NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Liposomal bupivacaine for treating post-operative pain

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of liposomal bupivacaine within its marketing authorisation for treating post-operative pain.

Background

Acute pain is a type of pain that typically does not last longer than 3 months and is common after surgical procedures that cause injury to tissue. The treatment of acute pain post-surgery is essential to facilitate recovery and restoration of function.

In 2019-20 the NHS in England performed 12,281,985 surgical procedures and interventions[1]. The perioperative quality improvement programme has collected data from 123 hospitals in England and Wales and found that in 2019 20% of people experienced severe pain at the site of surgery with a further 51% experiencing moderate pain[2]. The incidence and severity of post-operative pain will vary depending on the type of surgical procedure. Individuals also experience pain differently which can be influenced by biological responses, psychological state and traits and social context[3].

NICE guidance 180 recommends that the healthcare professional discusses the options for postoperative pain management with the person before they have surgery. They should take into account clinical features including comorbidities, age, frailty, renal and liver function, allergies, current medicines and cognitive function as well as whether the surgery is immediate, urgent, expedited or elective. The discussion with the person should include the likely impact of the procedure on the person's pain, their pain history, the potential benefits and risks, including long-term risks, of different types of pain relief and plans for discharge. There are several pharmacological interventions and delivery methods available to address post-operative pain which include paracetamol, non-steroid anti-inflammatory drugs (NSAIDs), opioids, ketamine and neuropathic nerve stabilisers. NICE guidance 180 recommends a multimodal approach to analgesia, selection should be adopted where a combination of analgesics with different mechanisms of action are combined. This approach aims to minimise potential side effects and maximise pain relief. The healthcare professional should also consider prescribing pre-emptive analgesia for use when local anaesthesia wears off.

The technology

Liposomal bupivacaine (Exparel, Pacira Ireland) is a non-opioid analgesic that consists of the active pharmaceutical ingredient bupivacaine combined with multivesicular liposomes. Bupivacaine is a local anaesthetic that blocks the generation and conduction of nerve impulses while multivesicular liposomes slowly release bupivacaine. Liposomal bupivacaine can be administered as a field block or as a brachial plexus or femoral nerve block.

Liposomal bupivacaine does not currently have a marketing authorisation in the UK for treating post-operative pain. It has been studied in clinical trials in adults as a single-dose infiltration to control post-operative pain following several different surgical procedures such as buccal mucosal graft harvesting, cystectomy, knee replacement and ankle fractures repaired with open reduction and internal fixation. It has also been studied in clinical trials as a nerve block for post-operative pain control following several different surgical procedures such as lung resection, total knee replacement and total shoulder replacement. Most trials compared liposomal bupivacaine with bupivacaine or placebo.

Intervention(s)	Liposomal bupivacaine
Population(s)	Adults with post-operative pain from small to medium sized surgical wound
Comparators	Established clinical management without liposomal bupivacaine (including but not limited to paracetamol, NSAIDs/COX-2 inhibitors, opioids, ketamine, neuropathic nerve stabilisers and local anaesthetics)
Outcomes	The outcome measures to be considered include: • pain reduction • use of rescue medications • length of hospital stay • length of stay in intensive care unit • hospital readmission • 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. 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 biosimilar 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	**Appraisals in development:** Bupivacaine–meloxicam for managing pain after surgery Proposed NICE technology appraisal [ID2728] Publication date to be confirmed. **Related Guidelines:** Perioperative care in adults (2020). NICE guideline [NG180] Moderate to severe acute post--operative pain: sufentanil sublingual tablet system (2016) NICE Evidence summary [ESNM71] **Related NICE Pathways:** Postoperative care (2020) NICE pathway http://pathways.nice.org.uk/
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domain 3. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Have all relevant comparators for liposomal bupivacaine been included in the scope?

Which treatments are considered to be established clinical practice in the NHS for post-operative pain management?

Will liposomal bupivacaine be used as an add-on therapy? If so at what stage in the pathway will it be used?

Will liposomal bupivacaine replace existing treatments? If so, will liposomal bupivacaine be used as a direct replacement or will it replace treatments that would usually be used at a later stage in the pathway?

Are the outcomes listed appropriate?

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

Should people receiving liposomal bupivacaine as a field block or nerve block be considered as separate subgroups and examined separately?

Where do you consider liposomal bupivacaine will fit into the existing NICE postoperative care pathway?

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 liposomal bupivacaine 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 liposomal bupivacaine 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 liposomal bupivacaine 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).

References

1. Hospital Admitted Patient Care Activity, 2019-20: Diagnosis (2020). NHS Digital. Accessed September 2020

2. Perioperative Quality Improvement Programme (PQIP) Annual Report 2018-19. (2019). Perioperative Quality Improvement Programme. Accessed September 2020

3. Small C, Laycock H. (2020) Acute postoperative pain management. British Journal of Surgery.107(2): 70-80