19th Expert Committee on The Selection and Use of Essential Medicines
April 8-12 2013
Expert peer review on application for HYDROMORPHONE HYDROCHLORIDE

1. Assessment of efficacy
   a. Have all relevant studies on efficacy been included
      Yes
   
   b. Summarize the data on efficacy, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)

   Table of Equianalgesic Potency Conversion
   Equianalgesic Dose (in mg)

<table>
<thead>
<tr>
<th>Opiate Agonist or Partial Agonist</th>
<th>Oral (mg)</th>
<th>Parenteral (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine sulfate</td>
<td>40 - 60</td>
<td>10</td>
</tr>
<tr>
<td>Hydromorphone hydrochloride</td>
<td>6.5 - 7.5</td>
<td>1.3 - 2</td>
</tr>
<tr>
<td>Oxymorphone hydrochloride</td>
<td>6.6</td>
<td>1 - 1.1</td>
</tr>
<tr>
<td>Levorphanol tartrate</td>
<td>4</td>
<td>2 - 2.3</td>
</tr>
<tr>
<td>Meperidine hydrochloride</td>
<td>300 - 400</td>
<td>75 - 100</td>
</tr>
<tr>
<td>Methadone hydrochloride</td>
<td>10 - 20</td>
<td>10</td>
</tr>
<tr>
<td>Nalbuphine hydrochloride</td>
<td></td>
<td>10 - 12</td>
</tr>
<tr>
<td>Butophanol tartrate</td>
<td></td>
<td>1.5 - 2.5</td>
</tr>
</tbody>
</table>

   Approximate Equianalgesic Doses for Conversion from Oral Opiate Agonists to Extended Release Hydromorphone Hydrochloride

<table>
<thead>
<tr>
<th>Opiate Agonist</th>
<th>Equianalgesic Oral Dosage (in mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydromorphone hydrochloride</td>
<td>12</td>
</tr>
<tr>
<td>Codeine phosphate</td>
<td>200</td>
</tr>
<tr>
<td>Hydrocodone bitartrate</td>
<td>30</td>
</tr>
<tr>
<td>Methadone hydrochloride</td>
<td>20</td>
</tr>
<tr>
<td>Morphine sulfate</td>
<td>60</td>
</tr>
<tr>
<td>Oxycodone hydrochloride</td>
<td>30</td>
</tr>
<tr>
<td>Oxymorphone hydrochloride</td>
<td>20</td>
</tr>
</tbody>
</table>

   Therapy with extended release hydromorphone hydrochloride should be discontinued by reducing the dose by 25-50% every 2-3 days until a dose of 8mg is reached
   
   c. Please provide any additional relevant information with reference

2. Assessment of safety
   a. Have all relevant studies on safety been included
      Yes
b. Summarize the data on safety, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)

ADR of hydromorphone hydrochloride as nausea, vomiting, constipation and euphoria may be less marked than with morphine hydrochloride

Risk Evaluation and Mitigation Strategy: US FDA has approved a Risk Evaluation and Mitigation Strategy (REMS) for hydromorphone extended release. The REMS program consists of the medication guide that must be dispensed with every prescription for hydromorphone hydrochloride extended release tablets. Clinicians who prescribe the extended release preparation must complete a training module regarding appropriate and safe use of the drug.

c. Please provide any additional relevant information with reference

3. Assessment of cost and availability
a. Have all relevant data on safety provided
  Yes

b. Summarize the data on cost and cost effectiveness, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)

  In comparison with morphine hydrochloride, the cost of hydromorphone is higher.

  Many hydromorphone products are available under trade names. Generic products are not available

c. Please provide any additional relevant information with reference

d. Is the product available in several low and middle income countries?

  Imported product to low and middle income countries from foreign manufactures/companies

4. Assessment of public health need
a. Please provide the public health need for this product (1-2 sentences)

  Hydromorphone hydrochloride as the opioid products (tablet and injectable) are drugs needed for public health to treat intense pain and pain not responsive to other analgesics in: post-traumatic patients, cancer patients, surgery ...

b. Do guidelines (especially WHO guidelines) recommend this product? If yes, which ones? List 1 or 2 international preferable

  No

5. Are there special requirements for use or training needed for safe/effective use?
If yes, please provide details in 1-2 sentences

Due to narcotic addition is a current social evil in many countries, it is necessary:

  1. To train the health staff to implement the Guidelines/Treatment Regimen relating hydromorphone hydrochloride and other narcotic safe/effective use for medical purposes
  2. To promulgate document and training materials for safe/effective use hydromorphone and opioid pharmaceutical products and narcotic products
3. To conduct control/inspection activities relating narcotic products
4. To supervise the implementation of Narcotic Law and regulatory documents relating narcotics

6. Is the proposed product registered by a stringent regulatory authority?
   Yes
   National Medicines Administration Authority and Narcotic Control Authority

7. Any other comments

8. What is your recommendation to the committee (please provide the rationale)
   Hydromorphone could be listed in WHO EML (complementary list) due to the higher efficacy and lesser ADR than morphine but high cost and unavailable generic products in low and middle income country.
   Measures for safe and rational use and for control of misuse and abuse of hydromorphone products should be taken