1. NAME OF THE MEDICINAL PRODUCT

Ecinq 30 mg film coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 30 mg ulipristal acetate.

Excipients with known effect:
Each tablet contains 240.0 mg of lactose (as monohydrate) and 1.35 mg sodium.

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Film-coated tablet
White, round, biconvex, film-coated tablet of 9.0 – 9.2 mm diameter embossed with *"U30"* on one side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Emergency contraception within 120 hours (5 days) of unprotected sexual intercourse or contraceptive failure.

4.2 Posology and method of administration

Posology

The treatment consists of one tablet to be taken orally as soon as possible, but no later than 120 hours (5 days) after unprotected intercourse or contraceptive failure.

This tablet can be taken at any time during the menstrual cycle.
If vomiting occurs within 3 hours of the tablet intake, another tablet should be taken.

If a woman's menstrual period is late or in case of symptoms of pregnancy, pregnancy should be excluded before the tablet is administered.

Special populations

Renal impairment
No dose adjustment is necessary.

Hepatic impairment
In the absence of specific studies, no alternate dose recommendations for Ecinq can be made.

Severe hepatic impairment
In the absence of specific studies, Ecinq is not recommended.

Paediatric population
There is no relevant use of ulipristal acetate for children of prepubertal age in the indication emergency contraception.

Adolescents: ulipristal acetate for emergency contraception is suitable for any woman of child bearing age, including adolescents. No differences in safety or efficacy have been shown compared to adult women aged 18 and older (see section 5.1).

Method of administration
Oral use.
The tablet can be taken with or without food.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1

4.4 Special warnings and precautions for use

Ulipristal acetate is for occasional use only. It should in no instance replace a regular contraceptive method. In any case, women should be advised to adopt a regular method of contraception.

Ulipristal acetate is not intended for use during pregnancy and should not be taken by any woman suspected or known to be pregnant. However, it does not interrupt an existing pregnancy (see section 4.6).

Ulipristal acetate does not prevent pregnancy in every case.

In case the next menstrual period is more than 7 days late, if the menstrual period is abnormal in character or if there are symptoms suggestive of pregnancy or in case of doubt, a pregnancy test should be performed. As with any pregnancy, the possibility of an ectopic pregnancy should be considered. It is important to know that the occurrence of uterine bleeding does not rule out ectopic pregnancy. Women who become pregnant after taking ulipristal acetate should contact their doctor (see section 4.6).

Ulipristal acetate inhibits or postpones ovulation (see section 5.1). If ovulation has already occurred, it is no longer effective. The timing of ovulation cannot be predicted and therefore the tablet should be taken as soon as possible after unprotected intercourse.

No data are available on the efficacy of ulipristal acetate when taken more than 120 hours (5 days) after unprotected intercourse.

Limited and inconclusive data suggest that there may be reduced efficacy of ulipristal acetate with increasing body weight or body mass index (BMI) (see section 5.1). In all women, emergency contraception should be taken as soon as possible after unprotected intercourse, regardless of the woman's body weight or BMI.

After the tablet intake menstrual periods can sometimes occur a few days earlier or later than expected. In approximately 7% of the women, menstrual periods occurred more than 7 days earlier than expected. In 18.5% of the women a delay of more than 7 days occurred, and in 4% the delay was greater than 20 days.

Concomitant use of ulipristal acetate and emergency contraception containing levonorgestrel is not recommended (see section 4.5).

Contraception after ulipristal acetate intake

Ulipristal acetate is an emergency contraceptive that decreases pregnancy risk after unprotected intercourse but does not confer contraceptive protection for subsequent acts of intercourse. Therefore, after using emergency contraception, women should be advised to use a reliable barrier method until her next menstrual period.

Although the use of ulipristal acetate for emergency contraception does not contraindicate the continued use of regular hormonal contraception, ulipristal acetate may reduce its contraceptive action (see section 4.5). Therefore, if a woman wishes to start or continue using hormonal contraception, she can do so after using ulipristal acetate, however, she should be advised to use a reliable barrier method until the next menstrual period.

Specific populations

Concomitant use of ulipristal acetate with CYP3A4 inducers is not recommended due to interaction (e.g. barbiturates (including primidone and phenobarbital), phenytoin, fosphenytoin, carbamazepine, oxcarbazepine, herbal medicinal products containing *Hypericum perforatum* (St. John's wort), rifampicin, rifabutin, griseofulvin, efavirenz, nevirapine and long-term use of ritonavir).

Use in women with severe asthma treated by oral glucocorticoid is not recommended**.**

Excipients
This medicine contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Potential for other medicinal products to affect ulipristal acetate

Ulipristal acetate is metabolized by CYP3A4 *in vitro*.

- *CYP3A4 inducers*
  In vivo results show that the administration of ulipristal acetate with a strong CYP3A4 inducer such as rifampicin markedly decreases C_{max} and AUC of ulipristal acetate by 90% or more and decreases ulipristal acetate half-life by 2.2-fold corresponding to an approximately 10-fold decrease of ulipristal acetate exposure. Concomitant use of Ecinq with CYP3A4 inducers (e.g. barbiturates (including primidone and phenobarbital), phenytoin, fosphenytoin, carbamazepine, oxcarbazepine, herbal medicinal products containing *Hypericum perforatum* (St. John's wort), rifampicin, rifabutin, griseofulvin, efavirenz and nevirapine) therefore reduces plasma concentrations of ulipristal acetate and may result in a decreased efficacy of Ecinq.
  For women who have used enzyme-inducing drugs in the past 4 weeks, Ecinq is not recommended (see section 4.4) and non-hormonal emergency contraception (i.e. a copper intrauterine device (Cu-IUD)) should be considered.

- *CYP3A4 inhibitors*
  In vivo results show that administration of ulipristal acetate with a potent and a moderate CYP3A4 inhibitor increased C_{max} and AUC of ulipristal acetate with a maximum of 2- and 5.9-fold, respectively. The effects of CYP3A4 inhibitors are unlikely to have any clinical consequences.

  The CYP3A4 inhibitor ritonavir can also have an inducing effect on CYP3A4 when ritonavir is used for a longer period. In such cases ritonavir might reduce plasma concentrations of ulipristal acetate. Concomitant use is therefore not recommended (see section 4.4). Enzyme induction wears off slowly and effects on the plasma concentrations of ulipristal acetate may occur even if a woman has stopped taking an enzyme inducer in the past 4 weeks.

Medicinal products affecting gastric pH
Administration of ulipristal acetate (10 mg tablet) together with the proton pump inhibitor esomeprazole (20 mg daily for 6 days) resulted in approximately 65% lower mean C_{max}, a delayed T_{max} (from a median of 0.75 hours to 1.0 hours) and 13% higher mean AUC. The clinical relevance of this interaction for single dose administration of ulipristal acetate as emergency contraception is not known.

Potential for ulipristal acetate to affect other medicinal products

Hormonal contraceptives
Because ulipristal acetate binds to the progesterone receptor with high affinity, it may interfere with the action of progestogen-containing medicinal products:

- Contraceptive action of combined hormonal contraceptives and progestogen-only contraception may be reduced
- Concomitant use of ulipristal acetate and emergency contraception containing levonorgestrel is not recommended (see section 4.4).

In vitro data indicate that ulipristal acetate and its active metabolite do not significantly inhibit CYP1A2, 2A6, 2C9, 2C19, 2D6, 2E1, and 3A4, at clinically relevant concentrations. After single dose administration induction of CYP1A2 and CYP3A4 by ulipristal acetate or its active metabolite is not likely. Thus, administration of ulipristal acetate is unlikely to alter the clearance of medicinal products that are metabolised by these enzymes.

P-glycoprotein (P-gp) substrates
In vitro data indicate that ulipristal acetate may be an inhibitor of P-gp at clinically relevant concentrations. Results *in vivo* with the P-gp substrate fexofenadine were inconclusive. The effects of the P-gp substrates are unlikely to have any clinical consequences.

4.6 Fertility, pregnancy and lactation

Pregnancy

Ecinq is not intended for use during pregnancy and should not be taken by any woman suspected or known to be pregnant (see section 4.2).

Ulipristal acetate does not interrupt an existing pregnancy.

Pregnancy may occasionally occur after Ecinq intake. Although no teratogenic potential has been observed, animal data are insufficient with regard to reproduction toxicity (see section 5.3). Limited human data regarding pregnancy exposure to ulipristal acetate do not suggest any safety concern. Nevertheless, it is important that any pregnancy in a woman who has taken Ecinq be reported to Aspen Healthcare Malta Limited. The purpose of this web-based registry is to collect safety information from women who have taken Ecinq during pregnancy or who become pregnant after Ecinq intake. All patient data collected will remain anonymous.

Breast-feeding

Ulipristal acetate is excreted in breast milk (see section 5.2). The effect on newborn/infants has not been studied. A risk to the breastfed child cannot be excluded. After intake of Ecinq for emergency contraception, breastfeeding is not recommended for one week. During this time it is recommended to express and discard the breast milk in order to stimulate lactation.

Fertility

A rapid return of fertility is likely following treatment with Ecinq for emergency contraception. Women should be advised to use a reliable barrier method for all subsequent acts of intercourse until

the next menstrual period.

4.7 Effects on ability to drive and use machines

Ulipristal acetate may have minor or moderate influence on the ability to drive or use machines: mild to moderate dizziness is common after Ecinq intake, somnolence and blurred vision are uncommon; disturbance in attention has been rarely reported. The patient should be informed not to drive or use machines if they are experiencing such symptoms (see section 4.8).

4.8 Undesirable effects

Summary of the safety profile

The most commonly reported adverse reactions were headache, nausea, abdominal pain and dysmenorrhea.

Safety of ulipristal acetate has been evaluated in 4,718 women during the clinical development program.

Tabulated list of adverse reactions

The adverse reactions reported in the phase III program of 2,637 women are provided in the table below.

Adverse reactions listed below are classified according to frequency and system organ class using the following convention: very common (≥1/10), common (≥ 1/100 to <1/10), uncommon (≥ 1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000) and not known (cannot be estimated from the available data).

MedDRA	Adverse reactions (frequency)		
System Organ Class	**Common**	**Uncommon**	**Rare**
Infections and infestations		Influenza	
Immune system disorders			Hypersensitivity reactions including rash, urticaria, angioedema**
Metabolism and nutrition disorders		Appetite disorders	
Psychiatric disorders	Mood disorders	Emotional disorder Anxiety Insomnia Hyperactivity disorder Libido changes	Disorientation
Nervous system disorders	Headache Dizziness	Somnolence Migraine	Tremor Disturbance in attention Dysgueusia Syncope

Eye disorders		Visual disturbance	Abnormal sensation in eye Ocular hyperaemia Photophobia
Ear and labyrinth disorders			Vertigo
Respiratory, thoracic and mediastinal disorders			Dry throat
Gastrointestinal disorders	Nausea* Abdominal pain* Abdominal discomfort Vomiting*	Diarrhoea Dry mouth Dyspepsia Flatulence	
Skin and subcutaneous tissue disorders		Acne Skin lesion Pruritus	
Musculoskeletal and connective tissue disorders	Myalgia Back pain		
Reproductive system and breast disorders	Dysmenorrhea Pelvic pain Breast tenderness	Menorrhagia Vaginal discharge Menstrual disorder Metrorrhagia Vaginitis Hot flush Premenstrual syndrome	Genital pruritus Dyspareunia Ruptured ovarian cyst Vulvovaginal pain Hypomenorrhea*
General disorders and administration site conditions	Fatigue	Chills Malaise Pyrexia	Thirst

*Symptom which could also be related to an undiagnosed pregnancy (or related complications)
**Adverse reaction from spontaneous reporting

Adolescents: the safety profile observed in women less than 18 years old in studies and post-marketing is similar to the safety profile in adults during the phase III program (Section 4.2).

Post-marketing experience: the adverse reactions spontaneously reported in post-marketing experience were similar in nature and frequency to the safety profile described during the phase III program.

Description of selected adverse reactions

The majority of women (74.6%) in the phase III studies had their next menstrual period at the expected time or within ± 7 days, while 6.8% experienced menses more than 7 days earlier than expected and 18.5% had a delay of more than 7 days beyond the anticipated onset of menses. The delay was greater than 20 days in 4 % of the women.

A minority (8.7%) of women reported intermenstrual bleeding lasting an average of 2.4 days. In a majority of cases (88.2%), this bleeding was reported as spotting. Among the women who received ulipristal acetate in the phase III studies, only 0.4% reported heavy intermenstrual bleeding.

In the phase III studies, 82 women entered a study more than once and therefore received more than one dose of ulipristal acetate (73 women enrolled twice and 9 enrolled three times). There were no safety differences in these subjects in terms of incidence and severity of adverse reactions , change in duration or volume of menses or incidence of intermenstrual bleeding.

Reporting of suspected adverse reactions
Reporting of suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the ADR Reporting Website: www.medicinesauthority.gov.mt/adrportal.

4.9 Overdose

Experience with ulipristal acetate overdose is limited. Single doses up to 200 mg have been used in women without safety concern. Such high doses were well-tolerated; however, these women had a shortened menstrual cycle (uterine bleeding occurring 2-3 days earlier than would be expected) and in some women, the duration of bleeding was prolonged, although not excessive in amount (spotting).
There are no antidotes and further treatment should be symptomatic.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Sex hormones and modulators of the genital system, emergency contraceptives. ATC code: G03AD02.
Ulipristal acetate is an orally-active synthetic selective progesterone receptor modulator which acts via high-affinity binding to the human progesterone receptor. When used for emergency contraception the mechanism of action is inhibition or delay of ovulation via suppression of the luteinizing hormone (LH) surge. Pharmacodynamic data show that even when taken immediately before ovulation is scheduled to occur (when LH has already started to rise), ulipristal acetate is able to postpone follicular rupture for at least 5 days in 78.6% of cases ($p<0.005$ vs. levonorgestrel and vs. placebo) (see Table).

Prevention of ovulation[1,§]			
	Placebo n=50	**Levonorgestrel** n=48	**Ulipristal acetate** n=34
Treatment before LH surge	n=16 0.0%	n=12 25.0%	n=8 100% p<0.005*
Treatment after LH surge but before LH peak	n=10 10.0%	n=14 14.3% NS†	n=14 78.6% p<0.005*
Treatment after LH peak	n=24 4.2%	n=22 9.1% NS†	n=12 8.3% NS*

1: Brache et al, Contraception 2013
§: defined as presence of unruptured dominant follicle five days after late follicular-phase treatment
*: compared to levonorgestrel
NS: non statistically significant
†: compared to placebo

Ulipristal acetate also has high affinity for the glucocorticoid receptor and *in vivo*, in animals,

antiglucocorticoid effects have been observed. However, in humans, no such effect has been observed even after repeat administration at the daily dose of 10 mg. It has minimal affinity to the androgen receptor and no affinity for the human estrogen or mineralocorticoid receptors.

Results from two independent randomized controlled trials (see Table) showed the efficacy of ulipristal acetate to be non-inferior to that of levonorgestrel in women who presented for emergency contraception between 0 and 72 hours after unprotected intercourse or contraceptive failure. When the data from the two trials were combined via meta- analysis, the risk of pregnancy with ulipristal acetate was significantly reduced compared to levonorgestrel (p=0.046).

Randomized controlled trial	Pregnancy rate (%) within 72h of unprotected intercourse or contraceptive failure2		Odds ratio [95% CI] of pregnancy risk, ulipristal acetate vs levonorgestrel[2]
	Ulipristal acetate	Levonorgestrel	
HRA2914-507	0.91 (7/773)	1.68 (13/773)	0.50 [0.18-1.24]
HRA2914-513	1.78 (15/844)	2.59 (22/852)	0.68 [0.35-1.31]
Meta- analysis	1.36 (22/1617)	2.15 (35/1625)	0.58 [0.33-0.99]

2: Glasier et al, Lancet 2010

Two trials provide efficacy data on ulipristal acetate used up to 120 hours after unprotected intercourse. In an open-label clinical trial, which enrolled women who presented for emergency contraception and were treated with ulipristal acetate between 48 and 120 hours after unprotected intercourse, a pregnancy rate of 2.1% (26/1241) was observed. In addition, the second comparative trial described above also provides data on 100 women treated with ulipristal acetate from 72 to 120 hours after unprotected intercourse, in whom no pregnancies were observed.

Limited and inconclusive data from clinical trials suggest a possible trend for a reduced contraceptive efficacy of ulipristal acetate with high body weight or BMI (see section 4.4). The meta-analysis of the four clinical studies conducted with ulipristral acetate presented below excluded women who had further acts of unprotected intercourse.

BMI (kg/m^2)	**Underweight 0 - 18.5**	**Normal 18.5-25**	**Overweight 25-30**	**Obese 30-**
N total	128	1866	699	467
N pregnancies	0	23	9	12
Pregnancy rate	0.00%	1.23%	1.29%	2.57%
Confidence Interval	0.00 – 2.84	0.78 – 1.84	0.59 – 2.43	1.34 – 4.45

A post-marketing observational study evaluating efficacy and safety of ulipristal acetate in adolescents aged 17 and younger showed no difference in the safety and efficacy profile compared to adult women aged 18 and older.

5.2 Pharmacokinetic properties

Absorption

Following oral administration of a single 30 mg dose, ulipristal acetate is rapidly absorbed, with a peak plasma concentration of 176 ± 89 ng/ml occurring approximately 1 hour (0.5-2.0 h) after ingestion, and with an $AUC_{0-\infty}$ of 556 ± 260 ng.h/ml.

Administration of ulipristal acetate together with a high-fat breakfast resulted in approximately 45% lower mean C_{max}, a delayed T_{max} (from a median of 0.75 hours to 3 hours) and 25% higher mean $AUC_{0-\infty}$ compared with administration in the fasted state. Similar results were obtained for the active mono-demethylated metabolite.

Distribution

Ulipristal acetate is highly bound (>98%) to plasma proteins, including albumin, alpha-l-acid glycoprotein, and high density lipoprotein.

Ulipristal acetate is a lipophilic compound and is distributed in breast milk, with a mean daily excretion of 13.35 µg [0-24 hours], 2.16 µg [24-48 hours], 1.06 µg [48-72 hours], 0.58 µg [72-96 hours], and 0.31 µg [96-120 hours].

In vitro data indicate that ulipristal acetate may be an inhibitor of BCRP (Breast Cancer Resistance Protein) transporters at the intestinal level. The effects of ulipristal acetate on BCRP are unlikely to have any clinical consequences.

Ulipristal acetate is not a substrate for either OATP1B1 or OATP1B3.

Biotransformation/elimination

Ulipristal acetate is extensively metabolized to mono-demethylated, di-demethylated and hydroxylated metabolites. The mono-demethylated metabolite is pharmacologically active. *In vitro* data indicate that this is predominantly mediated by CYP3A4, and to a small extent by CYP1A2 and CYP2A6. The terminal half-life of ulipristal acetate in plasma following a single 30 mg dose is estimated to 32.4 ± 6.3 hours, with a mean oral clearance (CL/F) of 76.8 ± 64.0 L/h.

Special populations

No pharmacokinetic studies with ulipristal acetate have been performed in females with impaired renal or hepatic function.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, and genotoxicity. Most findings in general toxicity studies were related to its mechanism of action as a modulator of progesterone and glucocorticoid receptors, with antiprogesterone activity observed at exposures similar to therapeutic levels.
Information from reproductive toxicity studies is limited due to the absence of exposure measurement in these studies. Ulipristal acetate has an embryolethal effect in rats, rabbits (at repeated doses above 1 mg/kg) and in monkeys. At these repeated doses, the safety for a human embryo is unknown. At doses which were low enough to maintain gestation in the animal species, no teratogenic effects were observed.

Carcinogenicity studies (in rats and mice) showed that ulipristal acetate is not carcinogenic.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:
Lactose monohydrate
Pregelatinised starch (Maize)

Sodium starch glycolate
Magnesium stearate

Coating:
Hypromellose (E464)
Hydroxypropylcellulose (E463)
Stearic acid (E570)
Talc (E553b)
Titanium Dioxide (E171)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store in original package in order to protect from light.

This medicine does not require any special temperature storage conditions.

6.5 Nature and contents of container

PVC-PVDC-Aluminium blister of 1 tablet.

The carton contains one transparent blister.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Aspen Healthcare Malta Limited
89, Level 0,
Triq is-Siggiewi
Siggiewi SGW2021
Malta

8. MARKETING AUTHORISATION NUMBER(S)

MA1243/00601

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 9th April 2021
Date of renewal: 27th March 2025

10. DATE OF REVISION OF THE TEXT

02/2026