

# Levonorgestrel Intrauterine System for Contraception: An Expert Panel Consensus Statement

Suchitra N Pandit<sup>1</sup>, Anahita R Chauhan<sup>2</sup>, Shobha N Gudi<sup>3</sup>, Priti S Vyas<sup>4</sup>, Jayanta Kumar Gupta<sup>5</sup>, Savitha Yelamanchi Devi<sup>6</sup>, Pratima Mittal<sup>7</sup>, Kannaki CV<sup>8</sup>, Jaishree Gajaraj<sup>9</sup>, Kola Sasikala<sup>10</sup>, Jayanthi L Reddy<sup>11</sup>, Uma Ram<sup>12</sup>, Sonia Naik<sup>13</sup>, Leela Bhagavan<sup>14</sup>

## ABSTRACT

**Aim:** The primary objective of this consensus document is to develop evidence-based consensus recommendations on the use of the levonorgestrel-releasing intrauterine system (LNG-IUS) for contraception in the Indian setting.

**Background:** The unintended pregnancy rate in India is among the highest in the world. Current contraceptive options for women in India include combined or progesterone-only contraceptive pills, vaginal ring, depot medroxyprogesterone acetate, copper intrauterine devices, LNG-IUS, and implants. However, currently, there are no India-specific guidelines/recommendations on the use of LNG-IUS in women. Therefore, an expert panel meeting was convened to arrive at practical recommendations for clinicians on the appropriate use of LNG-IUS.

**Review results:** The panel comprising 15 obstetrics and gynecology experts from India discussed appropriate patient profiles for LNG-IUS and available evidence for the general population and women with comorbidities. The panel thoroughly reviewed the existing literature on contraception and put forth definitive recommendations to be followed on the use of LNG-IUS in the Indian setting. Consensus-based clinical recommendations were developed to serve as a reference for clinicians, regarding the use of LNG-IUS in the general population and women with comorbidities.

**Conclusion:** The use of the LNG-IUS in selected population can ensure contraception and also enhance treatment outcomes. The consensus recommendations given in this document can guide clinicians toward the same in Indian settings.

**Clinical significance:** The LNG-IUS, while being effective for contraception, offers several advantages in terms of reversibility, reduced pelvic infections, etc. Clinicians should carefully select the specific patient profiles/subgroups who would benefit from the use of LNG-IUS.

**Keywords:** Contraception, India, Intrauterine device, Levonorgestrel-releasing intrauterine system, Pregnancy, Recommendations, Review article. *Journal of South Asian Federation of Obstetrics and Gynaecology* (2020): 10.5005/jp-journals-10006-1813

## BACKGROUND

Unintended/unwanted pregnancies are a huge and persistent public healthcare concern, both worldwide and in India. These have far-reaching consequences, starting from the mother's and child's health to the socioeconomic impact on families as a whole. Although recent years have witnessed a decreased trend in the unintended pregnancy rate, with the increased use of contraception, recent worldwide estimates indicate that 55 out of every 1,000 women have an unintended pregnancy.<sup>1</sup> Data collated from various sources in India highlight that approximately half of the 48.1 million pregnancies in the country were unintended (estimated incidence rate of 70.1/1,000 women aged between 18 years and 49 years). A total of 15.6 million unintended pregnancies in the country ended in abortions. Such staggering data on unintended pregnancy indicate a significant unmet need for contraception among women in India.<sup>2,3</sup> These data not only call for definitive policies and reforms from the government on effective and accessible contraception methods for women, but they also highlight the role of clinicians/healthcare providers in strengthening family-planning efforts.<sup>4</sup>

Family planning is not only crucial for achieving sustainable development goals for a country but also for reducing healthcare costs.<sup>4</sup> Presently, the various options available for contraception in India include oral contraceptive pills (combined and progesterone only), injectable contraceptives (depot medroxyprogesterone acetate), and intrauterine devices (IUDs; such as copper bearing and hormonal).<sup>5</sup> Among IUDs, the levonorgestrel (LNG)-releasing

<sup>1</sup>Department of Obstetrics and Gynecology, Surya Group of Hospitals, Navi Mumbai, Maharashtra, India

<sup>2</sup>Department of Obstetrics and Gynecology, Saifee Hospital, Mumbai, Maharashtra, India

<sup>3</sup>Department of Obstetrics and Gynecology, St Philomena's Hospital, Bengaluru, Karnataka, India

<sup>4</sup>Department of Obstetrics and Gynecology, Sangita Maternity-Surgical and Diagnostic Centre, Mumbai, Maharashtra, India

<sup>5</sup>Department of Obstetrics and Gynecology, Apollo Gleneagles Hospital, Kolkata, West Bengal, India

<sup>6</sup>Department of Obstetrics and Gynecology, Swapna Health Care, Hyderabad, Telangana, India

<sup>7</sup>Department of Obstetrics and Gynecology, VMMC and Safdarjung Hospital, New Delhi, India

<sup>8</sup>Department of Obstetrics and Gynecology, Thamarai Fertility Services, Coimbatore, Tamil Nadu, India

<sup>9</sup>Department of Obstetrics and Gynecology, Apollo Specialty Hospital, Chennai, Tamil Nadu, India

<sup>10</sup>Department of Obstetrics and Gynecology, Lakshmi Clinic, Hyderabad, Telangana, India

<sup>11</sup>JJ Hospital, Hyderabad, Telangana, India

<sup>12</sup>Seethapathy Clinic and Hospital, Chennai, Tamil Nadu, India

<sup>13</sup>Department of Obstetrics and Gynecology, Max Super Specialty Hospital, Saket, New Delhi, India

<sup>14</sup>Department of Obstetrics and Gynecology, Cloud Nine Hospital, Bengaluru, Karnataka, India

intrauterine system (IUS) is an effective and convenient method providing long-term reversible contraception in women. Evidence over the years has revealed a pregnancy rate of below 1/100 women per year with LNG-IUS 52 mg (contains 52 mg of LNG released at a rate of 20 mg/day for at least 5 years), which makes it comparable to sterilization. It offers the advantage of reversibility, reduced pelvic infections, lower ectopic pregnancy rate, reduction in anemia, and menstrual bleeding. Furthermore, its use is associated with a low discontinuation rate, high patient satisfaction, and increased quality of life (QoL).<sup>6</sup> Despite LNG-IUS being uniquely placed as a contraceptive and deemed efficacious, safe, and cost-effective for priority conditions by the World Health Organization (WHO),<sup>7,8</sup> there are several unmet needs related to its usage in developing nations such as India.

**Need for a Consensus Statement on LNG-IUS**

Providers of IUDs play a crucial role in the appropriate usage of IUDs. Hence, the foremost prerequisite for the clinician/healthcare provider—apart from being skilled—is sound knowledge of appropriate screening for medical eligibility of the patient.<sup>5</sup> Although information on the method of insertion, counseling, and follow-up is readily available, there is a lack of structured, evidence-based recommendations/guidelines on the selection of LNG-IUS among the various available options. There is also a lack of recommendations/guidelines for specific patient profiles/subgroups of women who stand to benefit from LNG-IUS use.

Although the WHO has laid down useful guidelines regarding the eligibility criteria for LNG-IUS use in women with a range of medical conditions,<sup>9</sup> there is a lack of structured, easily implementable clinical recommendations/guidelines for LNG-IUS specific to the country. The formulation of recommendations will not only help in achieving consistent use of LNG-IUS, but will also facilitate the medical fraternity in making informed decisions about selecting appropriate contraception options for specific subgroups of patients. Hence, this document has been prepared to chalk out

**Corresponding Author:** Suchitra N Pandit, Department of Obstetrics and Gynecology, Surya Group of Hospitals, Navi Mumbai, Maharashtra, India, Phone: +91 9820416474, e-mail: Bqpub2019@gmail.com

**How to cite this article:** Pandit SN, Chauhan AR, Gudi SN, *et al.* Levonorgestrel Intrauterine System for Contraception: An Expert Panel Consensus Statement. *J South Asian Feder Obst Gynae* 2020;12(5):307–312.

**Source of support:** Nil

**Conflict of interest:** None

definitive recommendations for Indian clinicians on LNG-IUS use in the country.

**REVIEW RESULTS**

The consensus-based, actionable clinical recommendations in this document were developed through the cumulative efforts of 15 India-based obstetrics and gynecology experts. The panel critically analyzed existing literature, including randomized clinical trials, systematic reviews, and meta-analyses, through a systematic search of MEDLINE (via PubMed), Cochrane-indexed databases, and guidelines on contraception.

Inputs/opinions on various topics related to LNG-IUS were discussed in a face-to-face meeting of all the experts in December 2018 in Mumbai. The clinical recommendations were validated and reviewed by the panel. The quality of evidence of the clinical recommendations was based on the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system by Guyatt et al.<sup>10</sup> (Fig. 1).

**Recommendations on Use of LNG-IUS**

The discussion on evidence on LNG-IUS from the expert panel churned out the following recommendations specific to India:

- The experts suggested and preferred the use of LNG-IUS 52 mg for 5 years as a long-term contraceptive in India for the following subgroups:

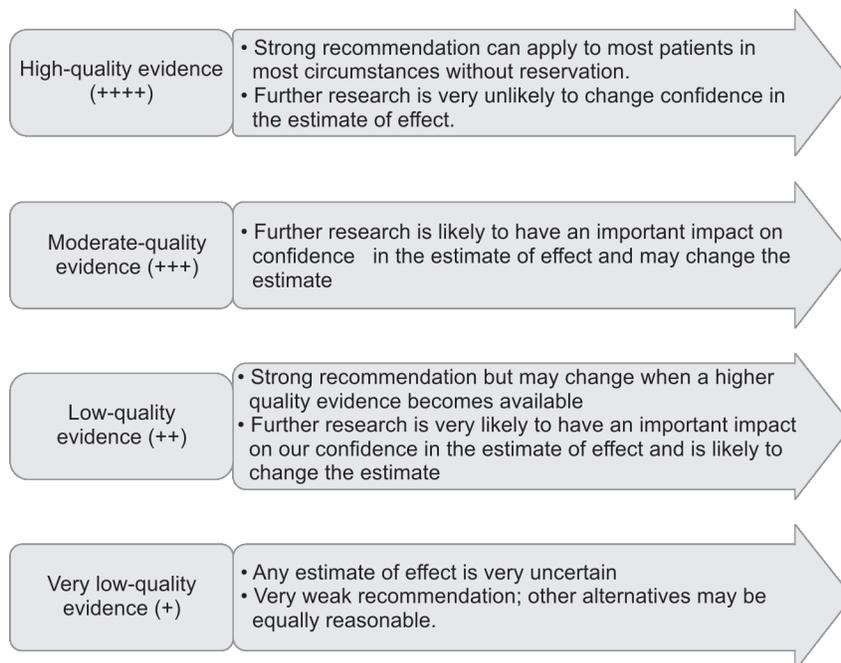


Fig. 1: Quality of evidence and interpretation<sup>10</sup>



- Perimenopausal women (++++)
- Women with heavy menstrual bleeding (HMB) (++++)
- Women with dysmenorrhea (++++)
- Women with comorbidities, such as:
  - Polycystic ovarian syndrome (PCOS) (++++)
  - Chronic medical disorders such as:
    - Chronic anemia (++++)
    - Stroke
    - Valvular heart disease
    - Hypertension and diabetes well controlled on medications
    - Connective tissue disorders
- Occupations requiring frequent traveling (+)
  - Globe trotters
  - Flight attendants

## DISCUSSION

### Evidence Supporting Recommendations

The LNG-IUS is a T-shaped device placed in the uterus; it exerts its contraceptive action through the release of a second-generation highly potent progestin—LNG. It causes the thickening of the cervical mucus, resulting in the inability of sperms to fertilize the egg. It also suppresses endometrial proliferation, thereby preventing implantation. The hostile environment created in the uterus affects sperm survival, motility, and capacitance—leading to the prevention of fertilization.<sup>9,11</sup>

### Evidence of LNG-IUS in the General Population and Specific Groups

The LNG-IUS has served as one of the most effective forms of contraception for preventing unintended pregnancy in recent times, with a cumulative global pregnancy rate of <0.5%.<sup>9</sup> Evidence on efficacy and safety of the LNG-IUS is summarized in the following sections.

#### *Efficacy and Safety of LNG-IUS in General Population*

A systematic review by French et al. comparing LNG-IUS 52 mg with nonhormonal IUDs revealed that although there was no significant difference in the pregnancy rate between the two methods, LNG-IUS 52 mg prevented ectopic pregnancies more effectively compared with nonhormonal IUD.<sup>12</sup> In a cross-sectional survey-based study involving 17,360 users of LNG-IUS, pregnancy with LNG-IUS *in situ* was rare. The 5-year cumulative pregnancy rate (per 100 users) in the study was 0.5 with a 5-year pearl rate of 0.11.<sup>13</sup>

In a multicentric, open-label, phase 3 clinical trial [A Comprehensive Contraceptive Efficacy and Safety Study of an IUS (ACCESS IUS)], pregnancy rates with LNG-IUS 52 mg were assessed in 1,600 women (aged 16–45 years) with regular menses based on the pearl index and safety. The 3-year cumulative pregnancy rate in the study was 0.55 [95% confidence interval (CI) 0.24–1.23]. Expulsion of the device during the 3-year study period was reported in <5% women, and pelvic infection was diagnosed in <1% women. Discontinuation of LNG-IUS 52 mg was primarily due to bleeding complaints and was only 1.6% during the study. Overall, the device was found to be a safe and effective method of contraception in nulliparous and parous women for over 3 years.<sup>14</sup>

Furthermore, in an ongoing 10-year continuation of the ACCESS IUS trial, the 5-year efficacy and safety data of LNG-IUS 52 mg were assessed in a total of 1,751 enrolled women (age 16–45 years). Of

the total women enrolled, 495 completed 5 years of LNG-IUS 52 mg use. The cumulative pregnancy rate in the study was 0.92% (95% CI 0.46–1.82). Device expulsion occurred in 3.8% of women, with discontinuation of the device in only 2.2%. The adverse event of pelvic infection was diagnosed in <1% of enrolled women. The results of the study indicated the use of LNG-IUS 52 mg to be effective and safe for over 5 years.<sup>15</sup> Bahamondes et al. conducted a chart review in 776 women who continued the use of LNG-IUS 52 mg for >60 months (61–184 months). No pregnancy was detected over 967 and 1485 women-years up to 7 to 15 years after the placement of the device.<sup>16</sup>

In addition to showing prolonged efficacy and safety, a retrospective chart review revealed a higher continuation rate for LNG-IUS 52 mg (77.8%) when compared with copper-based IUD (73.1%) and etonogestrel implant (75.9%).<sup>17</sup> LNG-IUS 52 mg, in addition to being an effective contraceptive, has a positive impact on women's QoL. In a multicenter observational study conducted among 201 women on LNG-IUS 52 mg, QoL was assessed using the Spanish Society of Contraception quality-of-life (SEC-QoL) questionnaire over 12 months. Apart from no reported pregnancy in the enrolled women, the results showed an overall improvement in the mean SEC-QoL score at 12 months when compared with baseline ( $p > 0.001$ ). The continuation rate for the device for 12 months was 93%.<sup>6</sup> In line with the evidence discussed above, the experts unanimously recommended the use of LNG-IUS 52 mg as a contraceptive in general parous and nulliparous women.

#### *Efficacy and Safety of LNG-IUS in Perimenopausal Women*

Besides, for use in the general population, LNG-IUS can be useful in perimenopausal women, by preventing the risk of unwanted pregnancy and checking menstrual disturbances as they transition into menopause. In an observational study conducted among 104 women, long-term clinical experience with LNG-IUS was assessed as women transitioned from the pre-, peri-, and postmenopausal stages. The included participants received a combination of LNG-IUS with supplemental estrogen therapy. The results revealed LNG-IUS to have good acceptability and tolerability. No expulsion of the device was observed. The combination therapy was found to be clinically applicable for the prevention of endometrial proliferation in the uterine cavity and for treating hyperplasia.<sup>18</sup>

Apart from the direct effect on the endometrium (suppression), LNG-IUS helps in preventing menorrhagia and pain, which are commonly observed in the premenopausal stage with mild hormonal adverse events, such as weight change, breast tenderness, and hirsutism.<sup>19</sup>

Consistent with the scientific evidence, the experts agreed on the usefulness of LNG-IUS in perimenopausal women and recommended the use of LNG-IUS 52 mg as a contraceptive measure in women transitioning to menopause.

#### *Efficacy and Safety of LNG-IUS in Women with Heavy Menstrual Bleeding, Dysmenorrhea, and Chronic Anemia*

A common medical condition seen in women during their reproductive age is heavy menstrual bleeding (HMB), which further leads to anemia or can be life-threatening in severe cases. After contraception, one of the main indications of LNG-IUS is for the treatment of HMB, as it causes endometrial suppression, thereby reducing bleeding.<sup>20,21</sup> In a benefit-risk review of LNG-IUS in HMB by Kauntiz et al., LNG-IUS was found to be associated with

greater menstrual blood loss (MBL) reduction compared with other treatment options, viz. oral contraceptives, tranexamic acid, and oral mefenamic acid. Within the first 3 months of LNG-IUS device use in women with normal menses, the endometrium becomes uniformly suppressed (characteristic of decidualization of the stroma and dilatation of numerous thin-walled venules). Numerous randomized clinical studies have shown LNG-IUS to cause the highest MBL reduction (>90%) within the first 3 months of its use. The trend of HMB (without known pathology) reduction with LNG-IUS use was further seen in nonrandomized trials as well. Although long-term efficacy data were limited, one of the studies suggested the effect is maintained through 4 years of device use.<sup>21</sup>

The device was also found to be safe with no uterine perforations observed in randomized clinical trials and a large, controlled Europe-based, surveillance study on IUDs. Randomized controlled trial evidence highlighted a partial or complete expulsion rate for the device of <5%. Additionally, a randomized controlled trial highlighted that LNG-IUS was more effective than combination oral contraceptives in reducing fibroid-related HMB. A 91% reduction in mean MBL was observed from baseline in the LNG-IUS group, compared with only 13% reduction with the combined oral contraceptive at 12 months ( $p < 0.001$ ). It is also cost-effective and exerts a positive impact on the overall QoL, when compared with endometrial ablation and hysterectomy.<sup>21</sup>

There is evidence that the device is beneficial in adenomyosis-associated HMB and dysmenorrhea.<sup>22,23</sup> A study was conducted to compare the effect of LNG-IUS and copper IUD on menses and dysmenorrhea. Compared with copper IUD, LNG-IUS was responsible for a significantly improved duration of menstrual bleeding, dysmenorrhea, and hemoglobin levels at 1 and 12 months' treatment. Moreover, LNG-IUS showed a significantly better safety profile compared with copper IUD.<sup>23</sup>

As monthly MBL is affected by LNG-IUS, the use of the device has the propensity to increase iron (ferritin) levels and reduce the prevalence of anemia among women. In a systematic review by Lowe et al., hemoglobin and serum ferritin levels at baseline and 1-year postuse of copper-based IUD or LNG-IUS were assessed. The results of the meta-analysis showed that the use of copper IUD resulted in a significant decrease in mean hemoglobin level after 1 year of use. However, after 1 year of use, there was a significant increase in hemoglobin levels in the LNG-IUS group. Although diet and other confounding factors are also related, the results of the meta-analysis indicated the likely benefit of LNG-IUS in borderline anemic women.<sup>24</sup>

The experts recommended the use of LNG-IUS in women with HMB, dysmenorrhea, and chronic anemia – based on results from published literature.

#### *Efficacy and Safety of LNG-IUS in Women with Comorbidities*

The benefits of LNG-IUS are further applicable to women with comorbid disorders.

The PCOS is a common reproductive disorder leading to hyperandrogenism and oligo-anovulation in women. The disorder is further linked to other clinical and metabolic comorbidities, such as dyslipidemia, diabetes, and cardiovascular disease (CVD). The clinical and metabolic impact of progesterone-only contraceptive (LNG-IUS) was assessed for 6 months in an observational controlled trial conducted among 30 women (aged 18–35 years) diagnosed with PCOS. Outcomes were compared between the LNG-IUS group and the control group (comprising 30 women without PCOS).<sup>25</sup>

Before LNG-IUS device insertion, women with PCOS had higher total testosterone levels, lower high-density lipoprotein levels, and significantly higher ovarian volume when compared with the control group. Six months after device insertion, the mean ovarian volume was 10% lower compared with baseline. The low-density lipoprotein levels postinsertion of IUD reduced by 5.2%, along with a significant reduction in total cholesterol levels by 6.7% ( $p < 0.01$ ), compared with baseline. The study concluded that LNG-IUS was not responsible for any significant change in clinical/metabolic markers in women without comorbidities, irrespective of whether they have PCOS.<sup>25</sup>

Although long-term evidence is limited regarding LNG-IUS use in PCOS, based on results from published literature, the experts recommended the use of LNG-IUS in patients with PCOS.

Progestogen-only contraceptive methods are not associated with a significantly increased risk of arterial or venous thrombosis. They are generally safe for all patients with cardiac disease. Thus, in women with conditions that carry an increased risk of venous or arterial thrombosis or paradoxical embolism, progestogen-only contraceptive methods are the preferred choice.<sup>26</sup>

Women with CVD include subgroups of various distinct disorders, and thorough counseling for pregnancy and contraception should be conducted for them.<sup>26</sup> A 15-year cohort European trial involving >150,000 women aged 15–49 years with no history of CVD or cancer assessed various contraceptive options for the risk of stroke and myocardial infarction (MI). The results of the study revealed that no progestin-only formulations, including LNG-IUS, significantly increased the risk of thrombotic stroke or MI.<sup>27</sup>

A retrospective chart review was conducted among women diagnosed with CVD who were either on copper-based IUD, LNG-IUS, or contraceptive implant. A total of 87.2, 7, and 4.8% of the women opted for LNG-IUS, copper IUD, and etonogestrel implant, respectively. No cases of perforation were observed in the study. No confirmed cases of infective endocarditis related to the use of long-acting reversible contraceptives (LARCs) were observed. The study concluded LARC devices to be a safe option for contraception in women with cardiovascular conditions.<sup>28</sup>

In a prospective trial conducted among women with CVD (inclusive of pulmonary hypertension) and on LNG-IUS 52 mg, gynecologic adverse events and the frequency of cardiovascular due to device use over the year after insertion were assessed. No cardiovascular event was identified a year after LNG-IUS insertion. The MBL decreased in the majority of women, and median hemoglobin levels increased significantly within a year, postdevice insertion. The study demonstrated LNG-IUS to be a safe and effective option for contraception in women with CVD.<sup>29</sup>

In addition to CVD, LNG-IUS has proven to be beneficial in other metabolic disorders such as diabetes. In a randomized controlled study conducted among 62 women with uncomplicated diabetes mellitus, participants were randomized to receive either copper-based IUD or LNG-IUS; and glucose metabolism was assessed over 12 months of device use. The results of the trial showed that LNG-IUS was not associated with any adverse effects on glucose metabolism, contrary to the classification by the WHO, which suggests that LNG-IUS is to be used with caution in women with insulin-dependent diabetes.<sup>30</sup>

In women with systemic lupus erythematosus (SLE), an unplanned pregnancy—especially during the active phase of the disease—can prove detrimental due to the teratogenic effects of immunosuppressive therapy on the developing fetus. Therefore,

women of reproductive age with SLE will require the use of highly effective contraception.<sup>31,32</sup> A retrospective cohort study by Rebelco et al. evaluated the effect of LNG-IUS 52 mg on disease activity and damage index scores in women with SLE with or without antiphospholipid syndrome (APS). Disease activity was assessed using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI-2K) scale, and disease damage was assessed using the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index for Systemic Lupus Erythematosus (SLICC/ACR-DI) scale. Women using LNG-IUS for contraception were followed up for a median of 5 years. The results of the study showed LNG-IUS use for a period of 5 years in women with SLE was not associated with an increase in disease activity or damage index scores; no significant differences were observed between women with and without APS.<sup>32</sup>

Another unique indication or area of use for LARC-LNG-IUS is situations requiring the indication of amenorrhea terrestrially. The use of LARCs is particularly helpful in astronauts; it is not associated with daily compliance issues, like the oral contraceptive pill, and leads to the generation of less waste. An average of 11 years of menstrual suppression/contraception is required for astronauts. Also, these devices do not interfere with the daily tasks of astronauts.<sup>33</sup>

Thus LNG-IUS can be used by individuals working in occupations requiring frequent traveling, as LNG-IUS offers the ease of long-term reversible contraception, good tolerability, reduced MBL, and improved QoL. All these cumulative benefits facilitate care-free contraception in individuals always on the go, with no adverse effect on health requiring urgent medical attention. The device reduces unwanted pregnancy, as it is functional for 5 years. Use of the device reduces reliance on other forms of conception such as condoms and contraceptive pills, which require supply, as against one-time insertion of LNG-IUS.

### Newer LNG-IUS

Two different low-dose formulations of LNG-IUS, viz. LNG-IUS 13.5 mg LNG-IUS 19.5 mg, are approved by the Food and Drug Administration. LNG-IUS 13.5 mg contains 13.5 mg LNG released at a rate of 12 µg/day for up to 3 years and was approved in 2013. LNG-IUS 19.5 mg contains 19.5 mg LNG released at a rate of 16 µg/day for up to 5 years and was approved in 2016. These low-dose devices have not shown altered systemic side effects compared with LNG-IUS 52 mg. They can be inserted easily and are associated with increased bleeding and reduced anovulation compared with LNG-IUS 52 mg. However, these are currently not available for clinical use in India.<sup>34,35</sup>

### CONCLUSION

Unintended pregnancy not only impacts maternal health, but it also has pronounced socioeconomic consequences, especially in a developing country such as India. The intrauterine contraceptive delivery of LNG via an IUS represents a unique option for LARC, and it is generally suitable for all women or women who require a specific contraceptive. In our endeavor, we aimed to establish a set of standard recommendations for the use of LNG-IUS in the country. The specific and practical consensus-based clinical recommendations were an outcome of the thorough approach followed by the participating experts. The document will not only guide Indian obstetricians/gynecologists on consistent use of LNG-IUS but will also ensure safe and consistent use of

the contraceptive in the region. We sincerely believe that these recommendations will serve as a steppingstone in empowering treating clinicians to make suitable decisions on the use of LNG-IUS across various healthcare settings in the country.

### CLINICAL SIGNIFICANCE

The LNG-IUS has been shown to be effective and safe for contraception in the general population and also beneficial for perimenopausal women and women with comorbidities. It is therefore essential that the clinicians carefully evaluate the patient profiles/subgroups of women who would benefit from the use of the LNG-IUS for contraception.

### ACKNOWLEDGMENTS

The authors thank BioQuest Solutions for providing editorial assistance.

### REFERENCES

1. Cristobal I, Neyro JL, Lete I. The new LNG-releasing IUS: a new opportunity to reduce the burden of unintended pregnancy. *Eur J Obstet Gynecol Reprod Biol* 2015;190:58–64. DOI: 10.1016/j.ejogrb.2015.04.016.
2. Singh S, Shekhar C, Acharya R, et al. The incidence of abortion and unintended pregnancy in India, 2015. *Lancet Glob Heal* 2018;6(1):e111–e120. DOI: 10.1016/S2214-109X(17)30453-9.
3. Iyengar K, Danielsson KG. A need for overhaul of policy on contraception and abortion in India. *Lancet Glob Health* 2018;6(1):e16–e17. DOI: 10.1016/S2214-109X(17)30473-4.
4. Muttreja P, Singh S. Family planning in India: The way forward. *Indian J Med Res*. 2018;148(Suppl 1):S1–S9.
5. Department of Family Welfare. Ministry of Health and Family Welfare. Government of India. Contraceptive Updates. Reference Manual for Doctors. Available at: <https://india.unfpa.org/sites/default/files/pubpdf/contraceptiveReferenceManualFinal7Nov2005.pdf> Accessed on: 30 May 2019.
6. Cristobal I, Lete LI, Viuda E, et al. One-year quality of life measured with SEC-QoL in levonorgestrel 52 mg IUS users. *Contraception* 2016;93(4):367–371. DOI: 10.1016/j.contraception.2015.12.014.
7. World Health Organization (WHO). WHO Model List of Essential Medicines. 20th List. (2017). Available at: <https://apps.who.int/iris/bitstream/handle/10665/273826/EML-20-eng.pdf?ua=1>. Accessed on: 30 May 2019.
8. World Health Organization. EML 2015 – application for the levonorgestrel-releasing intrauterine system (LNG-IUS). Available from: [https://www.who.int/selection\\_medicines/committees/expert/20/applications/LNG\\_IUS.pdf?ua=1](https://www.who.int/selection_medicines/committees/expert/20/applications/LNG_IUS.pdf?ua=1). Accessed on: 30 May 2019.
9. Beatty MN, Blumenthal PD. The levonorgestrel-releasing intrauterine system: safety, efficacy, and patient acceptability. *Ther Clin Risk Manag* 2009;5(3):561–574.
10. Guyatt G, Oxman AD, Akl EA, et al. GRADE guidelines: 1. Introduction - GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol* 2011;64(4):383–394. DOI: 10.1016/j.jclinepi.2010.04.026.
11. Grandi G, Farulla A, Sileo FG, et al. Levonorgestrel-releasing intrauterine systems as female contraceptives. *Expert Opin Pharmacother* 2018;19(7):677–686. DOI: 10.1080/14656566.2018.1462337.
12. French R, Sorhaindo AM, Van Vliet HA, et al. Progestogen-releasing intrauterine systems versus other forms of reversible contraceptives for contraception. *Cochrane Database Syst Rev* 2004(3):1–73.
13. Backman T, Rauramo I, Huhtala S, et al. Pregnancy during the use of levonorgestrel intrauterine system. *Am J Obstet Gynecol* 2004;190(1):50–54. DOI: 10.1016/j.ajog.2003.07.021.
14. Eisenberg DL, Schreiber CA, Turok DK, et al. Three-year efficacy and safety of a new 52-mg levonorgestrel-releasing intrauterine

- system. *Contraception* 2015;92(1):10–16. DOI: 10.1016/j.contraception.2015.04.006.
15. Teal SB, Turok DK, Chen BA, et al. Five-year contraceptive efficacy and safety of a levonorgestrel 52-mg intrauterine system. *Obstet Gynecol* 2019;133(1):63–70. DOI: 10.1097/AOG.0000000000003034.
  16. Bahamondes L, Fernandes A, Bahamondes MV, et al. Pregnancy outcomes associated with extended use of the 52-mg 20 µg/day levonorgestrel-releasing intrauterine system beyond 60 months: a chart review of 776 women in Brazil. *Contraception* 2018;97(3):205–209. DOI: 10.1016/j.contraception.2017.10.007.
  17. Sanders JN, Turok DK, Gawron LM, et al. Two-year continuation of intrauterine devices and contraceptive implants in a mixed-payer setting: a retrospective review. *Am J Obstet Gynecol* 2017;216(6):590.e1–590.e8. DOI: 10.1016/j.ajog.2017.02.003.
  18. Wildemeersch D. Why perimenopausal women should consider to use a levonorgestrel intrauterine system. *Gynecol Endocrinol* 2016;32(8):659–661. DOI: 10.3109/09513590.2016.1153056.
  19. Sitruk-Ware R. The levonorgestrel intrauterine system for use in peri- and postmenopausal women. *Contraception* 2007;75(6 Suppl.):S155–S160. DOI: 10.1016/j.contraception.2007.01.010.
  20. Sheng J, Zhang WY, Zhang JP, et al. The LNG-IUS study on adenomyosis: A 3-year follow-up study on the efficacy and side effects of the use of levonorgestrel intrauterine system for the treatment of dysmenorrhea associated with adenomyosis. *Contraception* 2009;79(3):189–193. DOI: 10.1016/j.contraception.2008.11.004.
  21. Gemzell-Danielsson K, Inki P, Heikinheimo O. Safety and efficacy of the levonorgestrel-releasing intrauterine system: recent insights. *Exp Rev Obstet Gynecol* 2014. 235–247.
  22. Kaunitz AM, Inki P. The levonorgestrel-releasing intrauterine system in heavy menstrual bleeding. A benefit-risk review. *Drugs* 2012;72(2):193–215. DOI: 10.2165/11598960-000000000-00000.
  23. Kelekci S, Kelekci KH, Yilmaz B. Effects of levonorgestrel-releasing intrauterine system and T380A intrauterine copper device on dysmenorrhea and days of bleeding in women with and without adenomyosis. *Contraception* 2012;86(5):458–463. DOI: 10.1016/j.contraception.2012.04.001.
  24. Lowe RF, Prata N. Hemoglobin and serum ferritin levels in women using copper-releasing or levonorgestrel-releasing intrauterine devices: a systematic review. *Contraception* 2013;87(4):486–496. DOI: 10.1016/j.contraception.2012.09.025.
  25. Da Silva AV, De Melo AS, Barboza RP, et al. Levonorgestrel-releasing intrauterine system for women with polycystic ovary syndrome. *Reprod Sci* 2016;23(7):877–884. DOI: 10.1177/1933719115623648.
  26. Hudsmith L, Thorne S. Contraception in women with cardiac disease. *Women's Heal* 2007;3(6):711–717. DOI: 10.2217/17455057.3.6.711.
  27. Lidegaard Ø, Løkkegaard E, Jensen A, et al. Thrombotic stroke and myocardial infarction with hormonal contraception. *N Engl J Med* 2012;366(24):2257–2266. DOI: 10.1056/NEJMoa1111840.
  28. Vu Q, Micks E, McCoy E, et al. Efficacy and safety of long-acting reversible contraception in women with cardiovascular conditions. *Am J Cardiol* 2016;117(2):302–304. DOI: 10.1016/j.amjcard.2015.10.026.
  29. Ueda Y, Kamiya CA, Horiuchi C, et al. Safety and efficacy of a 52-mg levonorgestrel-releasing intrauterine system in women with cardiovascular disease. *J Obstet Gynaecol Res* 2019;45(2):382–388. DOI: 10.1111/jog.13828.
  30. Rogovskaya S, Rivera R, Grimes DA, et al. Effect of a levonorgestrel intrauterine system on women with type 1 diabetes: a randomized trial. *Obstet Gynecol* 2005;105(4):811–815. DOI: 10.1097/01.AOG.0000156301.11939.56.
  31. Østensen M. Contraception counseling in SLE—an often forgotten duty? *Nat Rev Rheumatol* 2011;7(6):315–316. DOI: 10.1038/nrrheum.2011.54.
  32. Rebelo RC, Pignaton E, Valeria BM, et al. Disease activity and thromboembolic events in women with systemic lupus erythematosus with and without anti-phospholipid syndrome: users of the 52-mg levonorgestrel-releasing intrauterine system. *Arch Gynecol Obstet* 2019;299(6):1597–1605. DOI: 10.1007/s00404-019-05131-x.
  33. Kim J, Kwon J, Kim M, et al. Low-dielectric-constant polyimide aerogel composite films with low water uptake. *Polym J* 2016;48(7):829–834. DOI: 10.1038/pj.2016.37.
  34. Nelson AL. LNG-IUS 12: A 19.5 levonorgestrel-releasing intrauterine system for prevention of pregnancy for up to five years. *Expert Opin Drug Deliv* 2017;14(9):1131–1140. DOI: 10.1080/17425247.2017.1353972.
  35. Goldstuck ND. Clarification of the role of the Jaydess (Skyla) LNG-IUS 13.5mg and Kyleena LNG-IUS 19.5mg as intrauterine contraceptive systems. *Expert Rev Med Devices* 2017;14(8):593–599. DOI: 10.1080/17434440.2017.1350169.