Northern Treatment Advisory Group

# Minutes of meeting held on the 22nd November 2016, 9-12am,

# Meeting Room 4, The Durham Centre

**Present:**

- Tim Donaldson (TD) Chief Pharmacist, Northumberland, Tyne & Wear NHS Foundation Trust
- Ian Davidson (ID) Director of Quality and Safety, North Durham CCG & Chair of NTAG.
- Matthew Grove (MG) Consultant Rheumatologist and Head of Service, Northumbria Healthcare NHS Foundation Trust.
- Andrew Lloyd (AL) Consultant Anaesthetist and Chair of South Tees D&T, The James Cook University Hospital (JCUH)
- Graeme Kirkpatrick, Chief Pharmacist, County Durham and Darlington Foundation Trust (CDDFT)
- Bhavana Reddy (BR) Head of Prescribing Support, RDTC (professional secretary)
- Simon Thomas (ST) Consultant Physician, Newcastle upon Tyne NHS Foundation Trust
- Roger Wheeler (RW) General Medical Practitioner, Middlesbrough
- Janette Stephenson (JS) Head of Medicines Optimisation, North East Commissioning Support Unit.
- Ali Wilson (AW) Chief Officer, Hartlepool & Stockton-on-Tees CCG and Darlington CCG

Apologies were received in advance from: Toks Sangowawa, Tom Hall, Andrea Laudon and Chris Gray.

RW tendered his resignation and indicated that this meeting would be his last. The group thanked him for his involvement in NTAG.

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 September Meeting

The group approved the September minutes with no changes. A query was made regarding the Freestyle Libre recommendation and whether this could be linked to NICE criteria for CSM. The secretary noted that there was a link to the diabetes network criteria for use which in turn were based on NICE guidance. Actions within the minutes were verified.

**ACTION: Secretary to publish September minutes on the NTAG website.**

## 2) Matters Arising

### a) Lurasidone.

The group reviewed the joint cardiovascular and mental health clinical network letter that had been received. The secretary also gave the group a brief summary of the clinical evidence which the group had previously reviewed. It was noted that the company had

been in touch with extra data, however the majority of this was based on previous trial data that had already been reviewed and some was in the form of conference abstracts or data on file which couldn't be used as per the NTAG terms of reference. The overall position with regards to comparisons to aripiprazole however had not changed. There is still no direct comparative data against aripiprazole however in the absence of any head to head studies the company submitted an independent indirect mixed treatment comparison of 15 antipsychotics drugs and placebo. In terms of overall change in symptoms, or all-cause discontinuation, after six weeks of treatment, there was no significant difference between lurasidone and aripiprazole and both were better than placebo. Weight gain with lurasidone was not significantly different to placebo or aripiprazole; however, due to the short treatment duration, this result should be viewed cautiously. Treatment with lurasidone resulted in significantly more extrapyramidal symptoms and significantly larger increases in prolactin than aripiprazole. Whilst lurasidone would appear to have a favourable safety profile with regards metabolic side effects and weight gain, it does have higher rates of akathisia and or nausea than other antipsychotics so a risk benefit analysis would need to be carried out if recommended.

It was noted that whilst clinical trial data shows that lurasidone is superior to placebo and non-inferior to quetiapine, non-inferiority against risperidone was not demonstrated. It is also not suitable for treatment resistant patients. It may be suitable for a very small number of patients who are at risk of metabolic syndrome and who had experienced side effects with other treatment options.

The group agreed with the network that there was a clinical need to reduce the risk of weight gain and the development of metabolic syndrome and they liked the proposed algorithm from the network as a way of addressing this however there were concerns around the inclusion of lurasidone as an option after aripiprazole. The group noted that aripiprazole, low dose amisulpride, or haloperidol were also options for this patient group and they felt that these options should be tried first prior to moving onto lurasidone which is more expensive than all of these particularly as generic aripiprazole is now available. The group also commented that more detail was required under the lifestyle interventions section with defined goals i.e. weight reduction <7% of body weight etc. there also needs to be a review after three months following initiation of a new antipsychotic.

TD noted that most patients that don't tolerate aripiprazole are those that develop extra pyramidal side effects so it seems likely that they wouldn't tolerate lurasidone.

After much discussion and debate the group agreed that the current NTAG position on lurasidone would remain as it is currently and lurasidone is not recommended for use within the region. However the network should be encouraged to adopt a revised algorithm, updated based on the above comments and without the inclusion of lurasidone.

**ACTION: BR to feedback to network.**

## 3) Appraisal: Re-Review Capsaicin (Qutenza®) patch for neuropathic pain.

The appraisal report was introduced by the secretary. It was noted that the re-review had been requested by NoT APC and had also been identified through horizon scanning as there was now new data against pregabalin which had not been available at the time of the initial review. This new data was used by the SMC to update their initially negative recommendation. It was noted that indication approved was for those patients with peripheral neuropathic pain, who have not achieved adequate pain relief from, or have not tolerated, conventional first- and second-line treatments.

Qutenza is a cutaneous patch containing capsaicin 8%, considered to be a high concentration capsaicin preparation. It is licensed for treatment of peripheral neuropathic pain in adults. Capsaicin is thought to be useful for the treatment of pain due to stimulation and desensitisation of pain receptors in the skin.

The new data relates to a phase IV, open-label randomised trial which found that capsaicin 8% and oral pregabalin provide comparable pain relief, but that the onset of analgesia may be faster with capsaicin. The study was short (8 weeks) and therefore provides no data on how treatments compare in the long term.

Meta-analyses have assessed the efficacy of capsaicin 8% patches compared to capsaicin 0.04% patches. This comparator causes local skin reactions such as erythema and pain, but does not provide long term pain relief. It was chosen to prevent unintentional unblinding.

Capsaicin 8% was more likely than control to be associated with improvements in pain scores. However, the differences were small and may not be clinically important. In addition the studies were short, with endpoints assessed 8-12 weeks after treatment. The response to treatment in the control group was also highly variable, and several trials found no significant difference between Qutenza® and control.

A systematic review and indirect comparison of drugs for neuropathic pain found that the number of people needed to treat (NNT) to obtain a treatment response was higher with Qutenza® than pregabalin, gabapentin, tricyclic antidepressants or SNRIs, however the trials included were of varying quality and the authors noted that the evidence relating to capsaicin was of high quality.

There are no major safety concerns related to Qutenza® use. The majority of reported adverse effects are minor or moderate, and tend to be application site reactions such as pain and erythema. These can be treated with analgesia and local cooling, and are transient. Systemic adverse effects are not common with Qutenza® (incidence of 0-1.1%).

Qutenza® costs £210 per patch. It is licensed for use once every 90 days, but in practice is likely to be used less often. A cost-effectiveness model found Qutenza® to be more cost effective than pregabalin for treatment of neuropathic pain. However the model made several assumptions that may not reflect usual clinical practice. Costs for pregabalin are likely to change in the near future with the patent due to expire next year and an ongoing court battle regarding the patent for neuropathic pain.

The group agreed that there may be a place for this for those patients who have failed on pregabalin and other oral treatment options however this was still a fairly large cohort of patients so they were keen to get some feedback on how many patients' specialists envisioned using this treatment in. The group raised concerns that this may be used as well as pregabalin which would then increase costs substantially.
It was also noted that in those patients with intractable neuropathic pain, for whom no other treatment options are effective, Qutenza® may be cost effective as it would be used instead of spinal cord stimulators which can be expensive. It was agreed that a regional treatment algorithm outlining fourth line option after all oral therapies would be useful to identify place in therapy for Qutenza®. The group asked if the northern pain forum should be approached for further information to develop a regional pathway.

**The group therefore did not approve the use of Qutenza® and the current recommendation still stands however they would be minded to change this position if a regionally agreed treatment pathway for use of Qutenza® in neuropathic pain was developed and submitted to NTAG.**

**ACTION Secretary to update current recommendation as above.**

## 4) Appraisal: Lycra Garments for neurological and musculoskeletal conditions

This item was referred to NTAG via the south IFR panel as an increasing number of requests had been received. The secretary introduced the evaluation report.

Lycra garments are a type of orthotic device. They consist of sections of Lycra with strategically positioned reinforcement panels providing specific areas of resistance to stretch to aid corrective alignment of the body. The garments are made to measure and range from a glove for improved hand / upper limb function to a full body suit for whole body involvement. •They are predominantly used in children with cerebral palsy but are also advocated for other neurological and musculoskeletal conditions affecting movement and posture e.g. muscular dystrophy, multiple sclerosis, stroke, scoliosis, and head injury.

The garments are presumed to work by increasing sensory and proprioceptive awareness as well as producing a mechanical compressive effect. This is turn leads to reduction in abnormal tone, improved proximal stability, posture, movement and functional performance.

The flexibility and breathability of Lycra garments are viewed as advantages over conventional rigid/semi-rigid orthoses as they allow freedom of movement, intimate skin contact and user comfort.

There is limited evidence on which to base the clinical effectiveness of Lycra garments in the management of cerebral palsy and other neurological or musculoskeletal conditions. Available studies which have mostly been in children with cerebral palsy tend to be lacking in quality and have many limitations (e.g. small patient numbers, mostly case studies/series, non-standardised and/or subjective outcome measures and short duration). Only one published small randomised controlled trial (n=16) was identified.

The limited information suggests that wearing Lycra garments may improve stability, movement and function in some children with cerebral palsy in the short term, but are not conclusive. The lack of any robust data makes it difficult to identify which patients groups may benefit and if any proposed benefits are sustained in the long term. There is a need for well-designed RCTs to properly evaluate the effectiveness of Lycra garments although the group questioned what an adequate comparator would be.

Adverse effects reported in studies with various types of Lycra garments (full body suits, vests, shorts) include vomiting, cyanosis, hyperthermia, muscle weakness, inhibition of voluntary movement, respiratory compromise, constipation, friction sores and erythema. Long term safety is not known.

No published cost effectiveness studies were identified. Cost varies depending on the type of garment required and the manufacturer and can range from £90-£3000. The garments have an average life span of about 12 months but may need to be replaced more often in children as they grow.

Specialists with experience in using Lycra garments based at The Newcastle upon Tyne Hospitals NHS Foundation Trust were in agreement that the evidence base is limited. However, therapists reported that they have witnessed improvements in patients' function as a result of Lycra garment wear, and positive feedback is often received from patients and their families. It was suggested that from experience, Lycra garments may be beneficial for children with truncal weakness (poor core strength) to improve trunk stability and fine manipulative skills; children with dystonia to limit the range of involuntary movements at joints and improve joint stability; and for joint positioning (e.g. at the wrist, thumb or elbow).

The group reviewed the data provided from the South IFR panel and noted that there may be one or two specialists based in Tees that are prescribing these garments. The numbers across the patch are low however the majority appear to be from the Hartlepool and Tees locality. 26 applications had been approved at a cost of £46,412 over the last 24 months. The group felt that further information was required before a decision could be made. IFR data for the north of the region needed to be reviewed and it was suggested that specialists put forward a treatment pathway or define which patients they feel may benefit. The clinical data is sparse so an audit of current patients that have received these garments would be beneficial to aid decision making.

**This item will be deferred to the February meeting and further information will be sought in the meantime.**

**ACTION Secretary to contact NECS for north IFR data and to contact specialists asking for further information.**

## 5) Appraisal: Alfapump® for ascites due to liver cirrhosis.

This item was referred to NTAG via the IFR panel.

Ascites is a common complication of cirrhosis of the liver and metastatic cancer in the abdomen. It is a build-up of fluid which causes the abdomen to swell and may lead to discomfort, difficulty breathing, fatigue, nausea and poor appetite. The aim of treatment of ascites is to mobilise or remove the abnormal collection of intra-abdominal fluid. Medical

treatment with sodium restriction and diuretics is used in many patients for the management of ascites.

Ascites may occur in 60% of patients within 10 years of being diagnosed with cirrhosis of the liver. Refractory ascites can occur in up to 10% of patients with liver cirrhosis and ascites, and 50% of patients with refractory ascites will die within 6 months to 1 year. Ascites is considered to be refractory or diuretic resistant if there is no response to treatment with once daily 400mg spironolactone plus 160mg furosemide. For patients with treatment-resistant or recurrent ascites, treatment options include large-volume paracentesis, albumin infusion and insertion of transjugular intrahepatic portosystemic shunts (TIPSS). These procedures may be used to support a patient before liver transplantation. The guidelines recommend that patients with large or refractory ascites will require paracentesis. Following paracentesis, restarting diuretic therapy prevents recurrence of ascites in 80% of patients. The time interval between paracentesis procedures varies from patient to patient but is defined as frequent if the procedure is required more than three times per month. Expert opinion suggests that typically 1 to 2 paracentesis per patient per month are undertaken. Complications from paracentesis (bleeding) occur in up to 1% of patients but are rarely serious or life threatening. TIPSS may be used in selected patients who require frequent therapeutic paracentesis with appropriate assessment of the risk/benefit ratio. Clinical trials have shown TIPSS to be more effective in controlling ascites compared with large volume paracentesis and approximately two thirds of patients who undergo the procedure show an improvement in their ascites. However patients with advanced liver disease and/or encephalopathy are not usually suitable for a TIPSS procedure due to an increased risk of complications.

The Alfapump is a surgically inserted subcutaneous pump that works by automatically pumping ascitic fluid from the abdomen to the bladder, where it is excreted naturally from the body through urination. It is indicated for the management of refractory and recurrent ascites due to liver cirrhosis as well as the management of malignant ascites for palliative use.

Subcutaneous implantation of the Alfapump is required and is done under general anaesthesia, usually through 3 small incisions in the abdominal wall. A battery-powered pump with internal pressure sensors is implanted on the right side above the belt line. One catheter connects the pump to the peritoneal cavity, and another connects it to the urinary bladder. The pump and both catheters are secured with sutures to prevent migration. The implantation procedure takes under one hour and is minimally invasive. Following surgical insertion the doctor programs the pump wirelessly via the external handheld charging device, according to the needs of the patient (based on previous large-volume paracentesis requirements, observed accumulation of ascites and body weight). The hand-held device can also be used to collect data from the pump which can be downloaded to a computer for review by the doctor.

The only published study available to support the use of the Alfapump system is the Pioneer Study by Bellot et al. The Pioneer study was a non-randomized trial to assess the safety and efficacy of the Alfapump in the management of refractory ascites. The study enrolled 40 patients at nine centres in four European countries and patients were followed-up for 6 months after the insertion of the pump. The Alfapump was successfully inserted into all forty patients. In total, the 40 implanted Alfapump systems removed 4630 L of ascitic fluid over 4659 patient days, a mean of 0.99 L per patient per day. The median number of

paracentesis performed in the month preceding Alfapump implant was 3.4 (range 1–6) which dropped to 0.24 (range 0–5) per month after implant (p <0.01), 40% of the patients had no paracentesis after receiving their pump. Overall, there was a 90% reduction in the volume of ascitic fluid removed by paracentesis.

There is limited fully published safety data available on the use of the Alfapump device. In general, safety issues associated with the Alfapump include catheter occlusions, infections of the pump pocket, and pump malfunctions.

The group noted that NICE IPG479 states that current evidence on the safety and efficacy of subcutaneous implantation of a battery-powered catheter drainage system for managing refractory and recurrent ascites is inadequate in quantity and quality. Therefore, this procedure should only be used in the context of research. It does also state that the research (which may include observational studies) should clearly document the indications for use of the procedure and details of patient selection. Reported outcomes should include quality of life, overall survival and paracentesis-free survival, duration of function of the drainage system, nutritional parameters and any complications associated with its implantation or use. It was agreed that the specialists should be encouraged to audit their use of the alfapump® and record the outcomes listed above.

The cost of the entire system including pump device, catheters and programmer is £20,000 plus VAT. This includes lifelong maintenance of the device and free replacement in the event of device failure. The battery in the pump has a life span of two years. In comparison the PbR tariff for paracentesis is £815 (combined day case / elective tariff HRG FZ13Z including MFF). Therefore based on 24 hospital admissions per annum (based on 2 weekly) the cost of paracentesis is £19560 per patient per annum. A cost-utility analysis model carried out by the manufacturer suggests that the Alfapump® system in comparison with large volume paracentesis (LVP) over a time horizon of 9 months had lower cost (£26 798 and £39 702 respectively) and produced more benefits (0.87 QALYs and 0.67 QALYs respectively).

Specialists from the Freeman Hospital indicated that they would only consider use of the Alfapump® in those patients who have no other treatment options for refractory ascites such as liver transplant or TIPPS. Patients would be expected to have a survival rate >6 months and will be having very regular paracentesis (e.g. every 2 weeks). This appears to be in line with recommendations from other regions and Alfapump® may well prove to be cost effective in these patients. Specialists stated that patients report a huge increase in quality of life which doesn't come across in the clinical studies available to date although its understood trials are underway to look at this. it is expected that very few patients, ~5 per annum would fulfil this criteria across the North East and Cumbria Region.

**The group was minded to approve the use of the Alfapump® in the patient group as identified by specialists. i.e. those with a survival rate >6 months in whom other treatment options for refractory ascites are contraindicated and are having very regular (every 2 weeks) paracentesis.**

**ACTION Secretary to draft decision summary as above**

## 6) Regional Medicines Optimisation Committees (RMOC) Consultation

The group discussed the regional medicines optimisation committees' and the email that had been received regarding a nomination onto the RMOC steering group. It was noted that the communication around this hadn't been great as not all relevant personnel had received it and it was also noted that not all CCGs are members of NHS Clinical Commissioners. The group agreed that personnel should be put forward by NTAG. JC as a finance rep was suggested as well as ID as Chair.

**ACTION BR to send in NTAG nominations.**

## 7) 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 February meeting:

- Vagal Nerve stimulation for cluster headache.
- Hand held Iontophoresis

Both of the above items had arisen through requests to IFR panels. The group noted that the majority of requests that are received are now to do with devices.

## 8) AOB

The secretary raised the NICE consultation on changes to TAs and highly specialised technologies with the group for information. The group briefly reviewed the information and stated that more detail on how some of the new processes would work was required. For example how they would implement a fast track for those new technologies that have a cost per QALY of £10,000 or less? In addition the budget impact of £20 million for England is would mean a substantial number of drugs would fall into this category. The group agreed that these comments should be fed into the consultation.

No other business was raised and the meeting concluded.

The date of the next meeting was noted to be 28th February 2017

*Minutes produced by B Reddy, Professional Secretary to NTAG, 28th November 2016.*