Clinical Policy Recommendation Committee Minutes

Wednesday 28th June 2023
via Microsoft Teams

Present:

Name	Job Title	Organisation
Dr Glen Allaway	Chair	NHS Devon
Dr Andrew Craig	Voting Member	NHS Devon
Dr Lucy Harris	Voting Member	NHS Devon
Susan Masters	Deputy Chief Nursing Officer	NHS Devon
Dr Paul Melling	Voting Member	NHS Devon
Mac Merrett	Lay Public Member	
Chris Roome	Head of Clinical Effectiveness	NHS Devon
Mark Taylor	Lay Public Member	
Dr Emily Youngman	Consultant in Public Health Medicine	Devon County Council

Guests:

Dr Charles Dixon	Consultant Psychiatrist	DPT
Amanda Gulbranson	Lead Pharmacist	Children and Family Health Devon
Matt Howard	Clinical Evidence Manager	NHS Devon
Amy Rice	Clinical Effectiveness Pharmacist – Commissioning Projects Lead	NHS Devon

In attendance:

Fiona Dyroff	Clinical Effectiveness Governance Support Officer	NHS Devon
Rebecca Owen	Clinical Effectiveness Governance Manager	NHS Devon

1. Welcome and announcements

Apologies:

Name	Job Title	Organisation
Dr Kay Brennan	Voting Member	NHS Devon

Richard Croker	Deputy Director of Medicines Optimisation	NHS Devon
Paul Foster	Clinical Director of Pharmacy and Prescribing	T&SD
Dr Claire Hooper	Voting Member	NHS Devon
Barbara Jones	Head of Contracting	NHS Devon

Confirmation of voting members and Declarations of interest

The five voting members present were identified.

Dr Kay Brennan had delegated voting to Susan Masters
Dr Claire Hooper had delegated voting to Chris Roome

Declarations of Interest were collected and reported. No Declarations of Interest were made.

DRUG/ TECHNOLOGY TO BE CONSIDERED	PHARMACEUTICAL COMPANY/ MANUFACTURER/ SERVICE PROVIDER
Lurasidone (Latuda®) **in schizophrenia**	CNX Therapeutics Ltd (formerly Sunovion Pharmaceuticals Europe)
Alternative treatments:	
Amisulpride	Various manufacturers
Aripiprazole	Various manufacturers
Chlorpromazine	Various manufacturers
Clozapine (Clozaril®, Denzapine®)	Mylan, Britannia Pharmaceuticals Ltd
Haloperidol	Various manufacturers
Olanzapine	Various manufacturers
Quetiapine (Immediate release)	Various manufacturers
Quetiapine (Modified release)	Various manufacturers
Risperidone	Various manufacturers
Sulpiride	Various manufacturers

Notification of Any Other Business

The committee were asked if there were any items of AOB for discussion. One item was identified:

- Update on any changes to the future of the group.

2. Minutes of the meeting held on Wednesday 26th April and matters/actions arising

The minutes of the meeting held on Wednesday 26th April 2023 were approved.

Summary of actions			
	Action	**Lead**	**Status**
23/01	High Intensity Focussed Ultrasound for recurrent prostate cancer – Policy recommendation and QEIA to be prepared and subsequently progressed to final ICB approval and communication.	Rebecca Owen	Pending
23/02	Cryotherapy for recurrent prostate cancer – Policy recommendation and QEIA to be prepared and subsequently progressed to final ICB approval and communication.	Rebecca Owen	Pending
23/03	Focal hyperidrosis – Policy recommendation and QEIA to be prepared and subsequently progressed to final ICB approval and communication.	Rebecca Owen	Pending
23/04	Clinical Policy Recommendation Committee Annual Report 2022-23 to be submitted to the Strategy and Transformation SLT on behalf of NHS Devon ICB for information and assurance, and the risk posed by ongoing membership challenges to be escalated. <u>28/06/23</u> This action is progressing within the context of changes to organisational structures within NHS Devon	Rebecca Owen Chris Roome	Pending

3. Lurasidone for schizophrenia in adults

An application has been received from Devon Partnership Trust to consider the use of lurasidone for adults with schizophrenia. The proposal covers use in two distinct clinical scenarios. The first scenario is for use as a third line treatment option for patients who have not responded to, or not tolerated, prior treatment with amisulpride and aripiprazole. The second scenario is for use as a first line treatment option for patients with QTc prolongation.

This is the second time that lurasidone has been considered by the CPRC. The previous application, which was not supported, proposed that lurasidone was used earlier in therapy and so differs from the current application.

Amy Rice, Clinical Effectiveness Pharmacist presented a paper. Dr Charles Dixon, Consultant Psychiatrist, Devon Partnership Trust and Amanda Gulbranson, Lead Pharmacist, Children and Family Health Devon were present for discussion of this item.

NICE guidelines support antipsychotics for schizophrenia however, with the exception of clozapine, no specific drug choices are recommended.

There is no evidence to indicate that lurasidone would be effective in patients who have not responded to amisulpride and aripiprazole. No evidence of differences in adverse events have been found for lurasidone versus aripiprazole, which questions the role of lurasidone in those who have not tolerated aripiprazole. Evidence of a lower incidence of prolactin increases for lurasidone versus amisulpride suggests a potential role for lurasidone where amisulpride has been discontinued due to this adverse event only.

Currently, for patients who fail to respond to, or tolerate amisulpride and aripiprazole, third line options available in NHS Devon would be chlorpromazine, clozapine, haloperidol, olanzapine, quetiapine, risperidone, and sulpiride.

Two network meta-analyses found that lurasidone was less effective compared to clozapine, olanzapine and risperidone. Differences compared to chlorpromazine, haloperidol, quetiapine and sulpiride were not significant. There is no evidence that lurasidone is more effective than currently available third line options.

The applicant's rationale for using lurasidone as a third line option is based on a desire for an antipsychotic with a low propensity for weight gain, metabolic effects, and prolactin increases. A statistically significantly lower incidence of weight gain has been demonstrated for lurasidone when compared to chlorpromazine, clozapine, olanzapine, quetiapine and risperidone. Differences in the incidence of prolactin increase are however mixed with a statistically significantly lower incidence compared to haloperidol and risperidone but a statistically significantly higher incidence compared to clozapine and quetiapine. In terms of metabolic effects, a statistically significantly lower incidence of some, but not all, parameters have been found when compared to olanzapine and risperidone. Comparative metabolic effects against other third line options have not been evaluated. None of these comparisons consider whether differences are clinically significant and in comparisons of all-cause discontinuation rates, lurasidone failed to demonstrate a significantly lower discontinuation rate when compared to all seven of the currently available third line options. This suggests that any advantages in tolerability for lurasidone over other drugs were not sufficient to lead to significant differences in treatment discontinuation rate.

The applicant's rationale for using lurasidone in patients with QTc prolongation is based on risk classifications in the Maudsley Prescribing Guidelines. Lurasidone is classified as having 'no risk' of QTc prolongation which means there have been no reports of this event during therapeutic or supra-therapeutic use. However, these guidelines did not acknowledge an incidence of QTc prolongation reported in an RCT of lurasidone published in 2015. Since the publication of these guidelines, an additional case report of QTc prolongation with lurasidone has also been published. The same guidelines classify aripiprazole as a 'low risk' option. This is a recent change with the previous edition classifying it as a 'no risk' option. The rationale for this change in classification is based on only three case reports of QTc prolongation with aripiprazole, and given the much higher usage of aripiprazole does not represent a substantial difference in evidence compared to the two instances of QTc prolongation which have been reported following the use of lurasidone. Network meta-analyses report statistically significantly smaller changes in the QTc interval for lurasidone versus amisulpride, haloperidol, olanzapine, quetiapine, and risperidone, supporting lurasidone as a lower risk option compared to these drugs. However, the difference compared to aripiprazole was not significant which further questions the difference in risk between these two drugs.

Published cost-effectiveness studies of lurasidone have limited relevance as they do not consider its use in either of the scenarios proposed by the applicant. Any economic benefits demonstrated for lurasidone are driven by estimations of lower relapse rates however assumptions in model designs and data inputs affect the reliability of these findings. Furthermore, these benefits represent notional savings. Specialists estimate that lurasidone would be used in 24 patients per annum. This equates to an average increase in costs of approximately £10,600 per annum

compared to currently available third line options. The All-Wales medicines strategy group review of lurasidone published in 2015 estimated an uptake of lurasidone for 0.29% of patients at year one, rising to 2.94% of patients at year five. A review of NHS Wales prescribing data shows that actual uptake has however been much lower with lurasidone prescribing currently accounting for approximately 0.58% of antipsychotic prescription issues. However, a prescribing rate of 0.58% is still higher than that which has been proposed by specialists for Devon. If however the rate of 0.58% was seen in NHS Devon, it would equate to treating approximately 64 patients per annum with lurasidone. This would result in an increase in average costs of approximately £28,000 per annum compared to currently available third line options.

It is unclear whether the estimate of 24 patients per annum also includes the use of lurasidone in patients with QTc prolongation. An upper estimate of the incidence of QTc prolongation indicates potential for 155 patients per annum in Devon who would require an antipsychotic with a low QTc risk. Using lurasidone instead of aripiprazole would result in an increase in average costs of approximately £37,000 per annum. Due to a number of assumptions in this calculation it is however likely that this is a substantial overestimate. Regardless, for each affected patient, using lurasidone still costs on average £322 per annum more than using aripiprazole. As such, an alternative scenario was also considered whereby lurasidone is only used for patients with QTc prolongation who have not responded to, or not tolerated, aripiprazole. Predictions using the same parameters indicate a much lower increase in average costs of approximately £3,200 per annum however again, this is likely to represent an overestimate.

The committee considered issues pertinent to the routine commissioning of lurasidone for schizophrenia in adults:

- Efficacy: There is no evidence that lurasidone is more effective than other antipsychotics, including amisulpride and aripiprazole.
- Adverse events: Specialists reported that some patients find aripiprazole too alerting. Lurasidone offers an alternative which also has a low incidence of weight gain and metabolic effects. Specialist experience with lurasidone is limited but patients do not experience the same level of akathisia with some taking doses at bedtime. With current alternatives, the healthcare burden of metabolic effects can be significant. Clozapine may be more effective, but use is carefully regulated with regular blood tests required. Clozapine is not an option for all due to weight gain, constipation, and sedation.
- QT Prolongation: Specialists have requested that lurasidone be routinely commissioned as a first line treatment for patients with QTc prolongation. There may be benefits for adults around QT prolongation however this does not appear to be the same for children and adolescents. A lack of evidence for a lower risk compared to aripiprazole was acknowledged.
- Patient choice and shared decision making: Schizophrenia is a difficult condition to treat, current treatments are not suitable for all and bring health risks. Patients with schizophrenia have a reduced life expectancy. Specialists have requested lurasidone be made available as a third line option as it may have increased tolerability compared to current options. For some patients there is more concern about the side effects of a drug than its effectiveness. Patients can disengage from treatment due to side effects, including weight gain and sedation which can lead to relapse with potential for need for treatment under the Mental Health Act.
- Exceptional treatment Pathway: This may be used for patients who are at risk of disengaging from treatment due to side effects of routinely commissioned treatments.

The group were asked to consider lurasidone for schizophrenia in children and adolescents before voting on lurasidone for schizophrenia in adults.

The committee voted three to two in favour of routinely commissioning lurasidone as a third line treatment option.

The committee voted that for patients with QTc prolongation (at baseline or during treatment with an antipsychotic) lurasidone be routinely commissioned as a treatment option in patients who have not previously responded or have not tolerated aripiprazole.

ACTION: Policy recommendation and QEIA to be prepared and subsequently progressed to final ICB approval and communication.

4. Lurasidone for schizophrenia in children and adolescents

In 2020 the marketing authorisation for lurasidone was extended to include use in children and adolescents aged 13 to 17 years.

An application has been received from Children and Family Health Devon to consider the use of lurasidone as a second line option in children and adolescents aged 13 to 17 years, who have failed to respond to, or tolerate, previous treatment with aripiprazole. The rationale for using lurasidone is based on a desire for a second line treatment option with a low propensity for weight gain, metabolic effects and prolactin increase. Currently, second line treatment options available in NHS Devon are haloperidol or sulpiride, which are licensed for use in children and adolescents, and amisulpride, quetiapine, olanzapine, or risperidone, which are unlicensed in children and adolescents, but their use is supported in clinical practice. Clozapine is also available as a third line option and is licensed for use from 16 years of age.

Amy Rice, Clinical Effectiveness Pharmacist presented a paper. Dr Charles Dixon, Consultant physiatrist, Devon Partnership Trust and Amanda Gulbranson, Lead Pharmacist, Children and Family Health Devon were present for discussion of this item.

As for adults, NICE guidelines support the use of antipsychotics for schizophrenia but, with the exception of clozapine, no specific drug choices are recommended.

No studies have been published in which direct comparisons are made between lurasidone and other antipsychotics in children and adolescents. Three network meta-analyses report comparative efficacy and tolerability, but findings are inconsistent with a large reliance on indirect comparisons. No evidence has been published which indicates that lurasidone would be effective in children or adolescents who have not responded to aripiprazole. With no differences in the incidence of adverse events for lurasidone versus aripiprazole in the network meta-analyses, the role of lurasidone in patients who have not tolerated aripiprazole is also unclear. Compared to currently available second line options, none of the network meta-analyses reported a significantly greater response following short term use for lurasidone versus clozapine, haloperidol, quetiapine, olanzapine, or risperidone. No comparisons were made to sulpiride or amisulpride. In terms of tolerability, lurasidone had a statistically significantly lower incidence of weight gain compared to quetiapine, olanzapine, and risperidone, in addition to a statistically significantly lower incidence of prolactin increase for lurasidone versus haloperidol, olanzapine, and risperidone. The clinical significance of differences in adverse events was not evaluated, and comparisons of tolerability and all-cause discontinuation rates found no significant difference for lurasidone versus haloperidol, quetiapine, olanzapine, or risperidone. This suggests that advantages in tolerability were not sufficient to lead to significant reductions in treatment discontinuation. Comparisons following long term use were also reported in one network meta-analysis, but the reliability of these findings is limited by significant heterogeneity and inconsistencies.

Evaluation of the cost-effectiveness of lurasidone in children and adolescents is limited to one cost impact study, however the differing treatment sequences used in this comparison limits its relevance to local practice. Findings are driven by differences in relapse rates between antipsychotics however a lack of clarity in the source of the data used to underpin this input

places substantial uncertainty in the study findings. As such, the cost-effectiveness of lurasidone in children and adolescents remains unknown.

Specialists estimate that if approved for use as a second line option (after aripiprazole), lurasidone would be used in approximately four patients per year in Devon. Compared to currently available second line options this would equate to an average cumulative increase in costs of approximately £1,000 per annum. Whilst a figure of only four patients per annum appears to be small, this value is supported by calculations using current local prescribing data and lurasidone prescribing rates reported in NHS Wales.

The committee considered issues pertinent to the routine commissioning of lurasidone for schizophrenia in children and adolescents including:

- the need to ensure that policies for children and adolescents are joined up with the policy for adults.
- Evidence: There is little evidence published for the use of lurasidone in children and adolescents. Available evidence does not indicate that lurasidone is more effective than other antipsychotics. The rationale for using lurasidone is not based on efficacy but around presenting a licensed option with a low incidence of weight gain, metabolic effects and prolactin increase.
- Adherence to treatment: This is a difficult condition to manage and it is difficult to keep patients in school. Aripiprazole is generally used first line. If the child or adolescent has an enduring condition their first experience of treatment is key to adherence to future treatments. Fewer options are available with some patients having to received drugs which are not licensed in children and adolescents. If adherence is poor patients may require treatment under the Mental Health Act. Patients usually stay on the first treatment that works. 25% of people can stop medication within 5 years and 30% within 10 years.

The committee voted two to three in favour of the routine commissioning of lurasidone for children and adolescents (aged 13 to 17 years)] who have not responded to or not tolerated previous treatment with aripiprazole.

ACTION: Policy recommendation and QEIA to be prepared and subsequently progressed to final ICB approval and communication.

5. Update from NICE Planning Advisory Group (NPAG)

The committee received an update from the NPAG meeting which had taken place on Tuesday 11th April 2023.

The group had considered:

- Four ICB Commissioned Technology Appraisal
- Six NHS England Commission technology appraisals
- Two NHS England Commissioned Highly Specialised Technologies
- Six NICE guidelines
- Four Intervention Procedures Guidelines
- Four Medical Technology Guidelines
- One diagnostic guideline

6. NICE Planning Advisory Group (NPAG) Annual Report 2022-23

The committee received the NICE Planning Advisory Group (NPAG) annual report 2022-23. The report provides an account of the activity and governance of the group, and assurance to ICB of how its statutory responsibilities are fulfilled in respect of mandatory NICE guidance.

NPAG has ensured continuity of process following the establishment of the ICB, providing a forum for the ICB to fulfil its statutory responsibilities in respect of mandatory NICE Technology Appraisals and Highly Specialised Technologies and a route thought which the ICB is appraised of any obstacles to their implementation. NPAG also allows consideration to be given to the resource and service implications for all newly published NICE guidance and guidelines.

NPAG fulfils its role via reports on NICE guidance which include local service providers' assessment of the impact on their services and their plans in respect of it, identification of commissioning responsibilities, anticipated resource impact and any other impacts, e.g., on existing ICB commissioning policy. Issues arising are reported to the ICB locality managers and senior ICB officers are briefed on significant issues arising from NICE guidance in relation to their area of work.

There is an established process for ensuring that NICE Technology Appraisals and Highly Specialised Technologies are added to the local formulary within three months of publication (or 30 days if recommended through the fast-track appraisal process) in line with the ICB's statutory responsibilities.

NPAG also routinely considers NICE forward plans of guidance expected to be published over the forthcoming three-month period. They help identify the commissioner, provider/s, potential resource and capacity impact areas, as well as any other impacts, such as on an existing commissioning policy.

Outside of meetings, there has been continued post meeting liaison in respect of any issues highlighted or to support organisational awareness, for example to share details of guidance flagged as being of particular interest once published.

The team produces a monthly NICE bulletin detailing newly published and updated NICE guidance for the month, which is published and widely disseminated for local awareness. It also includes a list of current open NICE consultations for the benefit of those that may be interested in engaging upcoming topics.

There is also ongoing engagement by the team with national guidance and initiatives which link with NICE guidance to be able to support the organisation with relevant actions – such as the MedTech Funding Mandate and the Evidence Based Interventions Programme.

Updates from NPAG have continued to be a standing item on CPRC meeting agendas.

Five NPAG meetings were held during the year, receiving 137 reports relating to NICE guidance. Just over half of these related to mandatory guidance, which is prioritised on meeting agendas; the remainder split between clinical guidelines and other technology guidance.

There has also been an increase in the average number of pieces of guidance considered per meeting, which is now 27. The general trend is also for a year-on-year increase in the volume of guidance considered by NPAG since it was formed in 2013.

Over the year NICE published 201 new and updated guidance and guidelines (including 23 terminated appraisals). In line with the split of NPAG agendas, mandatory guidance accounts for nearly half of NICE's published guidance.

The group welcomed a number of observers to their meetings to enhance their understanding of the group and the ICB's NICE processes for the benefit of their roles. These were from a range of teams within NHS Devon, as well as Foundation Pharmacists from Royal Devon University Healthcare NHS Foundation Trust.

Looking ahead, a noted growth area for NICE is the publication of Healthcare Technology Evaluations (HTEs), which set out conditional recommendations while more evidence is generated to address any uncertainties. The aim of these HTEs is to support quicker access to promising health technologies that address national unmet need. The group supports the ambition to improve patient care through adoption of this approach; however, is also mindful of the potential challenges for the local health system and implications for patients in Devon, if technologies conditionally supported are subsequently not recommended by NICE for routine adoption in the NHS.

The planned delegation of NHS England functions to ICBs may have an impact on the future business of the group, with an increase in the areas for which the ICB is the responsible commissioner shaping the volume, depth and content of the papers brought to the meeting, as well as the discussion, implications and the subsequent actions which may be required.

CPRC was asked to receive the annual report for information and assurance. The report will be reported onwards in the organisation.

7. Update from Clinical Policy Engagement and Consultation Panel (CPEC)

The committee received an update from the Clinical Policy Engagement and Consultation Panel meeting which took place via Microsoft Teams on Wednesday the 25th May 2023.

The Clinical Policy and Engagement Panel had considered three items:

- High intensity focused ultrasound (HIFU) for recurrent prostate cancer
- Cryotherapy for recurrent prostate cancer
- Focal hyperhidrosis

The panel saw no reason for further engagement or consultation actions on any of the items discussed.

8. Clinical Policy Engagement and Consultation Panel (CPEC) Annual Report 2022-23

The group received the Clinical Policy Engagement and Consultation Panel (CPEC) annual report. The report gives an account of the activity and governance of the Panel in 2022-2023, from the period the ICB was established on 1 July 2022.

The panel has continued its function to support the organisation in determining the need for any further engagement or formal public consultation on recommendations made by CPRC. This process is prior to a final decision being taken by the ICB on any clinical policy recommendations.

The wider public interest issues are considered to determine the need for any further engagement or formal public consultation on clinical policy recommendations.

Since the transition to the ICB the panel has welcomed Thandi Hara (Non-exec director for citizen and community involvement) and Martyn Nicoll (Patient experience manager) as new members.

Two meetings were held during the (shorter) reporting period. During this period 10 clinical policy recommendations across a range of topics were considered.

CPEC made specific recommendations on the proposal to update the Assisted Conception Policy and the updated policy for Continuous Glucose Monitoring (CGM).

When the proposed update to the Assisted Conception policy was considered, the subjective nature of a 'stable' relationship was discussed, along with the appropriateness of a clinician making a moral judgement on this to determine eligibility to access assisted reproduction. There was concern that the definition was open to interpretation, and therefore potential challenge. The ICB was asked to consider further engagement work on this, within the context of other non-clinical factors relating to the social nature of relationships, which are a growing area and are broader than clinical factors for infertility.

The ICB took a decision to approve the policy amendment, noting that fertility specialists indicated that this was workable from their perspective and was consistent with the majority of other ICB areas. However, the wider issues relating to non-clinical and societal factors were flagged with the communications team to scope and consider how future engagement and/or consultation might be undertaken in this area.

Consideration of the updated policy for CGM highlighted the need for the previously produced clinical policy patient support information to be reviewed for ongoing relevance and updated as needed to support the publication and communication of any changes to commissioning policy.

CPRC was asked to receive the annual report for information and assurance. The report will be reported onwards in the organisation.

9. Any other business

Update on any changes to the future of the group

A committee member had asked for an update on any potential changes to the role of the Committee because of the restructuring of NHS Devon ICB.

It was noted that the ICB is going through a change. However, the organisation has stated that it wishes to keep CPRC. There is an aspiration to have greater secondary care involvement on the group. It was noted that the organisation is going to continue to need a robust decision-making process.

Summary of actions			
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23/05	Lurasidone for schizophrenia in adults – policy recommendation and QEIA to be prepared and subsequently progressed to final ICB approval and communication.	Rebecca Owen	Pending
23/06	Lurasidone for schizophrenia in children and adolescents - policy recommendation and QEIA to be prepared and subsequently progressed to final ICB approval and communication.	Rebecca Owen	Pending