Northern Treatment Advisory Group

Minutes of meeting held on the 1st September 2020, 9-11.30am

Virtual Online Meeting via StarLeaf

Present:

- Ian Davidson (ID) Medical Director, County Durham CCG & Chair of NTAG.
- Gavin Mankin (PGM) Principal Pharmacist – Medicines Management, RDTC (professional secretary)
- Matthew Grove (MG) Consultant Rheumatologist, Northumbria Healthcare NHS Foundation Trust.
- Toks Sangowawa (TS) Clinical Advisor/Locum Consultant in Public Health, South Tyneside MBC.
- Claire Sands (CS) Assistant Head of Finance, Newcastle Gateshead CCG.
- Alan Bell (AB) Head of Commissioning, Northumberland CCG
- Ewan Maule (EM) Head of Medicines Optimisation, Sunderland CCG.
- Helena Gregory (EL) Medicines Optimisation Pharmacist and Clinical Quality Team Lead North Cumbria CCG
- Matthew Lowery (ML) Formulary Pharmacist, Newcastle upon Tyne NHS Foundation Trust.
- Robert Lapham (RL) Formulary Pharmacist, South Tyneside & Sunderland NHS Foundation Trust.
- Andrew Lloyd (AL) Consultant Anaesthetist and Chair of South Tees D&T, The James Cook University Hospital (JCUH).
- Jim Welch (JW) Patient/Lay Representative.

In Attendance: Monica Mason, Head of Prescribing Support, RDTC – item 3

Apologies were received from: Joe Corrigan, Tim Donaldson, Nick Timlin, Siobhan Brown (represented by Alan Bell), Simon Thomas

The meeting was quorate.

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 Jim Welch declared the following:

- Agenda item 5 – JW is registered blind and chair of local blind support group – it was agreed that did not stop him participating in the discussion on this item as he does not have the condition for which brolucizumab is used, and does not advise patients/clinician directly on treatment choices.

Helena Gregory was welcomed to the meeting as the new CCG Medicines Optimisation representative following the retirement of Andrea Loudon.

1) Draft Minutes June 2020 Meeting

The group approved the June 2020 minutes.

ACTION: Secretary to publish June 2020 minutes on the NTAG website.

2) Matters Arising

- Review of NTAG recommendation on Sodium oxybate (Xyrem®) in the management of narcolepsy with cataplexy in adult patients in light of RMOC position statement - awaiting RMOC statement on Pitolisant before progressing as may change place in therapy and costings now generic Sodium oxybate available.
- Review of NTAG recommendations relating to the eye – awaiting feedback from NE Retina Group as to which recommendations require review.

3) Cost Modelling of Type 2 Diabetes Medicines (e.g. SGLT2, GLP-1s) in ASCVD, Heart Failure and CKD

The agenda item was introduced by the secretary based on a report from the RDTC.

Across the region type 2 diabetes guidelines and pathways are being presented for update to medicines management groups proposing the earlier use of SGLT2s and GLP1s to improve cardiovascular outcomes as demonstrated in recent trials. Whilst groups support the clinical basis of this approach, the cost effectiveness is more difficult to answer, and the impact on prescribing budgets which may result from the commissioning of cardiometabolic pathways is significant. The pressure is to use an SGLT2/GLP-1 either first line or as a standard first intensification in dual therapy with metformin, regardless of suitability of other drugs, SGLT2 (~£400 per year), sulfonylureas (~£20-25 per year), early use could cost millions of pounds. Whilst updated pathways have been supported clinically by APCs, the lack of robust economic modelling means these pathways cannot be approved for commissioning, as the cost benefit remains uncertain.

The group noted that in 2019 the SGLT2is and GLP1RAs together accounted for 7.7% of the items and 22.7% of the total spend on Drugs for Diabetes in England. The North of England has seen cost growth of 95% and 150% for the SGLT2is and GLP1RAs respectively between April 2017 & March 2020.

Current NICE guidance for type 2 diabetes does not cover evidence base for prescribing based on cardiovascular outcomes, since it pre-dates many of the relevant trials. An update of NICE guidance is planned, but no publication date is available. Other guidelines (e.g. ESC-EASD) do cover the evidence, and make recommendations for prescribing these drugs at an earlier point in the treatment pathway than NICE in order to reduce cardiovascular event rates. However ESC-EASD do not consider the cost-effectiveness or wider health economics for these agents in their recommendations. The agents in question are already in use in the NHS in line with NICE guidance, but placing them earlier in the treatment pathway would increase their use. One estimate puts the eligible population at roughly 1,480 per 1000,000, if the ESC-EASD advice were to be adopted.

The paper presented to NTAG discussed the economic/cost models currently available, and the limitations of these models. Assessing the impact of all nine relevant drugs is significantly more complicated that assessing one or two drugs at a time due to the number of variables that are unknown and must be estimated or assumed. RDTC searches for evidence conclude that models for the economic impact of introducing SGLT2is or GLP1RAs at an earlier stage of the treatment pathway than currently recommended by NICE are not yet available. It is therefore not possible at this time to estimate with any degree of confidence the impact of implementing the ESC-EASD guidance, beyond acknowledging that the likely eligible cohort is large, and therefore the number of events that could be averted (and cost of doing so) may also be large. Savings associated with

reduced rates of MI, stroke, hospitalisation for heart failure and so on are likely, but their magnitude cannot be estimated at present. Detailed economic modelling is therefore required to properly assess the impact in terms of costs and benefits.

In the absence of recent UK guidance or robust modelling data, the best path for NHS commissioners is therefore not clear. The CVOT data and ESC-EASD guidance have been available for some time, and both drug classes are well established in the NHS. It should therefore be acknowledged that, where prescribers are concerned that patients are at risk of CV events, it is likely that there is already some degree of prescribing of these agents outside of NICE guidance.

NTAG discussed the risks of doing nothing and awaiting updated NICE guidance. The CVOT data and ESC-EASD guidance have been available for some time, and both drug classes are well established in the NHS. It should therefore be acknowledged that, where prescribers are concerned that patients are at risk of CV events, it is likely that there is already some degree of prescribing of these agents outside of NICE guidance. It has been suggested that some local interim guidance could help rationalise prescribing, however the difficulty remains in assessing the financial impact and benefit of this required to proceed through the APC governance routes. NTAG concluded that national guidance supported by robust economic modelling is required as soon as possible. NTAG would be keen to engage with other medicines management groups across the region to press the case for NICE to update their current Type 2 diabetes guidelines as a priority, RMOC could be used as a vehicle to support this conversation. **Until then without significant investment from CCGs robust and accurate regional cost/economic modelling to support the financial case for approving updated or interim guidance ahead of NICE is not possible. CCG finance, commissioning and medicine optimisation representatives to NTAG were also asked to escalate this topic up through networks.**

ACTION:
ID to update County Durham & Tees Valley APC plus CCG Executive Committees

ID to ask Neil O'Brien to raise within STP

RDTC to communicate the request for NICE to expedite their guidance review, and share this conversation with GMMMG as requested.

4) Liposuction for Lipoedema and Lymphoedema

It is year since the Northern Treatment Advisory Group (NTAG) started considering issuing a regional commissioning position on Liposuction for Lipoedema and Lymphoedema.

Following the discussion at the February 2020 meeting of NTAG further information on the following was presented to NTAG as requested:

- Further definition on criteria for use particularly around functional ability after discussion with regional specialists.
- Published outcome data on the procedure from Dundee are still too broad and could impact on functional ability be further defined.

Current evidence on the safety and efficacy of liposuction for chronic lymphoedema is adequate to support the use of this procedure provided that an ongoing audit to gather outcome data is carried out. NICE IPG also supports use for lymphoedema. A likely estimate of the total number of patients referred from the region annually is around 10-12.

After discussion NTAG agreed to recommends the use of non-cosmetic liposuction in the management of chronic lymphoedema. patients who have failed conservative management in line with the current patient pathway for the treatment of lymphoedema. Patient selection should only be done by a specialist lymphoedema multidisciplinary team as part of a lymphoedema service pathway using the agreed regional criteria.

NTAG does not recommend the use of non-cosmetic Liposuction in the management of Lipoedema. Evidence for liposuction in the treatment of lipoedema is much more limited. Therefore, in light of the paucity of evidence to support this intervention, liposuction for this clinical indication cannot be supported at the present time.

ACTION: Secretary to draft recommendation as above.

5) Appraisal: Brolucizumab for wAMD

The appraisal report was introduced by the secretary. This had been added to the work plan via horizon scanning and following a formulary application submitted to Sunderland & South Tyneside APC in June 2020. The NICE TA has been delayed due to COVID-19, with no new date of expected publication. It is a CCG commissioned tariff excluded drug.

Brolucizumab would be another treatment option for AMD, with the potential to reduce the average number of patient visits and injections compared to other anti-VEGFs used in the management of wAMD.

The safety and efficacy of brolucizumab was assessed in two phase III trials (HAWK & HARRIER), both lasting 96 weeks and with a double-blind, parallel group non-inferiority design. Brolucizumab was non-inferior to aflibercept in both the HAWK and HARRIER trials at week 48 (primary outcome), and the benefits were maintained in both groups up to week 96. It should be noted that the trial design of HAWK and HARRIER does not represent the current treatment protocols used anti-VEGF treatments in the UK, which have shifted from PRN to Fixed dosing to current model of Treat & Extend.

No data on effectiveness in patients with prior inadequate response to other anti-VEGF treatments. There were no comparisons with ranibizumab, restricting conclusions that can be drawn regarding relative effectiveness. This is not unexpected however, since both ranibizumab & brolucizumab are marketed by the same company.

Differences in injection frequency should be interpreted with caution, since treat and extend regimens are available and licensed for aflibercept but were not included in HAWK or HARRIER. The EMA noted that this does not allow strong conclusions on the reduction of treatment burden with brolucizumab.

The majority of adverse effects observed in the trials were similar in both groups, and were known effects of intravitreal anti-VEGF inhibitors. The key exceptions were intravitreal inflammation (including uveitis, iritis, and vitritis) and retinal arterial occlusions, which were both more frequent with brolucizumab. Cautions have been added to the summary of product characteristics, and brolucizumab is contraindicated in patients with any active ocular inflammation.

The views of local clinicians were presented to NTAG. These all raised some concerns around increased incidence of side-effects with brolucizumab, which may limited uptake as 1st line treatment option as result. Clinicians also expressed the view that in the current COVID-19 and issues with capacity they would continue to prefer other more familiar more established anti-VEGF treatments over brolucizumab until such time as they had more service capacity to introduce brolucizumab safely with increased monitoring initially.

It was noted that the cost impact will depend on dose frequency, and, without better comparisons of flexible dosing, the overall impact is difficult to predict at present. If mean administration frequency is comparable to aflibercept in clinical practice brolucizumab is likely to be cost neutral, but further data on required administration frequency is required. Service changes in response to COVID-19 (e.g. where fixed rather than flexible dosing is in place) may also have an impact.

After discussion NTAG agreed not to recommend the use of Brolucizumab for the treatment of neovascular (wet) age-related macular degeneration (AMD) currently.
This recommendation was made taking into account the views of local clinicians because:

- **NTAG felt brolucizumab offered no clinical or cost advantage over current treatment options for wAMD to use ahead of NICE technology appraisal being issued.**
- **No published data on effectiveness in patients with prior inadequate response to other anti-VEGF treatments in wMAD.**
- **No direct comparisons with other treatments for wAMD other than alfibercept.**
- **Differences in injection frequency should be interpreted with caution, since treat and extend regimens are available and licensed for aflibercept but were not included in HAWK or HARRIER trials. The EMA noted that this does not allow strong conclusions on the reduction of treatment burden with brolucizumab.**
- **Overall safety message: rates of retinal inflammation and occlusions are higher with brolucizumab and caution is needed.**

The group noted that NICE is due to issue a technology appraisal for brolucizumab for the treatment of wAMD which when issued will superceed this NTAG recommendation.

ACTION: Secretary to draft recommendation as above.

6) Appraisal: Semaglutide (oral) for diabetes

The appraisal report was introduced by the secretary. This had been added to the work plan via horizon scanning as felt a regional position would be useful. It is the first oral GLP-1 analogue that is likely to have benefits as oral treatment compared with injectable formulations. There is no NICE TA planned and it was launched in August 2020.

A large phase III clinical trial programme found that semaglutide was generally associated with greater reductions in HbA1c, body weight and fasting plasma glucose than comparators, which included placebo, sitagliptin, empagliflozin, and liraglutide. The treatment differences against active comparators were not always clinically important. A cardiovascular (CV) outcomes trial found no difference between oral semaglutide and placebo for the compound risk of stroke, myocardial infarction and CV death compared to placebo in people with a history of CV disease or with CV risk factors. The safety profile of oral semaglutide was in line with subcutaneous

semaglutide, including an increased risk of diabetic retinopathy. The price is comparable to other drugs in class. Semaglutide provides an oral option for patients who require a GLP1RA, but other options should be considered for patients with CV risk.

After discussion NTAG agreed to recommend Semaglutide as an oral option for type 2 diabetes patients who require a GLP1RA, but other options with more robost cardiovascular outcome data should be considered for patients with cardiovascular risk.

ACTION: Secretary to draft recommendation as above.

7) Review of Current NTAG Transanal Irrigation Recommendation

NTAG reviewed the current NTAG recommendation from April 2016 for Transanal irrigation (TAI) systems (Peristeen®, Aquaflush®, Irypump® S and QuFora®) for neurogenic bowel dysfunction, chronic constipation and chronic faecal incontinence in light of new guidance issued by NICE in February 2018.

NTAG agreed to update its current recommendation to reference NICE MTG36 on Peristeen® from Feb 2018 and update the current Drug Tariff costs. No change itself to the actual current recommendation is required.

ACTION: Secretary to update recommendation

8) Review of Current NTAG Airsonett Recommendation

NTAG reviewed the current NTAG recommendation from April 2015 on the Airsonett® laminar flow device for treatment of uncontrolled asthma. No new evidence has been found to change current NTAG recommendation.

NTAG agreed to add a statement to current recommendation to say reviewed evidence based in September 2020 and found no evidence to support changing the current recommendation for use in adults. Plus note that NHSE does not routinely commission this device in children for this indication.

ACTION: Secretary to update recommendation as above.

9) Review of Current NTAG Gastroelectrical Stimulation for Gastroparesis Recommendation

NTAG reviewed its current recommendation from April 2010 on Gastroelectrical stimulation for gastroparesis as NTAG Policy to review recommendations every 2 years for new evidence. Currently Gastroelectrical stimulation with the Enterra™ device is not recommended for the management of gastroparesis by NTAG. Since April 2010 NHE England has published Clinical Commissioning Policy: Gastroelectrical stimulation for gastroparesis Reference: NHS England: 16025/P in July 2016 which states NHS England will not routinely commission gastroelectrical stimulation for gastroparesis. NHS England have concluded that there is not enough evidence to make the treatment available at this time.

NTAG therefore agreed to archive its current recommendation as superseded by NHS England Commissioning Policy in July 2016.

ACTION: Secretary to archive recommendation as above.

10) Cumberledge Review

The agenda item was introduced by the secretary. NTAG noted the publication of the Cumberledge Review in July 2020 and the continued need for NTAG to take all Declarations of Interest and the views of patients into account in its decision making. NTAG has an appropriate Declarations of Interest Policy in place with not changes required at this state. This includes making NTAG aware of any Declarations of Interest for anyone involved in preparing an appraisal for NTAG including clinicians who are consulted on place in therapy. Checks are also made of the ABPI database on payments made to individuals/organisations by the pharmaceutical industry.

11) Regional Medicines Optimisation Committee

No update on the Regional Medicines Optimisation Committees was available they have not met since February 2020 due to COVID-19. Their work plan and agendas can be found on the Specialist Pharmacy Services website.

12) NTAG Membership

Helena Gregory is now the new CCG Medicines Management/North Cumbria representative to NTAG replacing Andrea Loudon following her retirement.

13) Work Plan.

The group discussed the work plan.

- Buprenorphine long acting injection (Buvidal®) – has been referred to RMOC South and so advised to wait to see what further guidance is issued nationally by them plus timescales for this. Guidance was expected in May 2020 but delayed due to COVID-19.
- Dupilumab and Omalizumab for chronic rhinosinitis with nasal polyps – added to Nov 2020 NTAG agenda as no NICE TA not expected until July 2021.
- Andexanet alfa – review current NTAG recommendation if clinicians submit regional pathway/criteria for use but noted NICE TA in progress which will supersede current NTAG recommendation.
- Solriamfetol for narcolepsy and obstructive sleep apnoea - CCG commissioned tariff excluded drug. Licensed for both indications but awaiting launch + price. Two NICE TAs planned – OSA no date but in progress, narcolepsy – TA delayed due to COVID-19 and no date – provisionally added to Nov 2020 agenda.

Also agreed to add six monthly review of prescribing data for current NTAG recommendations to November 2020 NTAG agenda provisionally, together with the annual review of the NTAG Terms of Reference.

14) Changes to Policy for Publication of NTAG Appraisals on NTAG Website

Going forward it was agreed that the full appraisal will not be published on NTAG website but be available on request or via RDTC website for stakeholders. This is to ensure the full appraisal is only available to CCGs/Trust in NE&NC. CCGs pay RDTC to produce these appraisals for NTAG, and if made publically available risk other parts of UK using for free without permission, or using an out of date version. It also prevents the pharma/medical device industry from using NTAG appraisals in their promotional activities which has never been supported by NTAG. Non-stakeholder NHS organisations can still request a copy of the full appraisal and each request will be reviewed on case by case basis. The decision itself will still be published on NTAG website and be publically available.

15) AOB

No other business was raised and the meeting concluded.

The date of the next meeting was agreed to be 17th November 2020 and will be held virtually via StarLeaf.

Minutes produced by G Mankin, Professional Secretary to NTAG, 1st September 2020