Northern Treatment Advisory Group

Minutes of meeting held on the 7th September 2021, 9-11am

Virtual Online Meeting via Microsoft Teams

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.
- Claire Sands (CS) Assistant Head of Finance, Newcastle Gateshead CCG.
- Simon Thomas (ST) Consultant Physician, Newcastle upon Tyne NHS Foundation Trust
- Robert Lapham (RL) Formulary Pharmacist, South Tyneside & Sunderland NHS Foundation Trust.
- Jim Welch (JW) Patient/Lay Representative.
- Helena Gregory (EL) Medicines Optimisation Pharmacist and Clinical Quality Team Lead North Cumbria CCG
- Andrew Lloyd (AL) Consultant Anaesthetist and Chair of South Tees D&T, The James
- Cook University Hospital (JCUH).
- Tim Donaldson (TM) Chief Pharmacist, Cumbria, Northumberland, Tyne and Wear NHS Foundation Trust.
- Sarrah Seldon (SS) Senior Medicines Optimisation Pharmacist, Sunderland CCG.
- Toks Sangowawa (TS) Clinical Advisor/Locum Consultant in Public Health, South Tyneside MBC.

In Attendance:
Ewan Maule, Interim Lead Pharmacist – North East and North Cumbria ICS – for item 8.

Apologies were received from: Joe Corrigan

It was noted that Nick Timlin has resigned from NTAG due to clinical commitments and has been thank for his contributions to NTAG over the years. He will be replaced by his deputy Mike Milner, a GP in Tees Valley CCG.

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 none were declared.

1) Draft Minutes June 2021 Meeting

The group approved the June 2021 minutes with minor corrections to spelling and grammar.

ACTION: Secretary to publish June 2021 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.
- Cost Modelling of Type 2 Diabetes Medicines (e.g. SGLT2, GLP-1s) in ASCVD, Heart Failure and CKD – Regional Diabetes Network agreed to await for NICE but doing some general prescribing tips on SGLT2. NICE website has date of publication of updated guidance as 15th Feb 2022 with a consultation on draft guidance from 1.9.21 – 14.10.21. Agreed to remove from NTAG agenda as NICE updated guidance progressing.

3) Appraisal: Buprenorphine Prolonged-release Injection (Buvidal®) for Opioid Dependence

NTAG discussed whether it was within its remit to issue a recommendation on this topic as NTAG does not currently include representation from the appropriate commissioner, local authorities, within its membership and terms of reference. NTAG agreed it was important to have regional position on this topic. It agreed it could review Buprenorphine Prolonged-release Injection with a view to issuing a statement supporting its use clinically but that the financial case would need to be considered/approved by local authorities as the responsible commissioner for substance misuse services.

The agenda item was introduced by the secretary. This had been added to the work plan via horizon scanning and following a request for a regional position to go to local APCs from the North East Public Health Pharmacists Network.

Buvidal® is given as a once weekly or once monthly injection by a health care professional as an alternative to a daily buprenorphine tablet (which requires a prescription being received by a community pharmacy and then usually supervision of the dose at the pharmacy).

Based on national guidance, Buprenorphine Prolonged-release Injection does have a place in therapy as an option where there is a risk of diversion of opioid substitution medicines or concerns about the safety of medicines stored at home. It may also be an option for people who have difficulties adhering to daily supervised opioid substitution medication, such as for people who are working or in education, or who live in rural areas without easy access to a community pharmacy.

Ask is for NTAG to approve the use of long-acting injectable forms of buprenorphine by the Substance Misuse Service Providers (SMSPs). The model of supply/administration would then be agreed between the commissioner (local authorities) and the SMSP.

Buvidal® is significantly more expensive than generic SL buprenorphine (therefore will have a significant impact on the relatively limited drug budgets of SMSPs when provided by third party providers) however it is administered in a very different way (e.g. it is administered as a weekly or monthly injection and cannot be handled by a client) making an overall treatment cost comparison challenging.

NTAG reviewed the published NICE Evidence Summary and the RMOC Guidance for Buvidal®.

NTAG agreed to support the introduction of long-acting injectable formulations of buprenorphine by Substance Misuse Service Providers (SMSPs) (i.e. as additions to the local area formularies as RED drugs) as alternative option for the management of opioid dependence after oral methadone and/or oral buprenorphine. APCs will need to consider the products for inclusion, e.g. one product, a limited range or all available potential products.

Long-acting injectable formulations of buprenorphine may be an option in the following circumstances:

- **Where there is a risk of diversion of opioid substitution medicines or concerns about the safety of medicines stored at home.**
- **For service users who have difficulties adhering to daily supervised opioid substitution medication.**
- **For service users in custodial settings, where the risk of diversion and time needed for supervised consumption currently leads to challenges in supplying supervised medicines safely**

As part of this recommendation, it is important that through the Regional Drug and Alcohol Commissioner's Group there is:

1. Funding agreed with the local authorities as the commissioners of substance misuse services.
2. An agreed pathway for discharge from the prison service.
3. A consistency of approach to identification of eligible client cohorts in the community (e.g. in line with the recommendations in the NICE ES; and with a recognition that the benefits for use in a prison setting will be different from reasons/benefits for use in the community).
4. Monitoring of the use of long-acting injectable formulations of buprenorphine.
5. Sharing of best practice for the introduction of long-acting injectable formulations of buprenorphine by SMSPs.
6. Awareness is raised amongst wider partners across the region (e.g. CCGs, GP practices, Trusts and the NEAS) of Long-acting injectable formulations of buprenorphine, in particular the implications for pain management and overdose.
7. SMSPs inform GP practices of patients on long-acting injectable formulations of buprenorphine provision in a timely manner so that this can be recorded in the Summary Care Record for the purposes of pain management, potential drug interactions, clinical interventions, and the treatment of any overdose.

ACTION: Secretary to draft recommendation as above.

4) Review of Current NTAG Recommendation for Lurasidone (Latuda®) for the Treatment of Schizophrenia in Adults

NTAG reviewed the current NTAG recommendation from April 2015 for lurasidone (Latuda®) for the treatment of schizophrenia in adults. Currently NTAG does not recommend the use of lurasidone.

NTAG has been asked to consider changing NTAG recommendation by the mental health trusts in the North East and North Cumbria to approve use and include the new license extension from the age of 13 years old. This request is supported by the North East and North Cumbria Integrated Care System (ICS) Mental Health Programme.

An appeal against original NTAG decision was discussed at the April 2016 and November 2016 meetings, and no change to the original NTAG recommendation was made.

The reasons for this review of the current NTAG recommendation include:

- The current position prevents discharge of patients who are stable and treatment compliant - Patients who are well and currently prescribed lurasidone remain on mental health team caseloads - if approved they could be discharged to GP, creating specialist capacity at a time of rapidly escalating demand.
- Lurasidone is now licensed for adolescents.
- National and ICS drive to prevent obesity and/ or increased cardiovascular mortality in patients prescribed antipsychotics - a significant amount of resources are needed to support the patient with lifestyle interventions.
- Unlike most other anti-psychotics, there is good clinical evidence that lurasidone does not cause significant weight gain and other cardio metabolic harms.
- Felt by mental health that insufficient comparative data is too narrow an approach to justify exclusion from clinical use (comparative studies are lacking for many commonly prescribed medicines).
- The relative absence of weight gain with lurasidone offers improved medication adherence (compared to other antipsychotics), particularly in younger and female patients – so patients remain well, less likely to relapse, reducing demand on in-patient services.
- Minimal issues with weight gain with lurasidone so fewer GP appointments and less risk of developing long term conditions e.g. diabetes, cardiovascular disease.

Lurasidone costs fall within the existing price range of licensed antipsychotics and it is currently less expensive than paliperidone. But it is significantly more expensive than max dose aripiprazole, olanzapine or amisulpride. It was also noted that quetiapine is not widely used for schizophrenia. The patent of lurasidone is not due to expire until June 2026.

The difficulties around financial modelling for perceived better cardiovascular/metabolic outcomes with lurasidone compared other oral antipsychotics were discussed. Lurasidone would not be used routinely but reserved as a third line treatment for those tried on other antipsychotics. Other side-effects (e.g. akathisia) may also limit the uptake of lurasidone.

NTAG discussed the evidence presented and agreed with the proposal is to change the NTAG recommendation to approve use as follows:

As an option only for the treatment of schizophrenia in adults and adolecents aged 13 years and older who require antipsychotic treatment, who have previously had a trial of but not responded to or tolerated aripiprazole, where the patient does not fulfil the treatment resistance criteria as outlined in NICE Clinical Guideline 178 for the initiation of prescribing of clozapine, and who fulfil one of the following criteria:

- **Clinically significant weight gain on other antipsychotics (defined as greater than or equal to 5% gain in weight from baseline) and there is a need for the BMI to move towards the normal range**
- **Patients for whom there is a need to avoid weight gain and metabolic adverse effects, e.g. patients with diabetes, cardiovascular disease**
- **Patients with a prolonged QTc interval**

It was agreed that lurasidone was suitable for baseline monitoring + dose titration by specialist services with ongoing prescribing + monitoring thereafter transferred to primary care (in common with other second generation antipsychotics).

ACTION: Secretary to update recommendation as above.

5) Review of Current NTAG Recommendation for Daily vs On-demand PDE-5 Inhibitors for the Management of Erectile Dysfunction Following Treatment for Prostate Cancer

NTAG reviewed the current NTAG recommendation from March 2018 following a request from the Northern Cancer Alliance Clinical Lead for Urological Cancers. Currently NTAG recommends that on the basis of evidence available there is no evidence to recommend the use of daily dosing over on-demand dosing of PDE5 inhibitors, and there is no evidence that tadalafil is superior to sildenafil. On this basis NTAG recommends on-demand dosing using the PDE5 inhibitor with the lowest acquisition cost, currently this is generic sildenafil.

The reasons for this review of the current NTAG recommendation include:

- Erectile dysfunction is a subject at best sub-optimally managed for a variety of reasons. There is growing evidence that daily tadalafil helps support and maintain a man's erectile function for longer and he should not expect to only have access to treatment on an "ad hoc" basis.
- Daily treatment treats the pathology not the process. In the on-demand studies in erectile dysfunction (which included include patients with all causes of erectile dysfunction) there was unlimited medication, so men averaged 50mg (2.5 per week) i.e. more tadalafil than on the daily regime (35mg).
- On the basis that by continually restricting patient access to generic PDE5 inhibitors to one tablet a week (rather than prescribing quantities based on the individual patients clinical need can result in reduced efficacy (associated with performance related anxiety) and in turn this often results in requests for specialist management which may be more costly.
- Generic tadalafil is now available and costs have fallen since reviewed by NTAG in March 2018. Tadalafil 5mg once daily is now comparable in price to sildenafil alternate days which is currently used post-prostatectomy by some consultants in NENC. (£3.89 per month vs £3.50 to £4.06 per month).
- Daily dose tadalafil can be helpful in salvaging patients that are non-responders to on demand treatment with on demand PDE5 inhibitors including sildenafil & tadalafil, thereby preventing the need of more invasive/expensive treatment options e.g. intra-cavernosal injections.
- Studies have shown that 75-80% of the partners of men with erectile dysfunction have a preference for daily dosing and there is published evidence in favour of a reduced incidence of adverse side effects on daily dosing versus taking tadalafil 10mg/20mg on demand.
- Issues of equity of access across the NENC with some GPs happy to prescribe though non-formulary and others refusing as not recommended/on Do Not Prescribe Lists.

There are four oral PDE5 inhibitors licensed for treatment of ED in the UK; sildenafil, tadalafil, vardenafil, or avanafil. Sildenafil, tadalafil and vardenafil are available as generics, while avanafil

(Spedra®, Menarini) is still under patent. All four PDE5I's have been used as supportive therapy to rehabilitate erectile function successfully post-radical prostatectomy.

Six systematic reviews (with extensive overlap in included trials) and one additional double-blind RCT provide evidence in men who have undergone radical prostatectomy. Both regular (daily or three-times a week) and on-demand (prior to sexual activity) doses were effective but the studies are not designed well enough to draw firm conclusions which regimens offer the best treatment outcomes. There are no specific recommendations within available guidelines on which regimen(s) to choose.

A Q&A prepared by UK Medicines Information (UKMi) pharmacists for NHS healthcare professionals was published in May 2019 entitled "What rationale, guidance and evidence is there for the use of phosphodiesterase-5 inhibitors as supportive therapy to rehabilitate Erectile Function after nerve sparing radical prostatectomy?"

It was also noted that tadalafil once daily is included in the current NHSE guidance: Items of Low Clinical Value published in June 2019, NHSE aim is to review this guidance at least every 3 years to ensure it remains up to date. As such, NHSE plan to review this guidance document and its entire contents during the course of this financial year to ensure it remains relevant and up to date. NHSE do not anticipate that significant changes will be required but as part of this review will consider the latest evidence of clinical and cost effectiveness (taking into account any price changes) for each product, and make updates as necessary. NHSE anticipate that CCGs will continue to follow national guidance where possible, including any updates to current guidance that may be issued in the future. NTAG noted that some CCGs have backed off enforcing the NHSE recommendation not to use once daily tadalafil due to the fall in price of tadalafil since the NHSE guidance was produced.

NICE guidelines for prostate cancer recommend that men should have early and ongoing access to specialist erectile dysfunction services. The guidelines recommend that men with prostate cancer who experience erectile dysfunction (after radical treatment including radical prostatectomy) should be offered a PDE5I as the first line treatment to improve the chance of a spontaneous erection. However, NICE do not suggest which PDE5I to choose, which dosing regimen(s) to use or when to start the PDE5I after surgery.

The British Society for Sexual Medicine Guidelines on the Management of Erectile Dysfunction in Men (2017) recommends that PDE5Is are first-line therapy for ED (which includes men who have undergone prostatectomy). These guidelines state that daily or regular dosing regimens of PDEI's frequently salvage erectile dysfunction in men who have failed with on-demand PDE5I therapy.

The European Association of Urology (EAU) guidelines (2015) state that men with erectile dysfunction post radical prostatectomy are generally poor responders to PDE5I's and response rates depend on age, dosage, interval between surgery and starting therapy and degree of cavernous nerve damage. However PDE5I's are still the first-line therapy recommended for men who have undergone NSRP regardless of the surgical technique used. The guidance notes that lack of evidence to guide choice of PDE5I and suggests that the choice of drug should depend on the frequency of intercourse (to guide occasional use or regular therapy) and the patient's personal experience. This guidance notes that the early use of PDE5I's in penile rehabilitation is controversial but advises that ideally treatment should be started as soon as possible after surgery. This is because better long-term results are seen when treatment starts immediately post-

operatively. Perseverance with PDE5I therapy is suggested for at least 6-9 months because maximal response can take time to achieve.

Since generics of once daily 5mg tadalafil became available the cost has fallen from £715 per patient per annum in 2017 to £50.57 per patient per annum currently based on the August 2021 Drug Tariff. (Note: 2.5mg daily tadalafil = £253 per patient per annum currently)
So tadalafil 5mg daily is now cost-effective if using tadalafil when required dosing three times a week or more (i.e. 12 x a month) and cost effective against sildenafil if using sildenafil 25mg – 50mg five times a week (i.e. 20 x a month) or more OR sildenafil 100mg four times a week or more (i.e. 16 x a month).

After discussion NTAG agreed to recommend that once daily oral 5mg tadalafil may be considered as an option for the management of erectile dysfunction following treatment for prostate cancer. Oral 2.5mg tadalafil is not recommended by NTAG for this indication on the basis of cost.

This recommendation was made due to fall in price in tadalafil 5mg tablets since the NTAG last reviewed this in March 2018, and since the use of once daily tadalafil was included in 2017 by NHSE in their Items which should not routinely be prescribed in primary care: Guidance for CCGs.

ACTION: Secretary to update recommendation as above.

6) Regional Medicines Optimisation Committee

A verbal update on the Regional Medicines Optimisation Committee was given.

7) Work Plan

The group discussed the work plan.

- Inhaled levodopa for Parkinson's disease – still awaiting confirmation that product will be launched in the UK.
- Melatonin - agreed to remove from NTAG workplan as RMOC hopefully now looking at.
- Biosimilar insulin aspart (Trurapi®) – first one has now been launched so a review will be prepared for the November 2021 NTAG meeting.
- No other topics yet identified

8) Review of Current NTAG Terms of Reference and Membership

The NTAG Terms of Reference were last updated in November 2018, and although due for review the group had previously decided to wait until the proposed ICS structures were more fully developed. A verbal update on the proposed medicines optimisation structure within the ICS and the progress with setting this was given to NTAG by Ewan Maule, Interim Lead Pharmacist – North East and North Cumbria ICS

9) Updated NTAG Website

NTAG noted that the RDTC have a new website provider/developer so will be updating look of NTAG website in the coming months.

10) Proposed NTAG Meeting Dates 2022

Circulated for information.
It was discussed and agreed to review the day of the week that NTAG meets as part of the review of the NTAG Terms of Reference.

11) AOB

No other business was raised and the meeting concluded.

The date of the next meeting was agreed to be 16th November 2021 and will be held virtually via Microsoft Teams.

Minutes produced by G Mankin, Professional Secretary to NTAG, 7th September 2021