Northern Treatment Advisory Group

Minutes of meeting 25th November, 9-12am,

Meeting Room 4, The Durham Centre

Present:

- Joe Corrigan (JC) Chief Finance & Operating Officer, Newcastle & Gateshead Alliance CCGs
- Ian Davidson (ID) Director of Quality and Safety, North Durham CCG & chair of N-TAG
- Simon Howard (SH) Public Health Speciality Registrar, Public Health England
- Mike Lavender (ML) Consultant in Public Health Medicine, Durham County Council
- Carl Parker (CP) General Medical Practitioner, Hartlepool & Stockton-On-Tees CCG
- Bhavana Reddy (BR) Head of Prescribing Support, RDTC (professional secretary)
- Janette Stephenson (JS) Head of Medicines Optimisation, North East Commissioning Support Unit
- Mike Steward, Consultant Cardiologist, South Tees Foundation Trust
- Ali Wilson (AW) Chief Officer, Hartlepool & Stockton-On-Tees CCG

Apologies were received in advance from: Geoff Stephenson, Tim Donaldson, Sue Hunter, Helen Huck, Alison Thompson, Nicholas Quinn, Frank McAuley, Craig Steele, Simon Thomas & David Campbell.

The group noted that the meeting wasn't quorate (nine voting members needed to be present for quoracy) and therefore agreement on decisions made would need to be sought with the full membership via email before they could be published.

The Chair invited declarations of interest relating to the agenda. None were made.

1) Draft Minutes September Meeting

The group approved the September minutes with no changes.

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

2) Matters Arising

a) Patient Role.

The Secretary fed back that Health Watch Newcastle had been contacted with a view to filling the patient rep role on NTAG. Whilst Health Watch Newcastle had stated that they couldn't attend local meetings themselves they had put forward a volunteer. The Chair and Secretary met with the volunteer to discuss the patient role with the intention that he attends the November NTAG meeting however he had recently emailed to resign the post as he would no longer be able to attend. After discussion it was agreed that the two previous patient representatives who attended NETAG should be approached. It was also suggested that NTAG membership could contact local CCGs or Trusts to nominate a patient rep for the group.

ACTION: Secretary to investigate previous patient representatives at NETAG.

b) Review Criteria for Area Prescribing Committees.

The group discussed the document entitled '*what treatments will NTAG consider*'. JC fed back that he had discussed the financial threshold at the Chief Finance Officers meeting and they had suggested that a threshold of £50,000 per 100,000 population should be included as well as the per patient per annum figure. The document was approved as final following this update.

ACTIONS: Secretary to update document as above and publish on website.

c) Membership: letter from CD&D Trust

The group discussed the letter that was received from Professor Gray on behalf of County Durham and Darlington Foundation Trust requesting a place on NTAG. Whilst the group is keen to engage with all trusts, it was agreed that it was important to ensure that the group had balanced representation (with equal numbers of commissioners and providers). Therefore allowing CD&D to have their own place on the group wasn't straight forward as another place would have to be offered to primary care.

It was also noted that four other trusts don't have direct representation on the group and in the interests of fairness they would also have to be offered a place if the membership was to expand. Currently Gateshead Foundation Trust represented all district generals. It was agreed that increasing membership would make the meeting too large and unwieldy. It was therefore suggested that terms of office could be agreed and members rotated to allow all trusts to input into NTAG equally or that CD&D could be offered the deputy spot for Gateshead.

ACTION Secretary to contact CD&D Trust and offer them the deputy spot for District Generals.

Post meeting note: Gateshead Foundation Trust had indicated via email that they would be happy for CD&D Trust to represent district generals at NTAG as they were struggling to provide representation on a regular basis following internal changes within the Trust. They were keen however to remain on the distribution lists so they could input into discussions as necessary. After discussion with the Chair it was agreed that CD&D should be contacted and offered the vacant position.

3) Appraisal: Verteporfin with photodynamic therapy for chronic serous central retinopathy (re-review)

A request had been received from specialists at Newcastle to re-review the previous NETAG recommendation on verteporfin. SH provided an overview of the updated data regarding the use of verteporfin with photodynamic therapy for chronic serous central retinopathy (CSCR).

The majority of cases of CSCR resolve spontaneously, often within three months of diagnosis. However, there is a small cohort of patients for whom symptoms will persist,

producing chronic CSCR. Treatment options currently consist of either laser photocoagulation – which is not suitable for all cases – or conservative supportive care with no active treatment. The disease typically affects men in middle age.

Verteporfin PDT, using a half-dose regimen, has been investigated as a potential treatment option for chronic CSCR. While a large number of studies have now been published in this field, only a small minority report on the clinically relevant outcome of visual acuity, and still fewer use the treatment regimen proposed (others use varying doses of verteporfin or fluence).

It was noted that since the publication of the NETAG review in March 2011, a number of new studies have been published. However these studies are all small, vary widely in the treatment regimen used and typically have relatively short follow up periods.

All studies consistently demonstrated improvements in vision upon treatment with verteporfin PDT that strengthen the case for the observed effects being treatment related as opposed to spontaneous. However, it is notable that not all of the improvements described would be particularly clinically relevant, even where they are statistically significant. There are also no direct randomised comparisons with current standard therapies. No safety issues have been identified from this off-licence use of verteporfin to date

Treatment with verteporfin PDT is costly, at an estimated £1360 per treatment. Some patients require more than one treatment, though the proportion of patients this affects is unclear (especially in the long-term). However, the number of patients in the North East who might require treatment is estimated to be only 30 per annum. It should be noted that all of these estimated costs and patient populations rely on untested assumptions.

The group considered that the evidence base for verteporfin in chronic CSCR is still of an experimental nature and therefore there is not sufficient data to support widespread clinical use.

It was agreed that individual patients in exceptional circumstances may be suitable for treatment e.g. patients with poor sight in the other eye. Such cases must be referred via local individual funding request mechanisms.

ACTION Secretary to update previous decision summary with updated position as above

4) Appraisal: Biologic drugs for treatment-refractory moderately to severely active ulcerative colitis (UC) in younger patients.

The appraisal report concerning the use of biologic drugs for treatment-refractory moderately to severely active UC in younger patients was introduced by the secretary.

It was noted that this request had arisen from IFR and clinician requests. The group were made aware that a NICE multiple technology appraisal was underway which would look at three of the tumour necrosis factor inhibitors (TNFi) [adalimumab, golimumab and infliximab]

in more detail so the clinical data for these wasn't covered in depth in the review document although the current NICE ACD position was summarised. The clinical trial data for the new novel α4β7-integrin binding T-helper lymphocyte adhesion inhibitor, vedolizumab was included.

It was noted that this request was to use biologics in a small subgroup of the licensed population i.e. in younger patients in place of surgery.

There is no universally agreed pathway for management of patients with treatment-refractory moderately to severely active UC. Sub-optimal use of currently available treatments and lack of adherence have been identified as important causes of apparently refractory UC. Management focuses on confirming disease activity, exclusion of alternative diagnoses, attention to adherence and appropriate escalation of established therapies.

Surgery is considered to be largely curative of the gastrointestinal features of UC and to eliminate the risk of colorectal cancer. Among appropriately selected patients, surgery is associated with sustained improvements in quality of life. Surgery is, however, also associated with considerable risks and potential long-term adverse effects. A larger proportion of patients may opt for surgery due to chronic sub-acute disease or repeated exacerbations despite optimal management. People with UC are at increased risk of colorectal cancer and surgery may also be considered to prevent cancer in patients in whom polyps or dysplasia is detected during endoscopic surveillance and for patients who are at very high risk due to prolonged extensive disease. The advantages and disadvantages of extended trials of medical therapy in patients not responding well to standard treatments and for whom colorectal surgery is an option are not well established. It is unclear whether use of medical therapy would just delay surgery in this case.

The current NICE Appraisal Consultation Document does not recommend TNFi treatment for adults with treatment-refractory moderately to severely active ulcerative colitis.

For those patients for whom it was an option, colectomy dominated all of the treatments under evaluation and conventional therapy. For patients for whom colectomy is not an option, adalimumab was likely to be the most cost-effective option, but the base-case incremental cost-effectiveness ratio was considerably above the level considered to represent cost-effective use of NHS resources. NICE acknowledged several shortcomings in the evidence base and areas of uncertainty which may be pertinent to local decision making.

The group noted that the NICE appraisal does not consider the impact of surgery on fertility and the impact in younger patients has not been fully assessed.

An independent systematic review and meta-analysis combined the key TNFi trials with data from the one published trial of vedolizumab. The results suggested that infliximab may be more effective at inducing clinical response and mucosal healing than adalimumab. None of the other indirect comparisons reached statistical significance. There was no signal to suggest that vedolizumab might have advantages over the TNF inhibitors. No conclusions about relative efficacy of the four biologic therapies for maintenance of response and/or remission could be drawn.

The group discussed the patient impact of the disease and agreed that it was a difficult disease to manage. It was also noted that patients with UC that is poorly controlled despite optimum use of standard therapies and who are reluctant to or determined not to undergo surgery despite clinical advice currently have few options other than to tolerate their symptoms, the adverse effects of medication (possibly including long-term effects of exposure to corticosteroids), the increased risks of colorectal cancer and the regular endoscopic surveillance that this entails.

It was noted that if 10% of patients with ulcerative colitis experience chronic continuous disease activity, there could be approximately 775 patients in the North East and North Cumbria who might be considered for treatment with biologic drugs. The proportion of those patients who have moderately to severely active disease that cannot be controlled by optimising conventional therapy and the proportion of those whom colectomy might not be a reasonable treatment option is not known. Treating all 775 patients were treated with adalimumab could cost approximately £3.5 million.

It was noted that two biosimilar versions of infliximab (Inflectra®, Hospira and Remsima®, Celltrion) have marketing authorisation in the UK for the same indications as Remicade® however there are currently no approved UK list prices for these products yet. There is also currently no UK list price for vedolizumab.

The group did not support the use of biologics in treatment refractory UC in younger patients instead of surgery, due to an absence of supporting clinical and cost effectiveness data for this specific patient population.

However the group recognised that there may be certain individuals in exceptional circumstances for whom these treatments may be considered. Such cases must be referred via local individual funding request mechanisms.

ACTION Secretary to draft decision summary as above

5) Appraisal: Sativex® oramucosal spray for the management of non–MS pain.

The appraisal report concerning the use of Sativex® spray in the management of non-MS pain was introduced by the secretary. This appraisal was referred to NTAG from CCGs as Gp's have been getting an increasing number of requests to prescribe.

Sativex® is an oromucosal spray containing cannabis-derived active ingredients. It is not licensed in the UK for use as an analgesic and its use for the treatment of chronic non-MS related pain would be an off-license indication and therefore it isn't currently in the NICE work plan.

The anticipated place in therapy of Sativex® in the treatment of chronic pain associated with cancer and other non-MS related conditions is as an adjunct to existing opioid therapy and is not intended to replace current treatments. Sativex® is intended to address an unmet need in patients who experience moderate to severe pain despite the highest tolerated dose of

strong opioid therapy. It is thought that the non-opioid mechanism of action offers the prospect of pain relief without increasing opioid-related adverse side effects.

A number of randomised and non-randomised controlled studies of varying quality have examined the efficacy of Sativex® in the management of chronic non-MS related pain conditions. The main evidence base is for the use of Sativex in the treatment of chronic refractory cancer-related pain, and neuropathic pain of various origins. There are limited published data regarding its use in rheumatic disease.

Cancer Pain: The results of studies in patients with cancer are inconsistent, but suggest that Sativex® may have a role as an adjunct to opioid therapy for the treatment of cancer-related pain. However, the existing data are only preliminary; a clearer understanding of the role of Sativex® in the treatment of cancer pain should be confirmed upon completion of the comprehensive on-going phase III study programme.

Neuropathic pain: In patients with neuropathic pain of various origins the evidence for efficacy is limited, with only one study demonstrating that Sativex has a positive analgesic effect when used in addition to existing analgesic therapy.

Rheumatic Disease: A recent Cochrane Collaboration review concluded that Sativex® appears to improve pain and sleep to a modest degree in patients with RA, but given the CNS side effects profile, the potential harms appear to outweigh the modest benefits. It should be noted that this conclusion was based on the only published data available which was a phase II study.

Adverse effects with Sativex are frequent but are generally mild to moderate in severity and manageable.

Sativex® is a costly treatment, with an estimated mean annual cost per patient of £4,750 for the treatment of cancer pain, and £5,625 for the treatment of neuropathic pain. As the likely place in therapy of Sativex® is as an adjunct to opioid therapy, the cost will be in addition to existing therapy.

The group considered the clinical evidence for Sativex® in this indication to be of low quality and clear benefit was not demonstrated. Combined with a high acquisition cost, Sativex® was considered unlikely to meet conventional cost-effectiveness criteria.

ACTION Secretary to draft decision summary as above

6) Evaluation of ranibizumab cost models

The group were informed that this item had been referred to NTAG by NECS medicines management team. The Novartis budget impact model claims there are cost savings associated with prescribing ranibizumab for eye diseases when compared to aflibercept.

The secretary summarised the key points from the data presented:

- Both ranibizumab and aflibercept have been approved for use, by NICE, as a treatment option for people with wet AMD providing they fulfil certain criteria. Therefore both drugs would still need to be made available within Trust formularies.
- There has been a change to the ranibizumab license (changed in September 2014) which allows simpler dosing and monitoring for all indications when employing a 'treat and extend' regimen.
- These changes appear to reflect what was already happening in UK practice prior to the license change with patients no longer being monitored on a monthly basis for all indications and receiving injections less frequently than was suggested in the previous SPC.
- The budget impact model estimates budget impact over 5 years and it can look at individual indications or all indications together. All assumptions are drawn from the referenced clinical trials or the NICE TA 294 costing template.
- Previous models suggested high levels of savings however these savings were not real as they did not take into account current practice.
- Current practice across the NE and Cumbria is to use either ranibizumab or aflibercept on a PRN basis adapting treatment to individuals.
- If patients are being treated according to a treat-and-extend regimen, once maximum visual acuity is achieved and/or there are no signs of disease activity, the treatment intervals can be extended stepwise until signs of disease activity or visual impairment recur. The treatment interval should be extended by no more than two weeks at a time for wet AMD and may be extended by up to one month at a time for DMO.
- The current Novartis model suggests savings if trusts move to a 'monitor and extend' regimen from a 'prn' regimen when using ranibizumab, compared to licensed doses of aflibercept.
- This saving appears to be due to 2.3 fewer injections of ranibizumab in year 1. This saving is negated if more monitoring or injections are required subsequently or if aflibercept treatment is individualised in year 1 as is already happening locally.

It was therefore agreed that no changes to current practice were required regarding ranibizumab. The group endorses the current NICE recommendations on use of both ranibizumab and aflibercept as an option for wet AMD.

7) Updated Work Plan

The group discussed the current work plan and noted that some items no longer fulfilled the NTAG per patient per annum cost criteria. These items (lurasidone, protexo and rifaximin) were therefore discussed in more detail.

- It was agreed that due to the difficult nature of appraising medical devices - protexo temperature controlled laminar airflow device for asthma should still be considered by NTAG.
- It was suggested that mental health colleagues should be contacted regarding the review of lurasidone to check if a review by NTAG would be desirable.
- It was agreed that rifaximin (550mg TDS for 14 days) for IBD should be removed from the NTAG work plan and should be considered by local APC's.

The group agreed to add the following to the February agenda:

- Rituximab for thrombocytopenia purpura
- Protexo® temperature controlled laminar airflow device for asthma
- Lurasidone for schizophrenia *(pending agreement by mental health)*
- Aripiprazole and paliperidone LAI & protocol for use

The secretary agreed to add dates to the remaining medicines or technologies on the work plan and publish the updated work plan on the website.

ACTION: Secretary to add the above items to the agenda for the February meeting and to update the work plan as above.

8) AOB

No other business was raised and the meeting thus concluded.

The date of the next meeting was noted to be 24th February 2014, Meeting Room 4, The Durham Centre.

Minutes produced by B Reddy, Professional Secretary to NTAG, 2nd December 2014.