JAYDESS®/KYLEENA®
(levonorgestrel 13.5 mg/19.5 mg intrauterine delivery system)
EU Risk Management Plan
Part VI: Summary of the risk management plan

Summary of risk management plan for Kyleena

This is a summary of the risk management plan (RMP) for Kyleena. The RMP details important risks of Kyleena, how these risks can be minimised, and how more information will be obtained about Kyleena risks and uncertainties (missing information).

Kyleena's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Kyleena should be used.

I The medicine and what it is used for

Kyleena is used for contraception for up to 5 years.

Kyleena is a levonorgestrel (LNG, active substance) releasing intrauterine delivery systems (Levonorgestrel-Releasing Intrauterine System [LNG-IUS], total LNG content 19.5 mg). Kyleena is placed in the uterus with a preloaded, ready-to-use inserter.

Kyleena and Jaydess (Intrauterine System (71) with LNG content 13.5 mg) have similar inserter and T-body dimensions and are referred to as "LCS" in this document when data relate to both products (LCS = low-dose levonorgestrel contraceptive system; LCS12 = Jaydess and LCS16 = Kyleena).

II Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of Kyleena, together with measures to minimise such risks and the proposed studies for learning more about Kyleena's risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status — the way a medicine is supplied to the patient (e.g., with or without prescription) can help to minimise its risks

Together, these measures constitute *routine risk minimisation* measures.

In the case of Kyleena, these measures are supplemented with *additional risk minimisation measures* mentioned under relevant important risks, below.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including Periodic Benefit-Risk Evaluation Report/Periodic Safety Update Report (PBRER/PSUR) assessment, so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

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II.A List of important risks and missing information

Important risks of Kyleena are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely used. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Kyleena. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g., on the long-term use of the medicine).

Table Part VI-2: Summary of safety concerns for Kyleena

List of important risks and missing information	
Important identified risks	Pelvic inflammatory disease Ectopic pregnancy in case of contraceptive failure Uterine perforation
Important potential risks	Potential for medication error Potential for off-label use in indications other than contraception
Missing information	None

II.B Summary of important risks

Important identified risk: Pelvic inflammatory disease (PID)

Evidence for linking the risk to the medicine	As with other intrauterine contraceptives (IUCs) there is an increased risk of PID at the time of placement and during the first weeks after the placement (clinical trial evidence, epidemiological data).
Risk factors and risk groups	The risk of PID is increased in women with sexually transmitted infections, women who have multiple sexual partners and women who have had PID in the past.
Risk minimisation measures	**Routine risk minimisation measures:** SmPC: Section 4.2, 4.3, 4.4, 4.8 PIL: Section 2, 4 **Additional risk minimisation measures:** None

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Important identified risk: Ectopic pregnancy in case of contraceptive failure

Evidence for linking the risk to the medicine	Kyleena is very effective in preventing pregnancy. The absolute risk of ectopic pregnancy in LCS (LCS12/Jaydess and LCS16/Kyleena) users is low. However, when pregnancy occurs with LCS *in situ*, the pregnancy is more likely to be ectopic than in women who become pregnant without LCS in place. This is a risk which is common to all IUCs when contraceptive failure occurs (clinical trial evidence, observational study evidence). About half of the unintended pregnancies with LCS are ectopic pregnancies.
Risk factors and risk groups	The observed frequencies of ectopic pregnancy for LCS in subgroup analyses including age, parity and BMI gave no evidence for a higher incidence in any of the subgroups studied. Some of the subgroups were too small for a conclusive assessment. *Risk factors for ectopic pregnancy in general:* Women with a previous history of ectopic pregnancy, tubal surgery or pelvic infection carry a higher risk of ectopic pregnancy. Age, smoking, prior abortions, prior PID, prior history of tubal surgery or infertility are associated with a higher risk. In adolescents, prior PID and gonorrhoea/chlamydia trachomatis infection are the more important risk factors.
Risk minimisation measures	**Routine risk minimisation measures:** SmPC: Section 4.4, 4.6, 4.8 PIL: Section 2 **Additional risk minimisation measures:** Educational material

Important identified risk: Uterine perforation

Evidence for linking the risk to the medicine	Uterine perforation may occur with the use of all types of IUCs, including LNG-IUS (clinical trial evidence, observational study evidence)
Risk factors and risk groups	The risk of uterine perforation is increased in women who are breastfeeding at time of insertion or have given birth up to 36 weeks before insertion. The risk of perforation may be increased in women with fixed retroverted uterus.
Risk minimisation measures	**Routine risk minimisation measures:** SmPC: Section 4.2, 4.3, 4.4, 4.8 PIL: Section 2, 4 **Additional risk minimisation measures:** None

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Important potential risk: Potential for medication error

Evidence for linking the risk to the medicine	Mirena can be used for 8 years in the indication contraception and LCS16/Kyleena is approved for 5 years of use. LCS12/Jaydess is approved for 3 years of use. Each brand of LNG-IUS can be identified by its specific features. An incorrect decision on treatment continuation or IUS removal/replacement could theoretically occur in situations where the type of LNG-IUS that was inserted some years ago is not (no longer) known to the user or health care provider.
Risk factors and risk groups	Not applicable
Risk minimisation measures	**Routine risk minimisation measures:** SmPC: Section 3, 4.1, 4.2 **Additional risk minimisation measures:** Educational material and patient reminder card

Important potential risk: Potential for off-label use in indications other than contraception

Evidence for linking the risk to the medicine	LCS12/Jaydess or LCS16/Kyleena have not been studied in indications other than contraception. Off-label use of LCS12/Jaydess and LCS16/Kyleena in other indications Mirena is approved for (e.g., idiopathic menorrhagia, protection from endometrial hyperplasia during oestrogen replacement therapy) might occur but is expected to be low, since an effective treatment in the form of Mirena is available.
Risk factors and risk groups	Not applicable
Risk minimisation measures	**Routine risk minimisation measures:** SmPC: Clearly mentions approved indication in Section 4.1 PIL: Clearly mentions approved indication in Section 1 **Additional risk minimisation measures:** None

II.C Post-authorisation development plan

II.C.1 Studies which are conditions of the marketing authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of Kyleena. The results of the studies conducted with LCS12/Jaydess will be applicable for LCS16/Kyleena.

II.C.2 Other studies in post-authorisation development plan

There are no studies required for Kyleena by European Medical Agency (EMA) or any other national competent authority in the European Union (EU).