Peer Review Report #1

[Application for the levonorgestrel-releasing intrauterine system (LNG-IUS)]

(1) Does the application adequately address the issue of the public health need for the medicine?

Yes ☒ No ☐

Please provide brief details:
Unmet need for contraception remains high in many settings. It is highest among the most vulnerable in society including adolescents, the poor, those living in rural areas and urban slums, people living with HIV, and internally displaced people. In 2012, an estimated 222 million women had an unmet need for contraception. Long acting reversible contraception (LARC) including LNG-IUS has great potential in reducing these pregnancies as they are highly effective and do not rely a great deal on compliance and correct use.

(2) Have all important studies that you are aware of been included in the application?

Yes ☒ No ☐

Please provide brief comments on any relevant studies that have not been included:

(3) Does the application provide adequate evidence of efficacy/effectiveness of the medicine for the proposed use?

Yes ☒ No ☐

Briefly summarise the reported outcomes (e.g. clinical, surrogate, other) and comment, where possible, on the magnitude of clinical benefit associated with use of the medicine:
Information was identified and extracted from 139 studies. One-year Pearl Indices reported for short-acting user-dependent hormonal methods were generally less than 2.5. Gross life-table rates for long-acting hormonal methods (implants and the levonorgestrel releasing intrauterine system [LNG-IUS]) generally ranged between 0–0.6 per 100 at one year, but wider ranges (0.1–1.5 per 100) were observed for the copper intrauterine devices (0.1–1.4 per 100 for Cu- IUDs with surface area 300 mm2 and 0.6–1.5 per 100 for those with surface area less than 300 mm2).

(4) Is there evidence of efficacy in diverse settings and/or populations?

Yes ☒ No ☐

Please provide brief details:
139 studies done in different settings and/or populations. But the settings of these studies have not been specified in the application.

(5) **Has the application adequately considered the safety and adverse effects of the medicine? Are there any adverse effects of concern, or that may require special monitoring?**

   - Yes [ ]
   - No [x]

Please provide brief details:

**The application reported that there is Good** quality evidence suggests that LNG IUS is safe and potentially beneficial for woman with heavy or prolonged bleeding. There is no summary of the evidence or text summary of the included table.

**ADDITIONAL CONSIDERATIONS:**

(6) **Are there special requirements or training needed for the safe, effective and/or appropriate use of the medicine?**

   - Yes [x]
   - No [ ]

Please provide brief details:

There is a need for training on insertion of LNG IUS.

(7) **Are there any issues regarding the registration of the medicine by regulatory authorities?** (e.g., recent registration, new indications, off-label use)

   - Yes [ ]
   - No [x]

Please provide brief details:

The Mirena® IUS is registered in more than 120 countries worldwide, distributed commercially by Bayer Pharma. The LNG IUS provided by the ICA registered in three countries (Ghana, Kenya, and Nigeria), but is available through public-sector.

(8) **Is the medicine recommended for use in a current WHO GRC-approved Guideline (i.e., post 2008)?**

   - Yes [ ]
   - No [x]

Please provide brief details:

(9) **Please comment briefly on issues regarding cost and affordability of this medicine.**

The report did not comment on this issue which is very important especially in developing country settings.

(10) **Any additional comments?**
(11) Please summarise the action you propose the Expert Committee takes.

Though Levonoregstrrel IUS has some merits, being long acting contraceptive method, and can be used in other gynaecological indications (treatment of heavy menstrual bleeding), but the application as it stands, is lacking many important information concerning effectiveness and safety in different uses. Costs especially in developing countries are lacking. Application is proposing Levonorgestrel releasing intra-uterine system (Mirena®) which is available in private sector only! The reviewer is not endorsing this application at this stage.