Medicines & Healthcare products Regulatory Agency

DRUG SAFETY UPDATE (DSU)

Prolonged-release opioids: Removal of indication for relief of post-operative pain

Specialisms: *Pain management and palliation, Anaesthesia and intensive care*

Summary

The indication for the treatment of post-operative pain has been removed from the licences of all prolonged release opioids. These opioids should not be used post-operatively due to the increased risk of persistent post-operative opioid use (PPOU) and opioid-induced ventilatory impairment (OIVI). It is not recommended to use transdermal patches for the treatment of post-operative pain.

Advice for Healthcare Professionals:

- prolonged-release opioids provide relief from chronic severe pain, however, they should not be used for the treatment of acute pain following surgery
- prolonged-release opioids are associated with an increased risk of PPOU characterised as continued opioid use beyond 90 days following the operation, and an increased risk of OIVI causing serious respiratory depression, sedation, and depression of upper airway muscle tone
- before surgery, discuss with the patient the following:
  - explain the risks of PPOU, dependence and potential risk of addiction and withdrawal reactions
  - explain the risk of OIVI especially for patients with underlying respiratory conditions
  - immediate-release opioids are used for short-term treatment of pain
  - discuss with the patient pain management strategies involving the use of immediate-release opioids and multimodal analgesia and plan for end of treatment
- patients whose pain is managed with opioids pre-operatively should have their treatment reviewed before and after surgery in line with Consensus Best Practice Guidelines
- at discharge from hospital:
  - only prescribe and supply a sufficient amount of immediate-release opioids to treat acute post-operative pain to minimise the risk of PPOU, dependence, stock piling of unused opioids and potential for diversion

Advice for Healthcare Professionals *continued*:

- communicate the pain management plan with the primary care practice taking over care in the community and document in patient clinical notes
- it is important to report suspected dependence or respiratory depression to any medicine, including an opioid, via the Yellow Card Scheme

Advice for Healthcare Professionals to Provide to Patients:

- opioids provide relief from moderate to severe pain. Pain following an operation is usually short-lived and therefore should only require short-term treatment
- immediate release opioids are used for the treatment of short-term post-operative pain
- if you are taking prolonged release opioids before going into hospital for an operation, talk to your doctor to discuss your pain management and ongoing needs
- there is a greater risk of respiratory depression (problems breathing) and persistent post-operative opioid use with prolonged release opioids
- if you notice new or increased trouble with your breathing, dial 999 as this could be a sign of respiratory depression
- if you feel like you cannot stop taking opioids as you had originally planned, contact your doctor as this could be a sign of persistent post-operative opioid use (PPOU)
- if you are concerned for someone who has been using more opioids than prescribed, you can also seek advice from the NHS website or if you are in Northern Ireland from the Health and Social Care website

Background

Review of the benefits and risks of prolonged release opioids after surgery

Prolonged-release (modified release) opioids are indicated for moderate or severe pain and cancer pain, although NICE guidance [NG193] recommends that opioids are not used for chronic primary pain where there is no underlying condition accounting for the pain. A small number of prolonged release opioids containing morphine or oxycodone were also authorised for the treatment of post-operative pain, however concerns were raised on the potential for harm and an increased risk of PPOU and OIVI.

PPOU is defined as continued opioid use beyond 90 days from the day of operation. Dependence is a well-known side effect of opioids and we continue to communicate to raise awareness on this issue (see Drug Safety Update on opioids: risk of dependence and addiction).

Evidence from across the EU including the UK has shown that the incidence of PPOU ranges from 2% - 44% in patients treated with prolonged-release opioids. Also PPOU is

more prevalent (incidence up to 60%) in patients taking prolonged-release opioids pre-operatively.

Respiratory depression is also a well-known side effect of opioids, especially if taken in excess or in combination with other sedating medicines (for example benzodiazepines, pregabalin or gabapentin) which can lead to coma and potentially death.

OIVI is a serious form of respiratory depression associated with:

- depression of respiratory rate and/or depth of breathing – 'central respiratory depression'
- depression of consciousness – 'sedation'
- depression of supraglottic airway muscle tone – 'upper airway obstruction'

The reported incidence of OIVI is difficult to determine, although the international multidisciplinary consensus statement quotes an incidence of OIVI ranging from 0.4% to 41% depending on the identification measures used.

Following the conclusion of a safety review undertaken by the MHRA, and advice from the Commission on Human Medicines (CHM), the indication for the treatment of post-operative pain has been removed from the licences of prolonged release morphine and prolonged release oxycodone. The remaining prolonged release opioids are not recommended for acute post-operative pain relief and may already not be indicated for acute use or are contraindicated in acute pain relief.

The information considered by the CHM and the advice issued is presented in a Public Assessment Report.

Post-operative pain prescribing recommendations

Pain following surgery is usually short-lived, lasting between 5 – 7 days and therefore should only require short-term pain management best treated with immediate release opioids. However, many patients are discharged from hospitals with excessive amounts of opioids to meet their needs for acute post-operative pain management. This excess supply of opioids increases the risk of developing PPOU, dependence, addiction, or could lead to opioid diversion, and an increased risk of OIVI with unmanaged use. Therefore, patients should only be provided with a prescription for a sufficient amount of instant release opioids to manage their acute post-operative pain on discharge from hospital.

A Consensus Best Practice Guideline agreed between the Faculty of Pain Medicine, Royal College of Anaesthetists, Royal College of General Practitioners, Royal College of Surgeons of England, Royal College of Nursing, The British Pain Society, the Centre for Perioperative Care and endorsed by the Royal Pharmaceutical Society, recommend that pre-operative use of opioids should be reviewed prior to surgery.

Patients at increased risk

Adjustments in dose or dosing regimen might be necessary in patients at increased risk of experiencing these severe adverse reactions, including patients:

- with compromised respiratory function or respiratory disease

- with neurological disease
- with renal impairment
- with cardiovascular disorders
- using concomitant central nervous system (CNS) depressants
- older than 65 years
- with opioid tolerance
- using opioids pre-operatively

Patients and healthcare professionals are encouraged to discuss treatment regimens and agree a post-operative pain management plan prior to the proposed surgical procedure.

Reporting advice

If a patient experiences any side effect or is recognised by the prescriber to be experiencing a side effect related to post-operative analgesia to a medicine, prescribers, patients, or carers are asked to report this to the MHRA through:

- the Yellow Card website.
- the Yellow Card app; download from the Apple App Store or Google Play Store
- some clinical IT systems for healthcare professionals (EMIS, SystmOne, Vision, MiDatabank, and Ulysses)

This will assist the MHRA to monitor the rates reported in the UK and therefore to further protect public health.

When reporting suspected adverse drug reactions, please provide as much information as possible, including information about medical history, any concomitant medication, onset timing, and treatment dates.

Additional information

You can sign up to receive email updates on Drug Safety Updates.

References

Consensus Best Practice Guidelines surgery-and-opioids-2021.pdf

Sitter T and Forget P. Persistent postoperative opioid use in Europe. A systematic review. European journal of anaesthesiology 2021: volume 38, pages 505-511.

Srivastava D and others. Surgery and opioids: evidence-based expert consensus guidelines on the perioperative use of opioids in the United Kingdom. British Journal of Anaesthesia (2021): volume 126, pages 1208 – 1216.

Levy N and others. An international multidisciplinary consensus statement on the prevention of opioid-related harm in adult surgical patients. Anaesthesia 2021: volume 76, pages 520-536.

Stakeholder engagement:

- Faculty of Pain Medicine

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