Shortage of Diamorphine 5mg and 10mg injection

Update: 4th June 2020

Description of product affected

- Diamorphine is licensed for the treatment of severe pain associated with surgical procedures, myocardial infarction or pain in the terminally ill and for the relief of dyspnoea in acute pulmonary oedema.¹
- It is also used for labour pain in obstetrics and in women having a Caesarean Section. ²
- In addition, a small number of people in the UK may be receiving diamorphine for the management of opioid addiction.³
- Please note that in Cambridgeshire and Peterborough, morphine has superseded diamorphine as the end of life choice of injectable opioid in adults in primary and secondary care.
- In Cambridgeshire and Peterborough, diamorphine is still the end of life choice of injectable opioid in paediatric patients and in these instances, a discussion with the individual patient’s specialist involved in their care is required for appropriate alternative agents.

Background

- Accord have ongoing issues at their manufacturing plant in Europe and have been unable to support the UK with stock of diamorphine 5mg and 10mg injection, since summer 2019, this is not expected to resolve until summer 2020.
- Wockhardt, the only other UK supplier, have 5mg and 10mg strengths currently available with limited supplies.
- The indication from both supplies of diamorphine 5mg and 10mg strengths is that the supply will remain unpredictable for the foreseeable future.
- Both primary and secondary care will have to prepare for a complete out of stock of diamorphine 5mg and 10mg injection. Other strengths of diamorphine injection are not affected but there is not enough stock of these to support an increase in demand.

Alternative agents and management options

- The UK is the only country that uses diamorphine for medicinal analgesic purposes.
- Diamorphine is metabolised to morphine and in terms of analgesic efficacy and effect on mood, it has no clinical advantages over morphine by oral or subcutaneous/intramuscular routes.⁴
- In addition, morphine injection is less costly than diamorphine and does not have to be reconstituted.
- NICE guidance on the effective prescribing of strong opioids for pain in
palliative care recommends initiating subcutaneous opioids with the lowest acquisition cost.\textsuperscript{5}

- However, diamorphine is much more water soluble than morphine, and may be preferred to morphine in the very few patients where high dose injections are needed, as smaller volumes can be used.\textsuperscript{4}

- NICE however do support the preferential use of intrathecal or epidural diamorphine over morphine for women after a Caesarean section.\textsuperscript{2} They also recommend that for women who have had intrathecal opioids, there should be a minimum hourly observation of respiratory rate, sedation and pain scores for at least 12 hours for diamorphine and 24 hours for morphine.

\textbf{Action}

- \textbf{Sufficient supplies of morphine sulfate 10mg/ml injection are available from Ethypharm and Hameln to support this supply disruption. Please note that in Cambridgeshire and Peterborough, morphine has superseded diamorphine as the end of life choice of injectable opioid in adults in primary and secondary care.}

- These versions are available for epidural use.

- The Hameln presentation is preservative-free.

- Clinicians will need to decide whether morphine or another opioid is most appropriate for each patient. Care is needed when switching from one opioid analgesic to another to ensure equipotent dosage.\textsuperscript{6}

- According to BNF 3mg of diamorphine given parenterally is approximately equivalent to 5mg of morphine given parenterally.\textsuperscript{7} Therefore to convert diamorphine to morphine multiply the usual dose of diamorphine by 1.7 to give an approximately equivalent dose of morphine. However, it is strongly recommended that any dose conversion should be carried out after consultation with the specialist involved.

<table>
<thead>
<tr>
<th>Dose of parenteral diamorphine</th>
<th>Approximate equivalent dose of parenteral morphine</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.5mg</td>
<td>4mg</td>
</tr>
<tr>
<td>5mg</td>
<td>8 mg</td>
</tr>
<tr>
<td>10mg</td>
<td>17mg</td>
</tr>
<tr>
<td>15mg</td>
<td>25mg</td>
</tr>
<tr>
<td>20mg</td>
<td>35mg</td>
</tr>
<tr>
<td>30mg</td>
<td>50mg</td>
</tr>
</tbody>
</table>

- Patients should be carefully monitored after any drug switch and dose titration may be required.

- When converting from diamorphine to other subcutaneous drugs, consideration will also need to be given to drug compatibility in the syringe driver and the total volume of infused drugs.\textsuperscript{6}

- When converting to alternatives in regional anaesthesia, consideration will need to be given to use of preservative-free opioids.\textsuperscript{8}

- As morphine is not as soluble as diamorphine and the maximum concentration available is 30mg/mL, this may be an issue for patients requiring high doses of
subcutaneous morphine, particularly bolus doses for breakthrough pain where the volume given should not exceed 2mL. If volume is an issue, advice should be sought from the palliative care team.9

- Midwives administer diamorphine under Midwives Exemptions from the Medicines Act. This exemption also allows them to administer morphine.10 If stock of diamorphine run out, protocols need to be rewritten and midwives trained on administering morphine instead of diamorphine, as well as morphine added to Midwives Exemptions list on e-prescribing systems.

- NICE do recommend a different duration of monitoring for morphine (24 hours) than diamorphine (12 hours) after Caesarean delivery and local guidance may need to be reviewed. In reality it has been shown that the incidence of clinically significant respiratory depression seen with epidural morphine after caesarean delivery is very low - in one systematic review it was estimated to occur in between 1.08 and 1.63 cases per 10,000 women.11

- Patients in drug addiction treatment programmes may experience difficulties switching to alternatives12 and the community drug and alcohol team should be contacted for advice.

- Please refer to local guidance, the BNF or the Palliative care formulary for information on dose conversion to other opioids; and contact relevant specialist teams for advice on management of individual cases.

References

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7. BNF. Prescribing in palliative care, accessed online, 15 May 2019: https://www.medicinescomplete.com/#/content/bnf/PHP107735?hspl=palliative&hspl=care
8. Wockhardt UK Ltd. Morphine Sulfate 10mg/ml Injection BP: SPC, date of revision of text, 14/12/2018: https://www.medicines.org.uk/emc/product/2244/smpc
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