Northern Treatment Advisory Group

Minutes of meeting held on the 6th June 2017, 9-12am,

Meeting Room 4, The Durham Centre

Present:

- Ian Davidson (ID) Director of Quality and Safety, North Durham CCG & Chair of NTAG.
- Matthew Grove (MG) Consultant Rheumatologist, Northumbria Healthcare NHS Foundation Trust.
- Andrew Lloyd (AL) Consultant Anaesthetist and Chair of South Tees D&T, The James Cook University Hospital (JCUH)
- Bhavana Reddy (BR) Head of Prescribing Support, RDTC (professional secretary)
- Simon Thomas (ST) Consultant Physician, Newcastle upon Tyne NHS Foundation Trust
- Nick Timlin (NT) General Medical Practitioner, Hartlepool & Stockton-on-Tees CCG.
- Janette Stephenson (JS) Head of Medicines Optimisation, North East Commissioning Support Unit.
- Ali Wilson (AW) Chief Officer, Hartlepool & Stockton-on-Tees CCG.
- Hannah Willoughby (HW) Medicines Optimisation Pharmacist, Sunderland CCG.

Apologies were received in advance from: Tom Hall (Public Health), Andrea Laudon, Tim Donaldson (and Mental Health colleagues).

The group noted that as apologies from public health had been received the meeting wouldn't be quorate however BR stated that she would run all decisions by TH prior to issuing them.

No declarations were received prior to the meeting on receipt of the agenda and when the Chair invited any declarations of interest to be made, none were made.

1) Draft Minutes February Meeting

The group approved the February minutes with no changes.

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

2) Matters Arising

a) Qutenza® flowchart and specialist feedback.

Following the decision made at the last meeting regarding the re-review of Qutenza® patches the group had received a flow chart and outlined criteria for use from specialists. On reviewing the flow chart it was noted that patients would only be tried in patients with focal neuropathic pain who have had a trial of oral anti-neuropathic agents according to NICE guidance and where:

- Existing treatments have failed to control pain
- Patients report intolerance of existing treatments due to significant adverse events impacting quality of life

- Patients who have an allergy or any contraindications to existing therapy.

In addition specialists have indicated they would like to use capsaicin patches as a management step prior to the introduction of spinal and peripheral nerve stimulation which is more invasive and expensive. The group agreed that the proposed fourth line use (after other NICE approved therapies) seemed appropriate and that the protocol for use was reasonable. They agreed that there should also be clear criteria for stopping (as well as starting) and that the treatment should be stopped if no benefit was gained. One of the queries that the group had raised with specialists was the issue of just adding capsaicin patches to the patients other treatments such as pregabalin. The specialist stated that patients who were given capsaicin patches by the pain services would be under regular review and if therapy is successful (at least >30% pain relief) they would review all other medication and aim to wean them off. The group agreed that both initiation and ongoing treatment should remain with the specialist pain services.

As the protocol had a South Tees logo on it, it would need agreement from other specialists across the region before it could be approved. The group suggested the specialist liaise with the Northern Pain Forum to get agreement on proposed place in therapy and use of capsaicin patches.

ACTION: Secretary to update Qutenza® recommendation as above and liaise with specialist to gain approval of the pathway/protocol for use across the NE and Cumbria. Once approved to go on website alongside the recommendation.

3) Appraisal: Sodium Oxybate for Narcolepsy with Cataplexy.

The appraisal report was introduced by the secretary. This is a re-review of a previous recommendation; it had been referred to NTAG by the North of Tyne APC as specialist application had been received to enable the continuation of treatment when started as a child. NHS England now commissions the use of sodium oxybate for the above indication according to specific criteria for use in children up to the age of 19. CCGs are the responsible commissioner for adult patients.

Narcolepsy is often diagnosed either in adolescence or in middle age. Narcolepsy with cataplexy is estimated to affect around 35 per 100,000 of the population. For the NTAG area, this yields an estimated adult (age ≥18 years) prevalence of 879 patients who may have narcolepsy with cataplexy, although a large proportion of these patients will be undiagnosed. As might be expected, the condition often has a negative social impact, particularly with respect to driving, accident occurrence, and work-place and professional performance, with consequent effects on employment.

There is currently no cure for narcolepsy and so treatment relies upon lifestyle changes and symptomatic treatments for the different elements of day time sleepiness, disturbed night time sleep and cataplexy. Cataplexy is an episode of muscular weakness triggered by strong emotions such as laughter, anger and surprise. The loss of muscle tone ranges from a just-perceptible weakening of the facial muscles through weakness at the knees, to total collapse on the floor, which may cause injury.

NETAG reviewed the evidence for sodium oxybate in December 2009 and at the time the group did not recommend use. This was in line with the SMC and AWMSG. Although

clinically effective against placebo, sodium oxybate was considered unlikely to be cost effective even if limited to the most severe patients. There is also limited data on comparative efficacy against other treatments. Sodium oxybate differs from other treatments in that it aims to tackle all elements of the disease. (Daytime sleepiness, disturbed night time sleep and cataplexy). i.e. it is used to control multiple symptoms whereas other drug treatments are usually targeted at a single aspect.

There is limited new evidence since NETAG last reviewed sodium oxybate. A meta-analysis and systematic review published in 2012 summarises all of the available randomised controlled trial evidence. All of the efficacy outcomes reported favoured sodium oxybate and all were statistically significant, with the exception of the proportion of REM sleep. However, sample sizes for some comparisons were very small, and confidence intervals were wide in several cases, limiting the precision of these estimates of treatment effect.

Narcolepsy is an orphan disease, and clinical studies included small numbers of people for a short duration of time.

Adverse effects including gastrointestinal effects, dizziness and enuresis were more common with sodium oxybate than placebo. Discontinuation due to adverse effects occurred in 7-9% of patients.

The cost of sodium oxybate varies with the dose, which ranges from 4.5 g to 9 g daily. This results in an estimated cost per patient of £6,500 to £13,100 per year. Mean doses used in practice are likely to be in the middle of that range.

No cost-effectiveness studies were found. The number of patients eligible for treatment with sodium oxybate is expected to be low, both in terms of newly diagnosed adults and patients transitioning from paediatric services.

The group agreed that where paediatric patients fulfilled the NHS England criteria and had been started on sodium oxybate and benefited from its use these may be continued into adulthood. However as there is limited new information available it is not recommended for use in new adult patients. It was however noted that the patent expiry of sodium oxybate is around 2019 so costs should decrease at this stage when it may prove to be cost effective.

Use of sodium oxybate should be restricted to use by sleep specialist consultant with prior experience of use. It is classed as a RED drug in most localities across the North East. Sodium oxybate would be expected to be reserved for patients with severe cataplexy who have not responded to first line stimulants. In the NTAG region these patients are seen by two specialist consultant neurologists, one of whom estimated that they see one patient per year who they would like to treat with sodium oxybate. NHS England estimates that there are currently 10 children treated with sodium oxybate nationally, with a further 10 waiting for treatment. They also estimate that 10 children each year may be diagnosed with severe narcolepsy with cataplexy and qualify for sodium oxybate treatment.

ACTION Secretary to draft recommendation as above.

4) Appraisal: Pitolisant for narcolepsy and cataplexy in adult patients.

This item was introduced by the secretary; it had been added to the work plan via horizon scanning however specialists had indicated they were interested in using it.

Pitolisant is the first of a new class of medicine a histamine H3-receptor antagonist/inverse agonist, that is licensed to treat narcolepsy with or without cataplexy, and it is an additional option that was launched in September 2016.

The clinical evidence consists of two small randomised controlled trials of pitolisant 5–40 mg per day in adults with narcolepsy with or without cataplexy. Compared with placebo, pitolisant improved excessive daytime sleepiness, improved time awake in a darkened room and reduced the weekly cataplexy rate. Pitolisant was also compared with modafinil in a non-inferiority analysis (an analysis designed to test if it was not worse than modafinil for improving excessive daytime sleepiness by a pre-specified amount). Pitolisant 10mg to 40mg per day was not shown to be non-inferior to modafinil 200mg to 400mg per day for excessive day time sleepiness measured by the Epworth Sleepiness Scale (ESS). Non inferiority to modafinil was not shown.

The long-term safety data for pitolisant in people with narcolepsy are limited. However narcolepsy is an orphan disease, and clinical studies included small numbers of people for a short duration of time.

In both studies patients could remain on existing therapies such as sodium oxybate or antidepressants for treating cataplexy, therefore the findings may not be generalizable to patients who are not taking any other medicines for narcolepsy or cataplexy.

A high placebo effect was found on cataplexy rate which may reflect subjective and emotional triggers.

One of the clinical trials (HARMONY Ibis) which was considered pivotal for the license, hasn't yet been fully published so cannot be assessed.

The most common adverse events in the pitolisant groups were headache, insomnia, abdominal discomfort, nausea, irritability and anxiety. No participants in the pitolisant groups had withdrawal syndrome during the withdrawal phase.

The cost of 30 days treatment with pitolisant at a dose of 4.5 mg to 36 mg once daily is £310.00 to £620.00.

The cost of 30 days treatment with other medicines used for narcolepsy is £6.06 to £318.24 for stimulants such as modafinil, dexamfetamine or methylphenidate and £540.00 to £1,080.00 for sodium oxybate.

The group agreed that there was insufficient evidence of comparative efficacy and cost effectiveness at this stage to recommend use of this treatment in adult patients. There was acknowledgement however that it has less abuse potential than sodium oxybate and a better side effect profile compared to stimulants however further data is needed before it can be recommended on a population basis.

ACTION Secretary to draft recommendation as above.

5) Appraisal: Rituximab Biosimilar

This item was also referred to NTAG via the APCs.

Rituximab is a monoclonal antibody directed against the CD20 antigen found on the surface of immune system B cells. It is used in the treatment of inflammatory autoimmune disease and certain types of cancers.

In February 2017, a biosimilar formulation of rituximab was launched in the UK under the brand name Truxima®▼. The group reviewed the appraisal document which presented review on the comparability, efficacy, safety and cost of Truxima with respect to the reference product MabThera® for the RA indication only as this is the indication for which CCGs are the responsible commissioner. The following points were noted:

- A second biosimilar formulation of rituximab manufactured by Sandoz is expected to be licensed and launched in June/July 2017. However, there are currently no published data available for this product.
- To gain approval in the EU, biosimilar medicines must demonstrate that they are as safe and as effective as the reference medicine, and have the same quality characteristics. In an extensive comparability exercise it was shown that all major physicochemical characteristics and biological activities of Truxima® are comparable to those of MabThera®.
- In patients with RA, the clinical program consisted of a Phase 1 pharmacokinetic equivalence study (Study CT-P10 1.1), followed by a Phase 3 therapeutic equivalence study (Study CT-P10 3.2). In both studies efficacy in terms of DAS28 and ACR (standard measures in RA trials) were shown to be comparable between the two products. In addition, PK equivalence was demonstrated in terms of all PK parameters across all comparisons.
- Limited data from 56-week open-label study showed that in patients who switched from MabThera® to Truxima®, efficacy was sustained, and comparable to those maintained on Truxima®. However, this is a descriptive analysis and due to the small sample size no firm conclusions can be drawn.
- The overall safety profile of the two products appears broadly comparable although the incidences of AEs were generally lower for the reference products. The nature of TEAEs observed in clinical studies was in line with the well-characterised safety profile of MabThera® in RA populations. The majority of TEAEs were of mild to moderate severity, and no significant new safety signals were reported. Overall, a similar safety profile was observed between the maintenance and switch groups.
- On 1st September 2017, a new CMU contract which will include the biosimilars is due to start. MabThera® has an NHS list price of £349.25 and £873.15 for 2 x 100mg, and 1 x 500mg vials, respectively. Truxima® has a list price of £785.84 for 1 x 500 mg vials, which is represents a discount of around 10% on the corresponding price of MabThera®. However as with other biosimilar products locally negotiated discounts may be available.

The group approved use of the rituximab biosimilar first line, in those patients for whom rituximab is appropriate, in existing and new patients. For existing patients consideration should be given to switching where it is clinically appropriate and as part of a clinician led management programme which has appropriate monitoring in place. The group agreed that the recommendation should not be brand specific and that localities could agree which biosimilar product they would use.

ACTION Secretary to draft decision summary as above

6) Work Plan and Topics for next year.

The group discussed the work plan. It was noted that there were a few items for discussion for the September meeting. The Ozurdex treatment pathway hadn't been received so this may come to the September meeting. Members suggested that Saxenda® (liraglutide) for the obesity indication should be discussed by NTAG as it had now been launched and would be classed as high cost and would therefore fulfil the criteria for review. A few other items had been added to the work plan through horizon scanning:

- Andexanet alfa which is an anticoagulation reversal agent - antidote to oral factor Xa inhibitors – first in class.
- Dupilumab for atopic dermatitis/eczema – first in class for this indication.

It was also suggested that NTAG re-review the Collagenase recommendation as this had come up again in Durham. This was also added to the workplan.

7) AOB

Regional Medicines Optimisation Committees:

The group discussed the RMOC's; currently three members of NTAG had been recruited onto the membership of the RMOC (North). It was also noted that the RDTC would be providing the professional secretarial support to the RMOC. There were queries around the role of NTAG however it was noted that the RMOCs are currently concentrating on medicines optimisation issues which are outside the remit of NTAG so there was still a need for NTAG to continue meeting until the process for new drugs assessments had been finalised and approved. It seemed unlikely that any new drugs would be reviewed in this financial year.

Annual Report

The secretary noted that the annual report was now due and asked members if there was anything in particular they would like included. It was felt that the role of NTAG in assessing expensive devices should be highlighted as it was unclear whether any other group was looking at these devices, which often can be difficult to review. It was felt that the annual report should be taken to the September meeting of the northern forum and that the chair or secretary would be there to support it although AW as also a member of the forum so could also speak to the item should they not be able to attend.

No other business was raised and the meeting concluded.

The date of the next meeting was noted to be 5th September 2017.

Minutes produced by B Reddy, Professional Secretary to NTAG, 30th June 2017.