Northern Treatment Advisory Group

Minutes of meeting held on the 26th February 2019, 9-12am,

Meeting Room 4, The Durham Centre

Present:

- Ian Davidson (ID) Medical Director, North Durham CCG & Chair of NTAG.
- Gavin Mankin (PGM) Principal Pharmacist – Medicines Management, RDTC (professional secretary)
- Andrew Lloyd (AL) Consultant Anaesthetist and Chair of South Tees D&T, The James Cook University Hospital (JCUH)
- Matthew Grove (MG) Consultant Rheumatologist, Northumbria Healthcare NHS Foundation Trust.
- Toks Sangowawa (TS) Clinical Advisor/Locum Consultant in Public Health, South Tyneside MBC.
- Nick Timlin (NT) General Medical Practitioner, Hartlepool & Stockton-on-Tees CCG.
- Matthew Lowery (ML) Formulary Pharmacist, Newcastle upon Tyne NHS Foundation Trust
- Ewan Maule (EM) Head of Medicines Optimisation, Sunderland CCG.
- Claire Sands (CS) Assistant Head of Finance, Newcastle Gateshead CCG.
- Siobhan Brown (SB), Chief Operating Officer, Northumberland CCG

In Attendance: Nil

Apologies were received in advance from: Tim Donaldson, Joe Corrigan, Andrea Loudon, 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 it was declared that Matthew Lowery had participated in an advisory board for Rivaroxaban in August 2018. It was agreed that no action was required as an appraisal of rivaroxaban prevention of atherothrombotic events in adults with coronary artery disease or symptomatic peripheral artery disease was not going to be pursued by NTAG.

1) Draft Minutes November 2018 Meeting

The group approved the November 2018 minutes.

ACTION: Secretary to publish November 2018 minutes on the NTAG website.

2) Matters Arising

NTAG Terms of Reference – the updated Terms of Reference are going to the March 2019 meeting of the Northern CCG Joint Committee for approval together with a discussion around the future remit of NTAG and its accountability arrangements.

Freestyle Libre – following the announcement by NHS England that Freestyle Libre is to be made available on prescription from GPs or diabetes team for all patients who qualify for it in line with NHS clinical guidelines as of 1st April 2019 further guidance is still awaited nationally on how this will be funded and what will be the eligibility criteria for patients. A request for NTAG to consider making available regionally for Cystic Fibrosis Related Diabetes has been instead been fed into the national process for agreeing the patient eligibility criteria for flash glucose monitoring.

Rivaroxaban for prevention of atherothrombotic events in adults with coronary artery disease or symptomatic peripheral artery disease – following the last NTAG meeting it has been confirmed that NICE will issue a TA in August 2019 and prior to this a recommendation from RMOC North is expected imminently. It has been confirmed there is no pressure from cardiologist or vascular surgeons in the North East to prescribe and they await NICE guidance.

3) Appraisal: Doxylamine/Pyridoxine (Xonvea®) for nausea & vomiting in pregnancy

The appraisal report was introduced by the secretary. This had been added to the work plan via horizon scanning and because it was felt a regional position would be helpful. It is has a potential cost impact which is 3x NTAG Threshold for considering a drug.

The combination of doxylamine and pyridoxine has a long history of clinical use in the treatment of nausea & vomiting in pregnancy (NVP), being first introduced in the UK in 1958 as Debendox®. The product was reformulated in 1976, before being voluntarily discontinued by the manufacturer in 1983 due to the financial burdens of litigation and adverse publicity affecting the product. The current delayed-release formulation has been marketed in Canada as Diclectin® since 1979 and in the US as Diclegis® since 2013. Xonvea® contains the same active ingredients, dosage form, strength, route of administration and conditions of use as Debendox® as reformulated in 1976.

Despite widespread clinical use, there is limited evidence from randomised controlled trials demonstrating the efficacy and safety of this combination in the treatment of NVP. A single randomised 15-day trial compared Diclectin® to placebo in women with symptoms of NVP. At day 15, Diclectin® treatment was associated with a significantly greater improvement in symptoms of NVP compared with placebo, as assessed using the PUQE score (-0.9; p=0.006). The clinical significance of such a modest improvement in the PUQE score, less than one point on a 13-point scale has not been clearly established. However, the MHRA Assessment Report on Xonvea® states that the statistical differences represent improvements that are clinically meaningful for women suffering from NVP, and could represent a change from three hours of nausea per day to one hour or less. Due to the relatively short treatment period the longer-term efficacy and safety of this combination could not be evaluated in this study. Furthermore, the study did not include monotherapy arms; therefore the contribution of each component to the claimed effects could not be evaluated. The study only included women with mild-to moderate symptoms of NVP - the safety and efficacy in women with hyperemesis gravidarum was not assessed.

Doxylamine succinate is a sedating antihistamine, and safety concerns with Xonvea® are expected to be primarily related to this component. Pyridoxine hydrochloride is generally recognized as having no adverse effects. No new or unexpected safety concerns were identified in the pivotal study. The overall incidence and nature of adverse events in the two treatment groups was comparable, and there was no statistically significant difference between the groups for any adverse event.

Xonvea® is the only drug specifically licensed in the UK for the treatment of NVP. It is intended for use in women with symptoms of NVP that do not respond to conservative management. When conservative management has failed, the Royal College of Obstetricians and Gynaecologists (RCOG) recommends antihistamines (H1 receptor antagonists) and phenothiazines as first line antiemetics for NVP, as there are adequate safety and efficacy data to support this recommendation. Combinations of different drugs should be used in women who do not respond to a single antiemetic. Although none of these medicines are specifically licensed to treat NVP, there is reasonable experience with their (off-label) use in clinical practice, usually at doses consistent with their licensed use. RCOG Guidelines date from 2016 and are due for review 2019 but no date is available as to when this will be.

NTAG noted that NICE are due to issue an evidence summary on Xoneva® but there is no of expected date of publication as yet. The drug is also on the workplan for a national recommendation from the Regional Medicines Optimisation Committee but again there is no expected date of publication as yet

RDTC had also sought additional input from specialists within the region, who did not have any significant appetite to prescribe this drug. NTAG agreed that licensing was a key issue, and there was a discussion around the most appropriate placing in therapy. There were concerns around the lack of direct comparative evidence with other currently used options such as cyclizine.

The group also reviewed UK Teratology Information Service (UKTIS) monograph for Xonvea®.

NTAG felt that although Xonvea® is licensed, there was an insufficient evidence base at this time to support its use over options for which there is extensive clinical experience, and which are recommended in professional guidelines produced by RCOG. The group recognised that current treatment options are unlicensed in pregnancy but felt that guidance from RCOG was sufficient to justify current practice until such time that a national recommendation from RMOC is available, or RCOG guidelines are updated.

The Northern (NHS) Treatment Advisory Group agreed to not recommend the use of Doxylamine/Pyridoxine (Xonvea®) for the management of nausea & vomiting in pregnancy at this time. This NTAG recommendation will be reviewed in light of publication of a NICE and/or RMOC recommendation, or updated clinical guidelines from the Royal College of Obstetricians and Gynaecologists.

ACTION: Secretary to draft recommendation as above.

4) Appraisal: i-Port Advance® for use in children and adults with diabetes

The appraisal report was introduced by the secretary. This had been added to the work plan at the request of the regional diabetes network.

The i-Port Advance® manufactured by Medtronic is a subcutaneous insulin injection port suitable for multiple daily insulin administration in patients with type 1 and type 2 diabetes. It is classed as a medical device. It comes in two models, 6mm and 9mm catheter length which are both compatible with standard insulin pens and syringes. It is indicated for all ages and is inserted by the patient/carer following training using a disposable inserter supplied with it and no priming is required.. Both basal and bolus insulin can be given into the same port with minimum of 1 hour between doses. Each injection port has an expiry of 3 days (72 hours) or 75 injections – whichever

comes first. Based on expiry of 72 hours, a pack of 10 injection port is expected to last 30 days, resulting in an annual cost of around £870 per patient. The i-Port Advance® device can be worn when exercising, bathing or sleeping.

Clinical evidence for the use of i-Port Advance® device is limited. However, based on problems associated with insulin administration by injection(s), such as pain, anxiety (needle phobia), lipohypertrophy, and risk of infection, there may be some degree of acceptability for the device which may assist in achieving optimal glycaemic control reducing admissions from diabetic ketoacidosis (DKA) and reducing the insulin doses required. NTAG felt that if stops or delays progression to pump therapy it may be effective.

The i-Port Advance® device is not currently listed in the Drug Tariff. It can be obtained directly from Medtronic UK.

IFR requests to date have been refused as patient not demonstrated exceptionality and many of the requests relate to patients who have already tried/purchased the device themselves. NTAG agreed that formal commissioning position was required as not suitable for the IFR route.

NTAG noted that use of i-Port Advance® device may offer a cost saving in delaying the progression to insulin pump therapy and therefore may offer an alternative option to pump therapy in for patients meeting the NICE criteria for pump therapy. There was therefore no financial risk associated with approving the use of the i-Port Advance® device.

NTAG considered the place in therapy suggested by local paediatric diabetes specialists and felt these equally applied to adults.

The Northern (NHS) Treatment Advisory Group agreed to recommend the use of i-Port Advance® for use in children and adults with Type 1 diabetes as recommended by specialists for patients that fulfil the following criteria:

- **Children or adults with Type 1 diabetes**
- **As an alternative option in the following groups of patients who would otherwise meet the NICE criteria for insulin pump therapy**
    - **Patients in whom multiple daily injections are impractical and inappropriate where use of an injection port may avoid the need to move to insulin pump therapy**
    - **Patients with significant anxiety and needle phobia who are avoiding or missing injections**
    - **Patients with a raised HbA1C > 69mmol /l with poor compliance with treatment or who are injecting into lipohypertrophy despite support and advice to avoid these areas.**
- **Continued use of i-Port Advance® device to be reviewed every 3-6 months**

The i-Port Advance® device is not recommended for the treatment of people with type 2 diabetes mellitus it should only be for patients on multiple daily injection regimes and this is generally Type 1 diabetes patients rather than Type 2.

It is recommended that an ongoing audit of the of i-Port Advance® device is carried out to inform the evidence base for the use of device and demonstrate how long use of the device delays the progression to insulin pump therapy.

ACTION: Secretary to draft recommendation as above.

5) Apprasial: Medicinal Cannabis for CCG commission indications

The appraisal report was introduced by the secretary. This had been added to the work plan at the request of North Cumbria CCG. It was noted that patient interest in this topic is high and that NICE guidance is expected in Oct 2019.

After discussion it was agreed that no formal NTAG recommendation was required as North East & Cumbria Prescribing Forum have already issued an information sheet for GPs and a patient information leaflet on the use of medicinal cannabis. This guidance states that:

- Prescribing has been restricted to specialists, on a named patient basis.
- Prescriptions cannot be issued by general practitioners in primary care.
- Patients should not be referred to specialist doctors for the consideration of medicinal cannabis for the treatment of pain.
- Longer term guidance is expected from NICE by October 2019, but in the interim NHS England requested guidance from Guidance from the British Paediatric Neurology Association (BPNA) and the Royal College of Physicians (RCP) on the prescribing of CBPMs.
- BPNA supports use of these products in two rare forms of childhood epilepsy.
- RCP guidance supports prescribing for chemotherapy induced nausea and vomiting only, but not for any form of pain or any other indication.

NTAG supported the position taken by the North East & Cumbria Prescribing Forum.

6) Regional Medicines Optimisation Committee

A verbal update on the Regional Medicines Optimisation Committees was given to the group. Their workplan and agendas can be found on the Specialist Pharmacy Services website.

The group noted that it may need to review its recommendation from June 2017 on Sodium Oxybate for Narcolepsy in Adults in light guidance due from RMOC Midlands & East.

7) NTAG Membership

a) Secondary Care vacancies

Following the last NTAG meeting the North East & Cumbria Chief Pharmacists network have been approached again to seek a new provider Trust representative to attend NTAG but no response has been received as yet.

b) Primary care medicines vacancies

Still to contact stakeholder CCGs to seek a named deputy for the current GP representatives to NTAG.

ACTION:
Secretary to contact North East & Cumbria Chief Pharmacists Network to continue to seek one new provider Trust representative to attend NTAG.

ID/GM to write to stakeholder CCGs to seek a named deputy for the current GP representatives to NTAG.

8) Work Plan.

The group discussed the work plan.

It was agreed to add the following to the workplan for the June 2019 meeting:

- Liposuction for Lymphoedema and Lipoedema – request from IFR Panel North following a number of IFR requests which have all been refused.
- Alfapump for the treatment of refractory ascites – update of NTAG recommendation from 2016 to include new trial data and new NICE IPG631 published in Nov 2018.
- Freestyle Libre – may need a virtual meeting of NTAG to confirm regional position and responsibility for prescribing (primary or secondary care) once NHSE guidance available.

9) AOB

Nil

No other business was raised and the meeting concluded.

The date of the next meeting was agreed to be 4th June 2019.

Minutes produced by G Mankin, Professional Secretary to NTAG, 27th February 2019