited data suggest that rituximab treatment can induce a significant and durable response in many patients with ITP.

However, the optimal regimen and precise place in therapy of rituximab in the treatment of ITP remain uncertain.
In adults with ITP, response rates with rituximab ranged from 44% to 63%, and complete responses were seen in 30% to 44% of patients. However, relapse frequently occurs. Rituximab is a high cost PbR excluded drug. However it is likely that some of the cost of rituximab could be offset against potential savings realised through a reduction in blood transfusions, nursing time and rescue therapy. Rituximab is a one off treatment course given over 4 weeks, so whilst it may be expensive, it is cheaper than other second line options.

The off-label use of rituximab as a second-line therapy for ITP has been recommended in two recent international guidelines, and has been acknowledged in the NICE appraisal of romiplostim for ITP as being acceptable current practice. The group agreed that despite the unlicensed nature of the drug and the limited data available they had no reason to disagree with the position in the NICE and/or international guidelines. The group therefore approved rituximab as a second line option for ITP.

ACTION Secretary to draft decision summary as above

6) Appraisal: Airsonett® laminar flow device for treatment of uncontrolled asthma.

Airsonett® laminar flow device (previously Protexo®) is a CE-marked medical device, intended for use by people with persistent allergic asthma that has not responded adequately to high-intensity pharmacotherapy.
Although a number of trials have been conducted, the bulk of the clinical data relate to quality of life changes. The pivotal study (n=282) is a randomised double-blind trial with change in quality of life scores as the primary outcome. Patients used the Airsonett or an identical placebo (which did not filter or cool air) for one year. A significant improvement in quality of life, as measured by the mini asthma related quality of life questionnaire (AQLQ) or paediatric AQLQ, was more common with Airsonett than placebo (76% vs. 61%).
The effect was more pronounced in the people with poorly controlled asthma at baseline. However, this pre-specified subgroup was small, and there is no evidence that pharmacotherapy was optimised prior to starting treatment with Airsonett. There was a high response rate in the placebo arm, suggesting a response bias may be present.
Other published data show similar quality of life improvements. It has been proposed that the Airsonett® device be given to those patients who would otherwise be given omalizumab. Omalizumab whilst expensive, is however, known to significantly reduce rates of exacerbations in people with severe allergic asthma, and to improve rates of severe exacerbations and hospitalisation. There is no good quality evidence that Airsonett improves rates of asthma exacerbations, hospitalisation, medication use, or objective measures of respiratory function other than fractional exhaled nitric oxide.

No safety concerns were raised. While adverse events were reported commonly, none were considered to be related to study treatment. A small proportion of people discontinued treatment due to the draught or sound produced by the device causing a disturbance. The

annual rental cost of Airsonett is £2,088, including routine servicing and filter replacement. Additional costs may be incurred if damage occurs due to misuse.

Airsonett is intended to be used alongside optimised pharmacotherapy at BTS/SIGN step 4 (high-dose inhaled corticosteroids plus regular bronchodilators, with or without additional drugs). The cost will therefore be additive, particularly as omalizumab is commissioned by NHS England whilst the Airsonett® device would be CCG commissioned so proposed cost savings will not be seen in practice by CCGs.

The group noted that a large UK-based trial is currently investigating the effect on exacerbations, but results are not likely to be available until 2017. It was agreed that data from this trial, showing patient related outcomes, would be required before Airsonett® could be recommended for use.

ACTION Secretary to draft decision summary as above

7) Updated Work Plan

The group discussed the current work plan and noted that a couple of re-reviews had been requested by specialists.

These were:

- A re-review of the 2011 NETAG position on Omnipod® Insulin pump.
- A re-review of the 2012 NETAG recommendation on Orthotic functional electrical stimulation for drop foot of neurological origin.

After discussion the group agreed that Omnipod® should be re-reviewed as despite the procurement exercise relating to insulin pumps there was still inconsistency amongst CCGs around which patients should have access to Omnipod®. It was agreed that this would be added to the June agenda for further discussion and review.

The group agreed to discuss the orthotic FES re-review at the September meeting.
Other items for discussion at the June meeting were the two infliximab biosimilars and teriparatide.

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

8) AOB

No other business was raised and the meeting thus concluded.

The date of the next meeting was noted to be 2nd June 2015, Meeting Room 4, The Durham Centre.

Minutes produced by B Reddy, Professional Secretary to NTAG, 24th April 2015.