2. Elements for a Public Summary

2.1 Overview of disease epidemiology

Jaydess® is used for prevention of pregnancy (contraception) for up to three years.

Unintended (unplanned or unwanted) pregnancies and their consequences are widely recognized as serious public health issues in most countries. Pregnancy terminations due to unwanted or unplanned pregnancies are among the most commonly performed gynaecological procedures.

Contraception can greatly decrease the number of unwanted and unplanned pregnancies, and thereby help to avoid the psychological, health-related and social effects of unplanned pregnancy and prenancy termination. Reproductive and sexual health care, including provision of contraceptive services is a key service by which the health of women can be improved. Typically, a woman is able to become pregnant during more than 30 years of her life, starting from menarche (her first menstrual period) and ending at menopause (the end of menstrual periods). Therefore, contraceptive services have the potential to impact women's health and wellbeing over a large proportion of their lifetime.

2.2 Summary of treatment benefits

Jaydess® works by thickening the cervical mucus (in the part of the womb that opens to the vagina) and reducing the growth of lining of the womb. Its actions create an environment in the womb which prevents the sperm and egg coming into contact and so prevent egg fertilization.

Available contraceptive methods can be divided into two groups, short-acting methods (e.g. contraceptive pill, vaginal rings, or skin patches) and long-acting methods (e.g. contraceptive implants that are placed under the skin, or intra-uterine contraceptives which includes Jaydess®). Generally, all methods are effective in preventing pregnancy but short-acting methods require regular actions by the woman such as intake of a pill, change of a patch etc. In recent years, various medical groups have recommended wider use of long-acting methods because more unintended pregnancies occur with the use of short-acting contraceptives.

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The contraceptive efficacy of Jaydess® has been tested in a clinical study with 1432 women aged 18 to 35 years who were using Jaydess® for up to 3 years. This study was performed in Europe, the US and Latin America and showed that about 4 in 1000 women using Jaydess® become pregnant in the first year. Over a period of 3 years of use, about 9 in 1000 women become pregnant using Jaydess®.

2.3 Unknowns relating to treatment benefits

Jaydess® has been tested in a sufficiently large number of women to demonstrate its good contraceptive efficacy. No differences in the effectiveness in pregnancy prevention related to race, ethnic origin, or age of the woman is to be expected.

2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Infection of the womb or the fallopian tubes (pelvic inflammatory disease, PID)	As with other intrauterine contraceptives there is an increased risk of pelvic inflammatory disease at the time of placement and during the first 3 weeks after the placement. In studies with Jaydess®, the risk of pelvic infection was below 1%. Signs of PID are persistent lower abdominal pain, fever, pain in conjunction with sexual intercourse or abnormal bleeding. 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. PID may have serious consequences; it may impair fertility and increase the risk of a future ectopic pregnancy (pregnancy outside the womb).	Careful recording of history, testing for sexually-transmitted infections in women at risk. Prompt (antibiotic) treatment of PID may prevent serious consequences.
Pregnancy outside of the womb (ectopic pregnancy) in case Jaydess® fails	Jaydess® is very effective in preventing pregnancy. However, when a woman becomes pregnant while using Jaydess®, the risk that the pregnancy could develop outside the womb (have an ectopic pregnancy) is increased; about half of the unintended pregnancies with Jaydess® are ectopic pregnancies. In clinical studies, about 1.1 in 1,000 women using Jaydess® have an ectopic pregnancy per year. This rate is lower than in women not using any contraception (about 3 to 5 in 1,000 women per year). Women who have already had an ectopic pregnancy, surgery of the fallopian tubes or a pelvic infection carry a higher risk for this type of pregnancy. An	Early diagnosis of ectopic pregnancy may prevent serious complications and even surgery.

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	ectopic pregnancy is a serious condition, which calls for immediate medical attention.	
Perforation or penetration of the wall of the womb (uterine perforation)	Perforation of the womb may occur, most often during placement of an intra-uterine contraceptive. It may be associated with pain and bleeding but can also go unnoticed. A Jaydess® that has become lodged outside the womb is not effective at preventing pregnancy and should be removed to prevent any further complications. This may require surgery. Perforation occurs in less than 1 in 1,000 placements of an intrauterine contraceptive. The risk is higher (between 1 in 1,000 and 1 in 100) in breastfeeding women and women who had a delivery up to 36 weeks before insertion.	Jaydess® should only be inserted by physicians/ healthcare professionals who are experienced in insertions of intrauterine contraceptives and/ or have undergone training on the Jaydess® insertion procedure.
Risk associated with unintended pregnancy while Jaydess® is still in the womb	Jaydess® is very effective in preventing pregnancy. When a woman does become pregnant while Jaydess® is still in the womb, and the pregnancy is in the correct location (see above for "ectopic pregnancy"), she is at increased risk of suffering a miscarriage, infection or that she goes into labour before her due date. This is a risk which is common to all pregnancies occurring with intrauterine contraceptives.	Removal of Jaydess® as soon as the pregnancy is diagnosed may decrease the risk of complications during the later course of the pregnancy, but the removal itself may trigger a miscarriage
Ovarian cysts	Since the contraceptive effect of Jaydess® is mainly due to its local effect in the womb, ovulation (release of the egg) usually continues in fertile women while using Jaydess®. Sometimes an ovarian cyst may develop. In most cases there are no symptoms, although on occasion there may be pelvic pain or pain during intercourse. This cyst may require medical attention or, more rarely, surgery, but it usually disappears on its own. Development of ovarian cysts is a side effect common to all hormonal contraceptives that do not contain estrogen. In clinical studies with Jaydess®, more than 10% of women were found to have ovarian cysts. However, the study participants underwent regular ultrasound examinations of their pelvic organs which detected a high number of ovarian cysts without symptoms, and the number of women having Jaydess® removed due to symptomatic ovarian cysts was less than 1%.	Ovarian cysts cannot be prevented.
Jaydess® come out/is pushed out of the womb (expulsion)	Jaydess® may be pushed out of the womb (e.g. due to muscular contractions of the womb during menstruation) into the vagina. This can occur with any intrauterine contraceptive.	Correct placement of Jaydess®reduces the risk of expulsion. Checking that the removal threads

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	Symptoms may be pain or bleeding, but it can also happen without the woman noticing it. In clinical studies with Jaydess® expulsion occurred in around 4% of subjects. An expelled Jaydess® no longer prevents pregnancy.	are in place (by the woman herself), and checking the position (by the healthcare provider) when new symptoms of bleeding and pain occur helps to prevent unintended pregnancy due to undiagnosed expulsion.
Changes in the menstrual bleeding pattern	Jaydess® affects the menstrual periods of the majority of women. This is mostly caused by the effect of the hormone levonorgestrel on the endometrium (inner lining of the womb). Observed changes include spotting (a small amount of bleeding), shorter or longer periods, lighter or heavier bleeding, or no bleeding at all. Many women have frequent spotting or light bleeding in addition to their periods for the first 3-6 months after they have Jaydess® placed. Some women may have heavy or prolonged bleeding during this time. Overall, the amount and number of days of bleeding each month gets smaller over the duration of use. At the end of 3 years, 12% of women experienced no bleeding at all.	Changes in the bleeding pattern cannot be prevented.

Important potential risks

Risk	What is known (including reason why it is considered a potential risk)
Potential of medication error: Inadvertent mix-up between Jaydess® and Mirena	Jaydess® is approved for pregnancy prevention for up to 3 years. Mirena, another intrauterine contraceptive with higher content of levonorgestrel, is approved for pregnancy prevention for up to 5 years. Accidental use of Jaydess® beyond 3 years may occur if the woman does not remember which levonorgestrel intrauterine contraceptive she is using. This could result in unintended pregnancy.
Potential for off-label use in indications other than contraception	Jaydess® is approved for pregnancy prevention. Mirena, another intrauterine contraceptive with higher content of levonorgestrel, is approved - in addition to pregnancy prevention - for the treatment of heavy menstrual periods, and to protect the inner lining of the womb in women who use estrogen replacement therapy for menopausal symptoms. Theoretically, use of Jaydess® in these indications could occur despite the fact that there are no studies to show that Jaydess® works in these indications
Potential for use beyond 3 years	Jaydess® is approved for pregnancy prevention for up to 3 years. Mirena, another intrauterine contraceptive with higher content of levonorgestrel, is

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(approved duration of use)	approved for pregnancy prevention for up to 5 years. Theoretically, use of Jaydess® beyond 3 years may occur. This has not been studied; it could result in unintended pregnancy.

Missing information

Not applicable.

2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SmPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

This medicine has special conditions and restrictions for its safe and effective use (additional risk minimisation measures). How they are implemented in each country however will depend upon agreement between the manufacturer and the national authorities.

Additional risk minimisation measures implemented are for the following risks:

Pregnancy outside of the womb (ectopic pregnancy) in case Jaydess® fails

Risk minimisation measure: Information material to health care professionals highlighting the need to tell women about the risk
Objective and rationale: Early diagnosis of ectopic pregnancy may prevent the need for serious complications and even surgery. Health care professionals need to tell women using Jaydess® about this risk and about possible symptoms of an ectopic pregnancy so that they know when to see a doctor. Proposed action: Information material highlighting the risk, and emphasizing the need to tell women using Jaydess® about this, for health care professionals inserting Jaydess®.

Potential for medication error: Inadvertent mix-up between Jaydess®, LCS16 and Mirena

Risk minimisation measure: Reminder card for the woman
Objective and rationale: Jaydess® is approved for pregnancy prevention for up to 3 years. Accidental use of Jaydess® beyond 3 years may occur if the woman does not remember which levonorgestrel intrauterine contraceptive she is using. Proposed action:

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A reminder card to include the brand name Jaydess®, date of insertion, latest date of removal, and health care professional contact details, will be provided with every Jaydess® package to be filled in by the health care professional who inserts Jaydess® and to be handed out to the patient.
Risk minimisation measure: Information material to health care professionals regarding product differences between different levonorgestrel intrauterine contraceptives
Objective and rationale: In case of uncertainty, it is possible to distinguish Jaydess® from Mirena, another levonorgestrel intrauterine contraceptive, by the little silver ring on the Jaydess® T-body which can be seen during ultrasound examination. In addition, Jaydess® can be distinguished from LCS16, another levonorgestrel intrauterine contraceptive, by the colour of the removal threads (Jaydess®: brown color, LCS16: blue color). Since information on characteristics of other products cannot be included in the formal product information documents, additional information material is developed to point out the product differences and how to distinguish them. Proposed action: Information material for health care professionals to point out the product differences and how to distinguish them.

2.6 Planned post authorisation development plan

List of studies in post authorisation development plan

Study/activity (including study number)	**Objectives**	**Safety concerns/efficacy issue addressed**	**Status**	**Planned date for submission of (interim and) final results**
EURAS-LCS12: Large observational study	Assess risk of contraceptive failure including ectopic pregnancy, PID and other clinical outcomes in Jaydess® users as compared to users of other intrauterine contraceptives in real life	Unintended pregnancy Ectopic pregnancy PID	Protocol final	Final report Q2/2021 Annual interim reports
Database study of Jaydess® use in routine clinical practice (Sweden)	To investigate how Jaydess® is used (who is using it) in routine clinical practice	Potential off-label use	Protocol final	Final report Q4/2021

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Studies which are a condition of the marketing authorisation

The EURAS-LCS12 study is a condition of the marketing authorisation in Europe.

2.7 Summary of changes to the Risk Management Plan over time

Version	Date	Changes compared to previous version
2.0	DLP 23 Dec 2013	Part II: Missing information "Use in adolescent population" deleted, results of study in adolescent Jaydess® users included Missing information "Return to fertility" deleted, results of the return-to-fertility follow-up from the pivotal clinical study included Update of information on risk factors for identified risk "uterine perforation" based on the results of large observational study with other intrauterine contraceptives Part III: Protocols of planned post-authorization studies included with updated milestones
3.0	DLP 15 Jul 2015	The RMP is updated with the LCS12/Jaydess® and LCS16 data from ongoing and completed clinical studies where applicable. Parts III-V: LCS16 included. Part II, SVII-3.1.7 Bleeding changes-minor correction of bleeding pattern data for LCS12/Jaydess® because of programing error Part III, Section 4.1-correction of the classification of PASS Study EURAS-LCS12 Part III and V: Results of the internal survey on communication materials for LCS12/Jaydess® added Part VI split into VI.1 (Jaydess®) and VI.2 (LCS16) to present the summary of the relevant data for each product separately