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| <b>I.7</b>  | <b>Mifepristone-misoprostol – intrauterine fetal demise (IUFD) – EML</b>   |
| <b>Draft recommendation</b>   | <input checked="" type="checkbox"/> Recommended<br><input type="checkbox"/> Not recommended<br>Justification:<br>This regimen is in line with WHO recommendations. According to limited evidence it is effective and safe with minimal intervention at a reasonable cost.  |
| Does the proposed medicine address a relevant public health need?   | <input checked="" type="checkbox"/> Yes<br><input type="checkbox"/> No<br><input type="checkbox"/> Not applicable<br>Comments:<br>About 1% of all pregnancies are complicated by IUFD. Approximately 50% occur between 20 and 27 weeks of gestation (primarily from 20 to 23 weeks). IUFD has been associated with multiple and severe (potentially deadly) complications.<br>Additionally, currently there are no specific medicines in the EML for medical management of IUFD.   |
| Does adequate evidence exist for the efficacy/effectiveness of the medicine for the proposed indication?<br><br>(this may be evidence included in the application, and/or additional evidence identified during the review process) | <input checked="" type="checkbox"/> Yes<br><input type="checkbox"/> No<br><input type="checkbox"/> Not applicable<br>Comments:<br>Evidence from a systematic review (Cleeve, 2019) showed that women treated with this regimen had slightly higher rates of complete expulsion within 24 hours and a shorter expulsion time than women treated with misoprostol alone. Unfortunately, this outcome was only evaluated in one trial Chaudhuri, 2015. Authors graded the evidence as “very low certainty”.<br>Indirect evidence from the management of abortion should be considered. In this case the clinical effectiveness of the regimen was as high as 95%. |
| Does adequate evidence exist for the safety/harms associated with the proposed medicine?<br><br>(this may be evidence included in the application, and/or additional evidence identified during the review process)                 | <input checked="" type="checkbox"/> Yes<br><input type="checkbox"/> No<br><input type="checkbox"/> Not applicable<br>Comments:<br>Both drugs (in combination and individually) have been extensively used in the management of abortion. They have proved to be safe and have minimal harms associated (Minimal indirectness).<br>For the combination the most reported side effects include nausea, weakness, fever/chills, vomiting, headache, diarrhea, and dizziness.<br>Uterine rupture is potential side effect, but it is extremely rare (even in women with previous uterine incision)   |

24<sup>th</sup> WHO Expert Committee on Selection and Use of Essential Medicines  
Expert review

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| <p>Are there any adverse effects of concern, or that may require special monitoring?</p>  | <p><input checked="" type="checkbox"/> Yes</p> <p><input type="checkbox"/> No</p> <p><input type="checkbox"/> Not applicable</p> <p>Comments:</p> <p>Even when adverse events are rare there is potential for them to be severe such as uterine rupture, infection, and clinically significant bleeding.</p>  |
| <p>Are there any special requirements for the safe, effective and appropriate use of the medicines?</p> <p>(e.g. laboratory diagnostic and/or monitoring tests, specialized training for health providers, etc)</p> | <p><input checked="" type="checkbox"/> Yes</p> <p><input type="checkbox"/> No</p> <p><input type="checkbox"/> Not applicable</p> <p>Comments:</p> <p>Women must be monitored until expulsion is completed (This can be done by non-physician health care providers). These recommendations are extrapolated from the management of abortion.</p>  |
| <p>Are there any issues regarding cost, cost-effectiveness, affordability and/or access for the medicine in different settings?</p>   | <p><input type="checkbox"/> Yes</p> <p><input checked="" type="checkbox"/> No</p> <p><input type="checkbox"/> Not applicable</p> <p>Comments:</p> <p>Mifepristone, and misoprostol, either individually or as co-packed products are becoming more available. In some areas access to Mifepristone is limited.</p> <p>Where these medications are available price seems to be relative accessible.</p>  |
| <p>Are there any issues regarding the registration of the medicine by national regulatory authorities?</p> <p>(e.g. accelerated approval, lack of regulatory approval, off-label indication)</p>                    | <p><input type="checkbox"/> Yes</p> <p><input checked="" type="checkbox"/> No</p> <p><input type="checkbox"/> Not applicable</p> <p>Comments:</p> <p>Currently, mifepristone is registered in about 60 countries, while misoprostol is register in 110 countries.</p>   |
| <p>Is the proposed medicine recommended for use in a current WHO guideline?</p> <p>(refer to: <a href="https://www.who.int/publications/who-guidelines">https://www.who.int/publications/who-guidelines</a>)</p>    | <p><input checked="" type="checkbox"/> Yes</p> <p><input type="checkbox"/> No</p> <p><input type="checkbox"/> Not applicable</p> <p>Comments:</p> <p>World Health Organization. Abortion care guideline. 2022.</p> <p>Additionally, this approach is recommended by multiple international organizations:</p> <ul style="list-style-type: none"> <li>• United States Society of Family Planning</li> <li>• American College of Obstetricians and Gynecologists (ACOG)</li> <li>• U.S. Preventive Services Task Force (USPSTF)</li> <li>• Royal College of Obstetricians and Gynecologists (RCOG)</li> </ul> |