

# National Essential Anaesthesia Drugs List (NEADL)

March 2021



# Association of Anaesthetists

## The National Essential Anaesthesia Drug List (NEADL) 2021

The Association of Anaesthetists is pleased to present the 2021 edition of NEADL. This edition has been simplified to remove reference information available from other sources and to improve usability.

NEADL serves several purposes to a range of professionals involved in the delivery of anaesthesia. For suppliers, pharmacists and managers, NEADL offers advice on a minimum set of drugs that must be available wherever anaesthesia is to be conducted safely. This facilitates efforts focused on ensuring the sustainability of drug supply.

For anaesthetists, the list is in no way prescriptive. The use of alternatives is to be encouraged because it takes pressure off the supply of the NEADL drugs, making shortages less likely. This also spreads familiarity with the use of alternatives when there is a shortage of an essential drug.

Shortages principally affect generic injectables. When a shortage occurs, we look first to find a direct alternative, e.g. lorazepam for midazolam or vecuronium for rocuronium. Sometimes it will be necessary to look beyond injectables and develop protocols that make use of non-injectable formulations. For example, if injectable opioids were in shortage, a protocol for anaesthesia for orthopaedic surgery might include premedication with simple oral analgesics and long-acting opioids. Additional steps will help during shortages. They include:

- Decrease waste: only draw up what you will use, and consider alternatives to patient-controlled analgesia.
- Decrease use: develop alternative techniques such as regional analgesia during opioid shortage and vice versa.
- Decrease supplies: provide clinicians with the best alternatives, with advice on their safe use.
- Decrease activity: triage to protect emergency and live-saving surgical procedures.

Many of these mitigating strategies have been used to manage drug shortages during the SARS COV-2 global pandemic. Early communication between the Department of Health and Social Care (DHSC), the Medical Healthcare products Regulatory Agency (MHRA) and anaesthesia and critical care professionals, ensured the timely exchange of information and advice on drug shortage management. The principles of NEADL offer a structured approach to managing this crisis.

The Association of Anaesthetists would be pleased to see local solutions to drug shortages submitted as abstracts at WSM and Annual Congress meetings so that experiences might be shared.

Injectable generic drug shortage is a global issue affecting all countries irrespective of income. The causes of shortages and contributing factors are well known and are outlined in this text. Every step

in the supply chain can affect availability. Early detection, good communication and the ability to forward plan can help avoid unnecessary disruption to patient care.

We are grateful to of the original contributors and authors of NEADL 2015 and thank those who helped in the 2021 revision.

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The [British National Formulary online](#) (BNF online) offers the most up to date details of drugs available for anaesthesia. Drugs can be searched via the drug or treatment summary icons.

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## Essential, necessary and critical drugs

In this document, we will use the following definitions:

Essential medicines:	<b>E</b>	Those that satisfy the priority healthcare needs of the population, as defined by the <u>World Health Organization</u> .
Necessary drugs:	<b>N</b>	Those used to treat or prevent a serious disease or medical condition for which there is no alternative medicine available in adequate supply, as defined by the <u>US Food and Drug Administration</u> .
Critical drugs:	<b>C</b>	Those that are both necessary and vulnerable to shortage, as defined by the <u>US Drug Shortage Prevention Act 2012</u> .
Priority indications:	<b>P</b>	In times of shortage, these are the priority indications for which the drug should be reserved until further supplies are guaranteed.

## Medical gases

### Essential drugs name

Air **E N**

Oxygen **E N**

### Clinical indications

- Carrier gases for anaesthetic agents. **P**
- Air is used to drive medical equipment including ventilators and surgical tools.

### Alternative drugs or techniques

- **No alternative to oxygen.**
- Nitrous oxide (as a carrier gas).
- A self-inflating bag-valve-mask or draw-over system can be used to ventilate the lungs with air from the atmosphere.

### General comments

- Air and oxygen are necessary for the safe administration of anaesthesia
- Use of 100% oxygen during shortage of air risks oxygen toxicity and collapse of the lung (atelectasis).
- Nitrous oxide has been shown to be a safe carrier gas with weak anaesthetic and analgesic properties. Its tendency to provoke nausea and vomiting can be offset with anti-emetic therapy.

## Intravenous anaesthetics: propofol

### Essential drugs

**Propofol 10mg.ml (1%) E C**

Ketamine 10 mg.ml<sup>-1</sup> (1%) **E C N**

Propofol 20 mg.ml<sup>-1</sup> (2%)

### Alternative drugs

**Thiopental sodium C**

**Etomidate**

### Clinical indications

Induction of anaesthesia **P**

Maintenance of general anaesthesia

Sedation for critically ill patients being mechanically ventilated **P**

Sedation for procedures

### General comments

Patients may be sensitive to the drug or its diluent, in which case an alternative must be used

Propofol infusion syndrome may occur in children or adults after prolonged propofol infusion of larger doses particularly in ICU. It is often fatal.

## Inhalational anaesthetics: sevoflurane

Essential drug

**Sevoflurane E**

Alternative drugs or techniques

**Isoflurane**

**Desflurane**

Clinical Indications

**For the maintenance of general anaesthesia P**

**Induction of anaesthesia as an alternative to intravenous induction**

**General comments**

Volatile anaesthetic agents can be triggers for malignant hyperpyrexia.

All volatile agents are greenhouse gases. The most significant impact is caused by desflurane – 20 times that of sevoflurane per MAC hour.



## Antimuscarinic drugs

### Essential drugs

Atropine **E**

Glycopyrronium bromide **E**

### Alternative drugs

Hyoscine hydrobromide

### Clinical indications

- Treatment and prevention of intra-operative bradycardia. **P**
- An antisialagogue.
- Control of the muscarinic side effects of neostigmine.

### General comments

- Glycopyrronium has a similar onset and duration of action to neostigmine and is preferred to atropine for this indication.
- Glycopyrronium does not cross the blood–brain barrier, and therefore does not affect the sensorium.

## Benzodiazepines

### Essential drugs

Midazolam **E**

### Alternative drugs

Diazepam

Diazemuls

Lorazepam

Temazepam

### Clinical indications

- Premedication.
- Intra-operative sedation.
- Sedation in intensive care. **P**
- Co-agent for induction of anaesthesia.
- Emergency treatment of status epilepticus. **P**

### General comments

- Midazolam is available in a variety of concentrations and so has the potential for drug error.
- Overdose with high concentration midazolam during conscious sedation, outside the environment of anaesthesia and intensive care is one of the 2015/16 NHS England Patient Safety Never Events.
- All can be antagonised with flumazenil.

## Non-opioid analgesics

### Essential drugs

Paracetamol **E**

### Alternative drugs

Aspirin

Diclofenac

Ibuprofen

Ketoprofen

Nefopam

Parecoxib

### Clinical indications

- Analgesia. **P**
- Antipyretic. **P**
- Anti-inflammatory.

### General comments

- If there is a shortage of the injectable forms (where available), plan to use other routes of administration.
- Intravenous paracetamol was first licensed in the UK in 2000, since then it has formed an important part of peri-operative analgesic regimens. Paracetamol requires to be prescribed according to weight, age and comorbidities. It is also recommended that for patients weighing <33 kg, 50 ml vials should be used. Intravenous paracetamol remains under close monitoring from the MHRA and yellow card reporting should follow any adverse events.
- Injectable cyclo-oxygenase inhibitors as an alternative simple analgesic are either cyclo-oxygenase (COX)2 specific (parecoxib) or non-specific (ketorolac, diclofenac). The evidence for preferring one over another is slim.
- The Scottish Medicines Consortium has advised that parecoxib is not recommended for use within NHS Scotland.
- There is no good substitute for paracetamol as an anti-pyretic.

## Opioid analgesics

### Essential drugs

Fentanyl **E C**

Morphine **E C**

### Alternative drugs

Alfentanil

Buprenorphine

Codeine

Diamorphine

Dihydrocodeine

Methadone

Oxycodone

Pethidine

Remifentanil

Tramadol

### Clinical indications

- Intra-operative analgesia as part of a balanced technique. **P**
- Morphine is used for sedation as an infusion in critical care, especially neonatal and paediatric units. **P**
- Treatment of severe acute and chronic pain by various routes and under patient control.

### Alternative drugs or techniques

- Alfentanil.
- Remifentanil.

### General comments

- Fentanyl is 100 times more potent than morphine and produces respiratory depression in a dose-dependent manner. As a result of its haemodynamic stability, fentanyl can be used in very high doses while ventilation is controlled. Muscle rigidity (including the chest wall) can occur but is prevented by muscle relaxants. When used in small doses ( $1-2 \mu\text{g}\cdot\text{kg}^{-1}$ ), fentanyl's duration of action is 30–60 min, and this short duration of action is due to redistribution. However, when given in higher doses or after prolonged administration as an infusion, the effects last until the drug is eliminated from the body (terminal half-life: 3.5 h).

- Alfentanil has a shorter duration of action than fentanyl and morphine and is therefore not recommended for postoperative analgesia.
- Morphine causes histamine release that may lead to hypotension, rash, itching and bronchospasm.
- Caution in renal failure due to the accumulation of metabolites morphine-3-glucuronide and the active morphine-6-glucuronide.
- Remifentanil is used as a continuous infusion for intra-operative analgesia. It is not suitable for routine postoperative analgesia.
- When there is a shortage of injectables, consider enteral administration of opioid analgesics.

## Neuromuscular blocking drugs

### Essential drugs

Atracurium **E**

Suxamethonium **E C**

Rocuronium **E C**

### Alternative drugs

Cisatracurium

Mivacurium

Vecuronium

### Clinical indications

The establishment of neuromuscular blockade to facilitate a variety of anaesthetic interventions. **P**

- Tracheal intubation, including rapid sequence intubation (suxamethonium and rocuronium)
- Maintenance of mechanical ventilation
- Relief of laryngospasm and to modify the seizure activity associated with electroconvulsive therapy (suxamethonium at lower doses).

### General comments

- Rocuronium is associated with the highest incidence of IgE-mediated anaphylaxis amongst all the neuromuscular blockers.
- The block achieved with atracurium is not reversed by sugammadex
- Rocuronium can also be used for rapid sequence induction. With sugammadex immediately available, a short duration of action can be achieved.

## Drugs for reversal of neuromuscular blockade

### Essential drugs

Neostigmine (often in a premixed preparation with glycopyrronium bromide) **E**

Sugammadex **E**

### Alternative drugs

Edrophonium chloride

### Clinical indications

- Neostigmine can be used for competitive reversal of all non-depolarising neuromuscular blockade, primarily at the end of anaesthesia. **P**
- Sugammadex can be used to competitively reverse neuromuscular blockade of rocuronium and vecuronium.

### General comments

- Unwanted muscarinic effects of neostigmine such as bradycardia, bronchospasm and salivation are countered by concurrent glycopyrronium or atropine (hence the combined preparation).
- Edrophonium is a shorter-acting anticholinesterase. When used as an alternative to neostigmine, there is a risk of re-occurarisation.
- Sugammadex is only effective against neuromuscular block established with rocuronium and vecuronium.
- Exercise caution in patients with severe renal impairment due to uncertainty about excretion of the sugammadex-rocuronium complex.
- When using sugammadex, patients taking hormonal contraceptives should follow the advice for a missed dose. If non-oral hormonal contraception, additional use of non-hormonal contraception for the next 7 days should be advised. Refer to the product literature.
- In paediatrics, sugammadex is only recommended for routine reversal of rocuronium induced blockade in patients between the ages of 2 and 17 years.

## Antagonists of central and respiratory depression

### Essential drugs

Flumazenil **E**

Naloxone **E**

### Clinical indications

- Flumazenil reverses benzodiazepine-induced sedation. **P**
- Naloxone causes partial or complete reversal of opioid sedation, including respiratory depression. **P**

### Alternative drugs or techniques

- None

### General comments

- Flumazenil has a rapid action and effects are usually seen within 1–2 min. Repeated doses may be required.
- Patients show marked variation in their sensitivity to benzodiazepines and the ability to reverse enables safer use of the sedative.
- Naloxone has an extremely high affinity for  $\mu$ -opioid receptors and can produce rapid onset of withdrawal symptoms if not carefully titrated to effect. It can be given intravenously, intramuscularly, intranasally and as an infusion. Repeated doses may be required.



## Drug for malignant hyperthermia: dantrolene

### Essential drugs

Dantrolene sodium **ENC**

### Alternative drugs

None

### Clinical indications

- Malignant hyperthermia. **P**

### General comments

- An Association Safety Guideline recommends that 12 vials are available immediately to provide an initial dose of  $2.5 \text{ mg.kg}^{-1}$ . The total recommended maximum dose is  $10 \text{ mg.kg}^{-1}$ , so a treatment may require up to 48 vials.
- The treatment of acute malignant hyperthermia will also require rapid access to ice-cold normal saline 2 l, calcium chloride 10%, sodium bicarbonate 8.4%, glucose 20%, amiodarone 300 mg and a beta-blocker.
- Each vial contains mannitol 3g.

## Local anaesthetics

### Essential drugs

Hyperbaric bupivacaine **E**

Levobupivacaine **E N**

Lidocaine **E**

### Alternative drugs

Bupivacaine

Prilocaine

Ropivacaine

### Clinical indications

- Lidocaine:
  - Rapid onset local anaesthetic agent **P**
  - Vaughan Williams Class 1b anti-arrhythmic
  - Intravenous analgesic.
  - Modifies the pressor response to laryngoscopy
  - Used in the performance of awake fiberoptic intubation
  - Used for epidural anaesthesia for emergency caesarean sections.
  
- Levobupivacaine:
  - Slow onset, long-acting local anaesthetic agent, commonly used for long-acting peripheral nerve block. **P**
  - Used for epidural anaesthesia for emergency caesarean sections.
  
- Hyperbaric bupivacaine:
  - Intrathecal spinal anaesthesia for abdominal, obstetric, urological and lower limb operations. **P**

### General comments

- Available in combination with vasoconstrictors, which increases maximum safe dose and increases duration of action.
- Lidocaine is available in a variety of strengths and formulations, which are utilised in the performance of awake fiberoptic intubation.
- Hyperbaric bupivacaine was recommended for use in anaesthesia for hip fracture surgery in the National Hip Fracture Database Anaesthesia Sprint Audit of Practice.

## Drugs used for local anaesthetic overdose: lipid emulsion treatment

### Essential drugs

Lipid emulsion (Intralipid™ 20%) **E N C**

### Alternative drugs or techniques

10% solution of lipid emulsion

30% solution of lipid emulsion

### Clinical indications

- Severe local anaesthetic toxicity with cardiovascular or neurological impairment. **P**

### General Comments

- The Association has published a [Safety Guideline](#) on the treatment of severe local anaesthetic toxicity:
  - The initial dose of 20% preparation is  $1.5\text{ml.kg}^{-1}$  over 1 minute followed by a  $15\text{ml.kg}^{-1}$  infusion.
  - Repeated doses and increase of infusion rate (as per guideline may be required), in addition to prolonged CPR.
  - Maximum cumulative dose is  $12\text{ml.kg}^{-1}$ .
- A unique agent for management of severe local anaesthetic toxicity, which can be life saving. It should, therefore, be at hand whenever higher dose local anaesthetic is being administered.

## Anti-emetics

### Essential drugs

Dexamethasone **E**

Ondansetron **E**

### Alternative drugs

Cyclizine

Domperidone

Droperidol

Granisetron

Hyoscine hydrobromide

Metoclopramide

Prochlorperazine

### Clinical indications

- Dexamethasone:
  - Prevention of postoperative nausea and vomiting (PONV).
  - Suppression of inflammatory and allergic disorders. **P**
  - Treatment of cerebral oedema. **P**
- Ondansetron:
  - The prevention and treatment of PONV.

### General Comments

- PONV is a common cause of patient dissatisfaction after surgery and may cause a delay in day case surgery discharge.
- Ondansetron can lead to the prolongation of the QT interval – caution is advised in susceptible patients.

## Vasoconstrictor sympathomimetics

### Essential drugs

Adrenaline **E N C**

Ephedrine **E**

Metaraminol **E**

Noradrenaline **E C**

Phenylephrine **E**

### Alternative drugs

Dopamine

Dobutamine

Vasopressin

### Clinical indications

- Adrenaline
  - Cardiac arrest situations as part of the Advanced Life Support algorithm. **P**
  - For inotropic support in the critically ill with circulatory failure, either by intravenous bolus or infusion. **P**
  - Anaphylaxis. **P**
  - Nebulised to decrease symptoms associated with acute upper airway obstruction, post-intubation swelling and infectious croup.
  - Prolongs the action of local anaesthetics by decreasing local blood flow.
  - Topical haemostatic agent, e.g. used for peptic ulcers during endoscopy.
- Ephedrine
  - Hypotension in obstetric anaesthesia. **P**
  - Anaesthesia-induced hypotension.
- Metaraminol
  - Anaesthesia-induced hypotension. **P**
- Noradrenaline
  - Antihypotensive agent, administered by infusion. **P**
- Phenylephrine
  - Anaesthesia-induced hypotension. **P**

## General comments

- In critical care practice, a combination of noradrenaline and dobutamine is often preferred to adrenaline alone, giving greater control over heart rate and blood pressure.
- Ephedrine is a synthetic sympathomimetic with  $\alpha$ -agonist and  $\beta$ -agonist properties, increasing heart rate, force of contraction and blood pressure. Exhibits tachyphylaxis as a result of its indirect effects, as stores of noradrenaline (norepinephrine) at nerve endings are depleted.
- Ephedrine is commonly used to treat hypotension in obstetric anaesthesia as it may maintain uterine and placental blood flow more efficiently than some other sympathomimetics. If in short supply, it should be reserved for this indication.
- Phenylephrine is slightly safer to use in the presence of monoamine oxidase inhibitors than indirectly acting sympathomimetics such as ephedrine and metaraminol, although caution should still be taken.
- Phenylephrine is most frequently used as a bolus or infusion in obstetric theatre after spinal anaesthesia and to treat epidural-related postoperative hypotension. Can be safely given as a short-term peripheral intravenous infusion.

## Magnesium sulfate

Essential drug

Magnesium sulfate **E N**

Alternative drug

None

Clinical indications

- Seizure prevention and control when caused by pre-eclampsia or eclampsia. **P**
- Severe tetanus. **P**
- Acute severe asthma. **P**
- Magnesium sulfate is valued as an adjunctive agent during anaesthesia. It is thought to improve analgesia, relaxation and to protect against cardiac arrhythmia.

## Appendix 1 – Summary

Drug name	Essential	Alternatives	Necessary	Critical
Adrenaline	✓		✓	✓
Air & oxygen	✓		✓	✓
Atracurium	✓	✓		
Atropine	✓	✓		
Dantrolene	✓		✓	✓
Dexamethasone	✓	✓		
Ephedrine	✓	✓		
Fentanyl	✓	✓		✓
Flumazenil	✓			
Glycopyrronium	✓	✓		
Hyperbaric bupivacaine	✓	✓	✓	
Ketamine	✓	✓	✓	✓
Levobupivacaine	✓	✓	✓	
Lidocaine	✓	✓		
Lipid emulsion	✓		✓	✓
Magnesium sulfate	✓		✓	
Metaraminol	✓	✓		
Midazolam	✓	✓		
Morphine	✓	✓		✓
Naloxone	✓			
Neostigmine	✓	✓		
Noradrenaline	✓	✓		✓
Ondansetron	✓	✓		
Paracetamol	✓	✓		
Phenylephrine	✓	✓		
Propofol	✓	✓		✓
Rocuronium	✓	✓		✓
Sevoflurane	✓	✓		
Sugammadex	✓	✓		
Suxamethonium	✓	✓		✓



## Appendix 2 – Licensed and unlicensed drugs

Once a medicine has met the appropriate regulatory standards, the Medicines and Healthcare products Regulatory Agency (MHRA) provides marketing authorisation or a product licence for use in the UK. A licensed medicine is assessed for efficacy, safety, quality, presence of accompanying information and labelling.

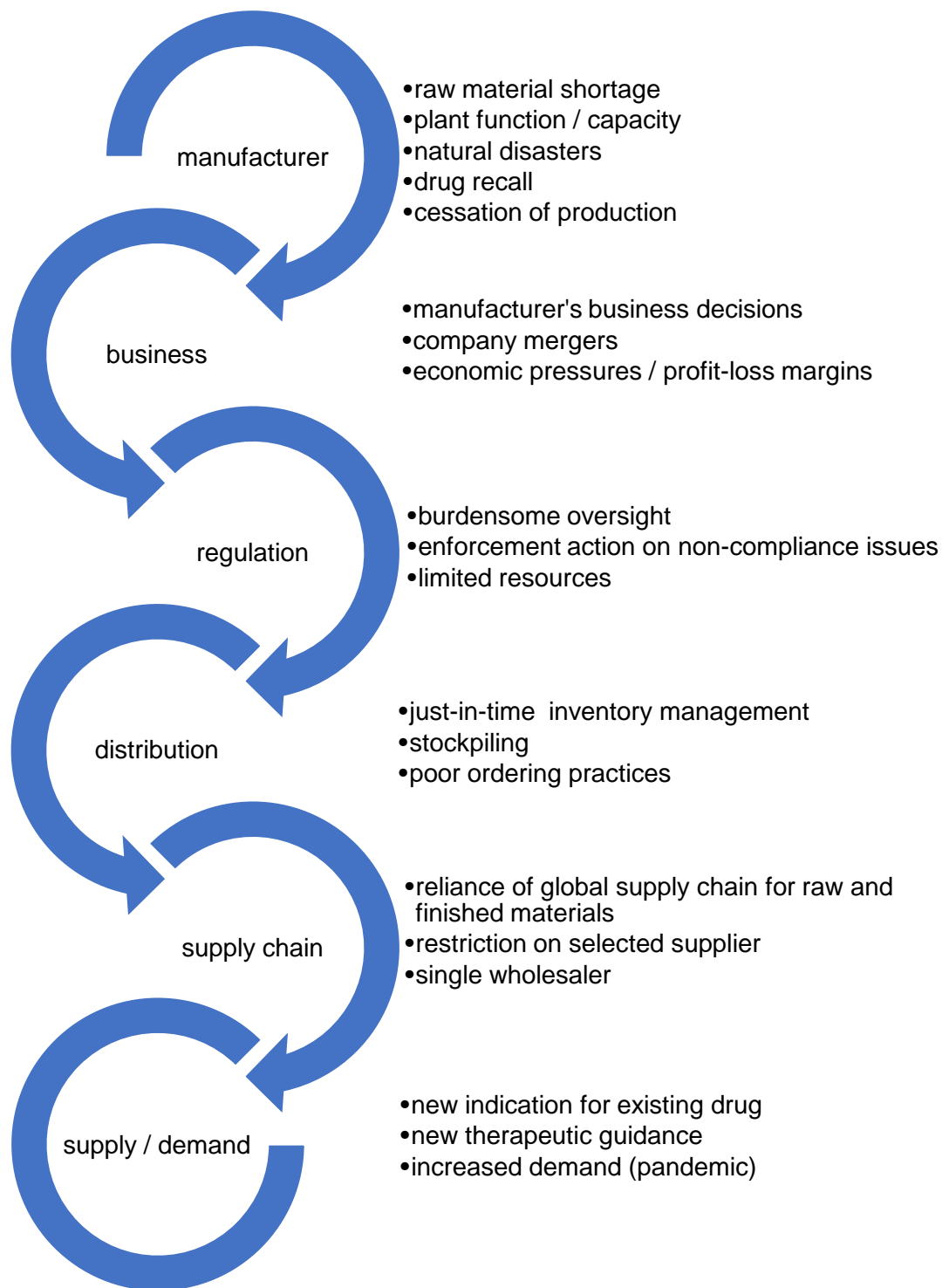
Using a drug for an indication which is not included in the summary of product characteristics is called off-label use.

Using a drug that has not received a product license from the MHRA is considered unlicensed use. The prescriber may assume a greater responsibility for prescribing an unlicensed drug than when prescribing licensed medicines.

Marketing Authorisation Holders (MAH) are required under Health Services Product Regulations to report any drug shortage to the Department of Health and Social Care (DHSC) as soon as possible and preferably with 6 months' notice of recognising a threat to the supply chain.

Under specific circumstances, which may include drug shortage, the MHRA may permit the import of unlicensed medicines for use in the UK.

## Appendix 3 – Drug manufacture to delivery pathway – potential steps leading to shortage



## Appendix 4 – An audit tool for departments – drug shortages

<p>Why do this audit</p>	<p>Drug shortages may adversely affect the safety and quality of care delivered to patients. Injectable anaesthetic drugs are one of the most common group of drugs to suffer shortage of supply. Many reasons might account for these shortages. A frequent reason is that most anaesthetic drugs are generic and no longer on patent, providing the manufacturer with minimal profit margin. Drug production can then become an unviable business model.</p> <p>In recent years, anaesthetists in the UK and Ireland have experienced shortages of induction drugs, local anaesthetics, muscle relaxants, opioid analgesics and antibiotics. Being aware of impending shortages facilitates preparation of contingency plans to ensure safe drug stock levels for primary indication procedures.</p>
<p>Best practice</p>	<p>The Department of Health and Social Care (DHSC) states: “Marketing Authorisation Holders (MAH) are expected to be fully accountable for their supply chain to the UK market and are required to understand the potential impact on UK patients should supplies of their products become unavailable”.</p> <p>In the UK the responsibility for the security of the supply chain lies with the DHSC.</p> <p>The Association of Anaesthetists has defined a National Essential Anaesthetic Drug List (NEADL) which outlines best practice in managing anaesthetic drug shortages.</p>
<p>Suggested indicators</p>	<ul style="list-style-type: none"> <li>• Monthly and ad hoc reports from pharmacy procurement leads</li> <li>• Monthly and ad hoc reports from medication safety officers</li> <li>• Link to Specialist Pharmacy Services to review drug shortage lists</li> <li>• Senior staff receive reports on theatre drug reconciliation</li> <li>• Departments agree with pharmacy the level of stock which triggers a shortage report to the DHSC</li> </ul>
<p>Proposed standards</p>	<ul style="list-style-type: none"> <li>• 100% of anaesthetic drug shortages are notified to the theatre liaison pharmacists within the 6-month period stipulated in the DHSC mandate.</li> <li>• Departments of anaesthesia have a pharmacy liaison anaesthetist who is in receipt of details of potential drug shortages</li> <li>• Departments of anaesthesia receive regular and timely updates on drug supply from the theatre liaison pharmacist</li> <li>• Strategies outlined in NEADL are used to inform on local contingency planning</li> </ul>
<p>Data to be collected</p>	<p>See indicators above</p>
<p>Reasons for failure to meet the standard</p>	<ul style="list-style-type: none"> <li>• Failure to appreciate the risk to patient care of anaesthetic drug shortage</li> <li>• Failure to agree local communication plan</li> </ul>

## Appendix 5 – Standard Operating Procedures for managing drug shortages (to be adapted locally)

- The Trust's chief pharmacist should inform the theatre liaison pharmacist of any shortage of drugs used in anaesthetic practice
- The theatre liaison pharmacist should inform the department of anaesthesia's head of service and clinical director of any drug noted to be in short supply as soon as this information is known.
- The head of service and clinical director should ensure all anaesthetists and anaesthetic assistants (nurses and operating department assistants) are informed of the potential drug shortage.
- The senior staff clinical advisory committee should agree the primary clinical indication for the drug in shortage.
- The head of service and clinical director should put measures in place to ensure that the drug in shortage is retained for its primary indication before local stock levels become critical to service delivery (this level should be ascertained in collaboration with the liaison pharmacist).
- The senior staff clinical advisory committee should agree alternative drugs to be used for secondary indications.
- Alternative drug choices should be shared with all anaesthetists and anaesthetic assistants.
- Once the shortage issue has resolved, this information should be communicated and any restrictions on use should be rescinded immediately.

Guidance for marketing authority holders is outlined by the [Department of Health and Social Care](#).