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## **NOTICE: RECOMMENDED THERAPEUTIC ALTERNATIVES FOR CLONIDINE TABLETS**

The newly released Paediatric Hospital Level Standard Treatment Guidelines (STGs) and Essential Medicines List (EML) 2023, 5<sup>th</sup> edition, has included clonidine tablets for various indications.

Clonidine was also previously registered in South Africa by Boehringer Ingelheim however the company has since discontinued the product in year 2000. The current sole registered supplier of clonidine 0.25mg tablets in South Africa, Aspen Pharmacare, is currently experiencing supply challenges. It is however expected that this product will become available at the end of September 2023.

The following therapeutic alternative recommendations are proposed until stock becomes available:

| <b>Indication:<br/>Hospital Level<br/>(Paediatrics)</b>                           | <b>Current recommendation in STGs and EML</b>  | <b>Therapeutic alternative</b>   |
|---|--|--|
| <b>14.10 Tic Disorders</b>  | <ul style="list-style-type: none"> <li>• Risperidone, oral.               <ul style="list-style-type: none"> <li>○ Starting dose: 0.25 mg/day (&lt; 20 kg) and 0.5 mg/day (&gt; 20 kg).</li> <li>○ Recommended average dosage: 1 mg/day.</li> <li>○ Dosage range: 0.25–3 mg.</li> </ul> </li> </ul> <p>If risperidone cannot be tolerated due to side effects:</p> <ul style="list-style-type: none"> <li>• Clonidine, oral, daily.               <ul style="list-style-type: none"> <li>○ Starting dose at 25 mcg and titrate gradually to 3–5 mcg/kg.</li> <li>○ Divide doses larger than 0.1mg/kg/day into 2 doses (morning and evening)</li> </ul> </li> </ul> | <ul style="list-style-type: none"> <li>• Risperidone, oral.               <ul style="list-style-type: none"> <li>○ Starting dose: 0.25 mg/day (&lt; 20 kg) and 0.5 mg/day (&gt; 20 kg).</li> <li>○ Recommended average dosage: 1 mg/day.</li> <li>○ Dosage range: 0.25–3 mg.</li> </ul> </li> </ul> <p>If risperidone cannot be tolerated due to side effects:</p> <ul style="list-style-type: none"> <li>» Discuss alternative with a specialist</li> </ul>   |
| <b>21.1.1.1 Acute pain<br/>Children with severe neurological impairment (SNI)</b> | <p>Patients with SNI may suffer from neuro-irritability, which can be associated with pain. In a child with recurrent pain behaviour episodes (3 or more prolonged episodes per week or a monthly cycle of frequent episodes for 1–2 weeks each month), initiate:</p> <ul style="list-style-type: none"> <li>• Clonidine, oral, 1–3 mcg/kg 6–8 hourly.</li> <li>• Amitriptyline, oral, 0.5–1 mg/kg 8 hourly.               <ul style="list-style-type: none"> <li>○ Maximum: 25 mg/dose.</li> </ul> </li> </ul>  | <p>Patients with SNI may suffer from neuro-irritability, which can be associated with pain. In a child with recurrent pain behaviour episodes (3 or more prolonged episodes per week or a monthly cycle of frequent episodes for 1–2 weeks each month), initiate:</p> <ul style="list-style-type: none"> <li>• Amitriptyline, oral, 0.5–1 mg/kg 8 hourly.               <ul style="list-style-type: none"> <li>○ Maximum: 25 mg/dose.</li> </ul> </li> </ul>   |
| <b>22.1.2.1 General anaesthesia preparation</b>                                   | <p><b>Premedication</b><br/><u>Midazolam:</u></p> <ul style="list-style-type: none"> <li>• This is a commonly used premedication agent that is generally well tolerated.</li> <li>• Can be safely used in most children, but caution is advised in children with:               <ul style="list-style-type: none"> <li>○ Risk factors for paradoxical excitation, e.g., children under 3 years,</li> <li>○ Attention Deficit Hyperactivity Disorder (ADHD), Autism Spectrum Disorder (ASD).</li> </ul> </li> </ul>   | <p><b>Premedication</b><br/><u>Midazolam:</u></p> <ul style="list-style-type: none"> <li>• This is a commonly used premedication agent that is generally well tolerated.</li> <li>• Can be safely used in most children, but caution is advised in children with:               <ul style="list-style-type: none"> <li>○ Risk factors for paradoxical excitation, e.g., children under 3 years,</li> <li>○ Attention Deficit Hyperactivity Disorder (ADHD), Autism Spectrum Disorder (ASD).</li> </ul> </li> </ul> |

| Indication:<br>Hospital<br>Level<br>(Paediatrics) | Current recommendation in STGs<br>and EML  | Therapeutic alternative   |                               |       |       |      |                               |           |      |                             |       |              |           |       |             |                  |     |           |      |            |       |          |      |            |    |              |           |    |               |           |    |
|---|--|---|-------------------------------|-------|-------|------|-------------------------------|-----------|------|-----------------------------|-------|--------------|-----------|-------|-------------|------------------|-----|-----------|------|------------|-------|----------|------|------------|----|--------------|-----------|----|---------------|-----------|----|
|   | <ul style="list-style-type: none"> <li>○ Avoid in patients with obstructive sleep apnoea (OSA), as can cause respiratory depression.</li> </ul> <p><b>OR</b><br/><u>Clonidine:</u></p> <ul style="list-style-type: none"> <li>• Preferred agent in children with:                             <ul style="list-style-type: none"> <li>○ Behavioural disorders such as ADHD, and children with ASD.</li> <li>○ Obstructive sleep apnoea.</li> </ul> </li> <li>• Does not cause respiratory depression.</li> <li>• Can cause bradycardia, which is clinically insignificant.</li> <li>• Provides analgesia in addition to anxiolysis and sedation.</li> <li>• Is tasteless and well tolerated. Even smaller children will swallow the tablets, but they can also be crushed and added to juice or water.</li> </ul> <p><b>Alternative in certain circumstance</b><br/><u>Ketamine:</u></p> <ul style="list-style-type: none"> <li>• Is cardio stable and does not cause respiratory depression.</li> <li>• Provides analgesia in addition to anxiolysis and sedation.</li> <li>• In exceptional circumstances, can be used IM, e.g. when dealing with a combative child who is unable to understand what is needed and will not accept other routes of administration.</li> </ul>   | <ul style="list-style-type: none"> <li>○ Avoid in patients with obstructive sleep apnoea (OSA), as can cause respiratory depression.</li> </ul> <p><b>OR</b><br/><b>Alternative in certain circumstance</b><br/><u>Ketamine:</u></p> <ul style="list-style-type: none"> <li>• Is cardio stable and does not cause respiratory depression.</li> <li>• Provides analgesia in addition to anxiolysis and sedation.</li> <li>• In exceptional circumstances, can be used IM, e.g. when dealing with a combative child who is unable to understand what is needed and will not accept other routes of administration.</li> </ul> |                               |       |       |      |                               |           |      |                             |       |              |           |       |             |                  |     |           |      |            |       |          |      |            |    |              |           |    |               |           |    |
|   | <table border="1"> <thead> <tr> <th data-bbox="368 1050 539 1088">Agent</th> <th data-bbox="539 1050 746 1088">Route</th> <th data-bbox="746 1050 1123 1088">Dose</th> <th data-bbox="1123 1050 1394 1088">Time to peak effect (minutes)</th> </tr> </thead> <tbody> <tr> <td data-bbox="368 1088 539 1167" rowspan="3">Midazolam</td> <td data-bbox="539 1088 746 1117">Oral</td> <td data-bbox="746 1088 1123 1117">0.25–0.5 mg/kg (max. 15 mg)</td> <td data-bbox="1123 1088 1394 1117">10–30</td> </tr> <tr> <td data-bbox="539 1117 746 1146">Intranasal**</td> <td data-bbox="746 1117 1123 1146">0.3 mg/kg</td> <td data-bbox="1123 1117 1394 1146">10–15</td> </tr> <tr> <td data-bbox="539 1146 746 1167">Intravenous</td> <td data-bbox="746 1146 1123 1167">0.025–0.1 mg/kg*</td> <td data-bbox="1123 1146 1394 1167">3–5</td> </tr> <tr> <td data-bbox="368 1167 539 1187">Clonidine</td> <td data-bbox="539 1167 746 1187">Oral</td> <td data-bbox="746 1167 1123 1187">3–5 mcg/kg</td> <td data-bbox="1123 1167 1394 1187">60–90</td> </tr> <tr> <td data-bbox="368 1187 539 1265" rowspan="3">Ketamine</td> <td data-bbox="539 1187 746 1216">Oral</td> <td data-bbox="746 1187 1123 1216">6–10 mg/kg</td> <td data-bbox="1123 1187 1394 1216">30</td> </tr> <tr> <td data-bbox="539 1216 746 1236">Intranasal**</td> <td data-bbox="746 1216 1123 1236">1–5 mg/kg</td> <td data-bbox="1123 1216 1394 1236">20</td> </tr> <tr> <td data-bbox="539 1236 746 1265">Intramuscular</td> <td data-bbox="746 1236 1123 1265">2–4 mg/kg</td> <td data-bbox="1123 1236 1394 1265">20</td> </tr> </tbody> </table> <p>*Titrate to effect. Repeat dose at 5-minute intervals until desired level of sedation is achieved.</p> |   |                               | Agent | Route | Dose | Time to peak effect (minutes) | Midazolam | Oral | 0.25–0.5 mg/kg (max. 15 mg) | 10–30 | Intranasal** | 0.3 mg/kg | 10–15 | Intravenous | 0.025–0.1 mg/kg* | 3–5 | Clonidine | Oral | 3–5 mcg/kg | 60–90 | Ketamine | Oral | 6–10 mg/kg | 30 | Intranasal** | 1–5 mg/kg | 20 | Intramuscular | 2–4 mg/kg | 20 |
| Agent   | Route  | Dose  | Time to peak effect (minutes) |       |       |      |                               |           |      |                             |       |              |           |       |             |                  |     |           |      |            |       |          |      |            |    |              |           |    |               |           |    |
| Midazolam   | Oral   | 0.25–0.5 mg/kg (max. 15 mg)   | 10–30                         |       |       |      |                               |           |      |                             |       |              |           |       |             |                  |     |           |      |            |       |          |      |            |    |              |           |    |               |           |    |
|   | Intranasal**   | 0.3 mg/kg   | 10–15                         |       |       |      |                               |           |      |                             |       |              |           |       |             |                  |     |           |      |            |       |          |      |            |    |              |           |    |               |           |    |
|   | Intravenous  | 0.025–0.1 mg/kg*  | 3–5                           |       |       |      |                               |           |      |                             |       |              |           |       |             |                  |     |           |      |            |       |          |      |            |    |              |           |    |               |           |    |
| Clonidine   | Oral   | 3–5 mcg/kg  | 60–90                         |       |       |      |                               |           |      |                             |       |              |           |       |             |                  |     |           |      |            |       |          |      |            |    |              |           |    |               |           |    |
| Ketamine  | Oral   | 6–10 mg/kg  | 30                            |       |       |      |                               |           |      |                             |       |              |           |       |             |                  |     |           |      |            |       |          |      |            |    |              |           |    |               |           |    |
|   | Intranasal**   | 1–5 mg/kg   | 20                            |       |       |      |                               |           |      |                             |       |              |           |       |             |                  |     |           |      |            |       |          |      |            |    |              |           |    |               |           |    |
|   | Intramuscular  | 2–4 mg/kg   | 20                            |       |       |      |                               |           |      |                             |       |              |           |       |             |                  |     |           |      |            |       |          |      |            |    |              |           |    |               |           |    |

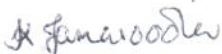
**Note:**

» The National Department of Health will advise when the supply of clonidine tablets is resumed.

**Circular dissemination**

Provinces and Healthcare Facilities are requested to distribute and communicate this information in consultation with the Pharmaceutical and Therapeutics Committees and all other relevant stakeholders.

Kind regards



**MS K JAMALOODIEN**  
**CHIEF DIRECTOR: SECTOR-WIDE PROCUREMENT**  
 DATE: 14/18/2023