NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Remimazolam for sedation for people having diagnostic or therapeutic procedures

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of remimazolam within its marketing authorisation for sedation for people having diagnostic or therapeutic procedures.

Background

Procedural sedation is used to intentionally suppress the consciousness level of people undergoing different clinical procedures including bronchoscopy, colonoscopy and endoscopy. The intended depth of sedation varies according to the procedure and patient factors. The depth of sedation can be categorised as 'mild', 'moderate' and 'deep'. Under minimal or mild sedation, the person responds normally to visual commands. Under moderate sedation the person responds purposefully to verbal commands alone or when light touch is also used. Under deep sedation, the person cannot be easily aroused but has purposeful response to noxious stimulation[1].

The number of people in hospital in the UK receiving procedural sedation is unknown. Data collected by NHS anaesthetists in 2013 showed that the annual number of cases managed by an anaesthetist requiring sedation was 308,800 cases (8.6%)[2]. Another study conducted in 2013 in the South West of England reported that most sedation occurred in endoscopy units (56.4%), followed by operating theatres (30.3%) and cardiology departments (7.2%)[3].

The choice of pharmacological agents for procedural sedation depends on several factors including the nature of the procedure, the planned level of sedation and differences between individuals. Doses and routes of administration also need to be tailored. NICE guideline CG112 'section in under 19s: using sedation for diagnostic and therapeutic procedures' recommends midazolam for upper gastrointestinal endoscopy and fentanyl in combination with midazolam for lower gastrointestinal endoscopy. It also recommends nitrous oxide or midazolam for dental procedures. This guideline does not include adults. The Royal College of Emergency Medicine has produced a best practice guideline on pharmacological agents for procedural sedation and analgesia in the emergency department. This guideline states that common pharmacological agents for procedural sedation and analgesia in adults include propofol, midazolam, ketamine and ketofol[1].

The technology

Remimazolam (Aptimyda, Paion AG) is an ultra-short-acting benzodiazepine sedative and anaesthetic. It is rapidly metabolised in the body to an inactive metabolite. Remimazolam specifically acts on the GABA-A receptor and has CYP-independent metabolism. Its actions can be reversed with flumazenil to rapidly end sedation if necessary. It is administered intravenously.

Remimazolam does not currently have a marketing authorisation in the UK for sedation for people having diagnostic or therapeutic procedures. It has been studied in clinical trials for sedative use in adults undergoing a colonoscopy or bronchoscopy.

Intervention(s)	Remimazolam
Population(s)	People having diagnostic or therapeutic procedures
Comparators	Established clinical management without remimazolam
Outcomes	The outcome measures to be considered include: • success of procedure • time to start of procedure • time to fully alert • time to ready for discharge • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost-comparison may be carried out. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	The availability and cost of biosimilars and generic products should be taken into account. Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	**Technology Appraisals:** None **Related Guidelines:** Sedation under 19s: using sedation for diagnostic and

	therapeutic procedures (2010). NICE guideline [CG112] Reviewed December 2018. **Related NICE Pathways:** Sedation in children and young people (2019) NICE pathway http://pathways.nice.org.uk/pathways/sedation-in-children-and-young-people
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 4 & 5 https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Which pharmacological agents are considered to be established clinical practice in the NHS for sedation for diagnostic or therapeutic procedures?

Are different pharmacological agents used for specific procedures in clinical practice? If yes, please provide detail.

Are the outcomes listed appropriate?

What outcomes are important for patients and clinicians?

Are there any subgroups of people in whom remimazolam is expected to be more clinically effective and cost effective or other groups that should be examined separately?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which remimazolam will be licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider remimazolam to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of remimazolam can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?
- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?
- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?
- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1. The Royal College of Emergency Medicine. Pharmacological Agents for Procedural Sedation and Analgesia in the Emergency Department. 2017. Available from: https://www.rcem.ac.uk//docs/College%20Guidelines/Pharmacological%20Agents%20for%20Procedural%20Sedation%20and%20Analgesia%20(Jan%202017%20Revised).pdf Accessed July 2020

2. Sury MRJ, Palmer JH, Cook TM et al. (2014) The state of UK anaesthesia: a survey of National Health Service activity in 2013, British Journal of Anaesthesia 113(4): 575-584.

3. South West Anaesthetic Research Matrix (2015) Sedation practice in six acute hospitals – a snapshot survey, Anaesthesia 40(4): 407-415.