ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

ORSERDU 86 mg film-coated tablets
ORSERDU 345 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

ORSERDU 86 mg film-coated tablets

Each film-coated tablet contains elacestrant dihydrochloride equivalent to elacestrant 86.3 mg.

ORSERDU 345 mg film-coated tablets

Each film-coated tablet contains elacestrant dihydrochloride equivalent to elacestrant 345 mg.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet

ORSERDU 86 mg film-coated tablets

Blue to light blue biconvex round shaped film-coated tablet with ME debossed on one side and plain face on the opposite side. Approximate diameter: 8.8 mm.

ORSERDU 345 mg film-coated tablets

Blue to light blue biconvex oval shaped film-coated tablet with MH debossed on one side and plain face on the opposite side. Approximate size: 19.2 mm (length), 10.8 mm (width).

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

ORSERDU monotherapy is indicated for the treatment of postmenopausal women, and men, with estrogen receptor (ER)-positive, HER2-negative, locally advanced or metastatic breast cancer with an activating *ESR1* mutation who have disease progression following at least one line of endocrine therapy including a CDK 4/6 inhibitor.

4.2 Posology and method of administration

Treatment with ORSERDU should be initiated by a physician experienced in the use of anticancer therapies.

Patients with ER-positive, HER2-negative advanced breast cancer should be selected for treatment with ORSERDU based on the presence of an activating *ESR1* mutation in plasma specimens, using a CE marked in vitro diagnostic (IVD) with the corresponding intended purpose. If the CE-marked IVD

is not available, the presence of an activating *ESR1* mutation in plasma specimens should be assessed by an alternative validated test.

Posology

The recommended dose is 345 mg (one 345 mg film-coated tablet), once daily.

The maximum recommended daily dose of ORSERDU is 345 mg.

Treatment should continue as long as clinical benefit is observed or until unacceptable toxicity occurs.

Missed dose
If a dose is missed, it can be taken immediately within 6 hours after the time it is usually taken. After more than 6 hours, the dose should be skipped for that day. On the next day, ORSERDU should be taken at the usual time.

Vomiting
If the patient vomits after taking the ORSERDU dose, the patient should not take an additional dose on that day and should resume the usual dosing schedule the next day at the usual time.

Dose modifications

The recommended elacestrant dose modifications for patients with adverse reactions (see section 4.8) are provided in Tables 1 and 2:

Table 1: ORSERDU dose reduction for adverse reactions

ORSERDU dose level	**Dose and schedule**	**Number and strength of tablets**
Dose reduction	258 mg once daily	Three 86 mg tablets

If further dose reduction below 258 mg once daily is required, discontinue ORSERDU.

Table 2: ORSERDU dose modification guidelines for adverse reactions

Severity	**Dose modification**
Grade 2	Consider interruption of ORSERDU until recovery to Grade ≤ 1 or baseline. Then resume ORSERDU at the same dose level.
Grade 3	Interrupt ORSERDU until recovery to Grade ≤ 1 or baseline. The dose should be reduced to 258 mg when resuming therapy. If the Grade 3 toxicity recurs, interrupt ORSERDU until recovery to Grade ≤ 1 or baseline. The reduced dose of 258 mg may be resumed if at the discretion of the treating physician if the patient is benefiting from treatment. If a Grade 3 or intolerable adverse reaction recurs, permanently discontinue ORSERDU.
Grade 4	Interrupt ORSERDU until recovery to Grade ≤ 1 or baseline. The dose should be reduced to 258 mg when resuming therapy. If a Grade 4 or intolerable adverse reaction recurs, permanently discontinue ORSERDU.

Use of ORSERDU with CYP3A4 inhibitors
Concomitant use of strong or moderate CYP3A4 inhibitors should be avoided and an alternative concomitant medicinal product with no or minimal potential to inhibit CYP3A4 should be considered.

If a strong CYP3A4 inhibitor must be used, the elacestrant dose should be reduced to 86 mg once daily with careful monitoring of tolerability. If a moderate CYP3A4 inhibitor must be used, the elacestrant dose should be reduced to 172 mg once daily with careful monitoring of tolerability.

Subsequent dose reduction to 86 mg once daily may be considered with moderate CYP3A4 inhibitors based on tolerability.

If the CYP3A4 inhibitor is discontinued, the elacestrant dose should be increased to the dose used prior to the initiation of the CYP3A4 inhibitor (after 5 half-lives of the CYP3A4 inhibitor) (see sections 4.4, 4.5 and 5.2).

No dose adjustments are required for coadministration of ORSERDU with mild CYP3A4 inhibitors (see section 4.5).

Use of ORSERDU with CYP3A4 inducers
Concomitant use of strong or moderate CYP3A4 inducers should be avoided and an alternative concomitant medicinal product with no or minimal potential to induce CYP3A4 should be considered.

If a strong or moderate CYP3A4 inducer must be used for a short duration of time (i.e. ≤ 3 days) or intermittently (i.e. treatment periods ≤ 3 days separated by at least 2 weeks or 1 week + 5 half-lives of the CYP3A4 inducer, whichever is longer), continue elacestrant without increasing the dose.

No dose adjustments are required for coadministration of ORSERDU with mild CYP3A4 inducers (see sections 4.4, 4.5 and 5.2).

Special populations

Elderly
No dose adjustment is required on the basis of patient age. Limited data are available in patients ≥ 75 years of age (see section 5.2).

Hepatic impairment
No dose adjustment is recommended for patients with mild hepatic impairment *(Child-Pugh A).* In patients with moderate hepatic impairment *(Child-Pugh B)*, ORSERDU dose should be reduced to 258 mg. Elacestrant has not been studied in patients with severe hepatic impairment *(Child-Pugh C)*, therefore no dose recommendation can be made for patients with severe hepatic impairment (see section 4.4).

Renal impairment
No dose adjustment in subjects with renal impairment is necessary. Elacestrant has not been studied in patients with severe renal impairment, therefore no dose recommendation can be made for patients with severe renal impairment (see section 5.2).

Paediatric population
The safety and efficacy of ORSERDU in children from birth to 18 years of age has not been established. No data are available.

Method of administration

ORSERDU is for oral use.

The tablets should be swallowed whole. They should not be chewed, crushed or split prior to swallowing. Patients should take their dose of ORSERDU at approximately the same time each day. ORSERDU should be administered with a light meal. Administration with food may also reduce nausea and vomiting (see section 5.2).

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

Hepatic impairment
ORSERDU is metabolised by the liver, and impaired hepatic function can increase the risk for adverse reactions. Therefore, ORSERDU should be used cautiously in patients with hepatic impairment and patients should be regularly and closely monitored for adverse reactions. Administration of elacestrant should be undertaken with caution at a dose of 258 mg once daily in patients with moderate hepatic impairment (see section 4.2). In the absence of clinical data, elacestrant is not recommended in patients with severe hepatic impairment (Child-Pugh C) (see section 4.2).

Concomitant use with CYP3A4 inhibitors
Concomitant administration of ORSERDU with strong CYP3A4 inhibitors including, but not limited to: clarithromycin, indinavir, itraconazole, ketoconazole, lopinavir/ritonavir, nefazodone, nelfinavir, posaconazole, saquinavir, telaprevir, telithromycin, voriconazole, and grapefruit or grapefruit juice should be avoided. An alternative concomitant medicinal product with no or minimal potential to inhibit CYP3A4 should be considered. If the strong CYP3A4 inhibitor cannot be avoided, ORSERDU dose adjustment should be applied (see sections 4.2 and 4.5).

Concomitant administration of ORSERDU with moderate CYP3A4 inhibitors including, but not limited to: aprepitant, ciprofloxacin, conivaptan, crizotinib, cyclosporine, diltiazem, dronedarone, erythromycin, fluconazole, fluvoxamine, grapefruit juice, imatinib, isavuconazole, tofisopam and verapamil should be avoided. An alternative concomitant medicinal product with no or minimal potential to inhibit CYP3A4 should be considered. If the moderate CYP3A4 inhibitor cannot be avoided, ORSERDU dose adjustment should be applied (see sections 4.2 and 4.5).

Concomitant use with CYP3A4 inducers
Concomitant administration of ORSERDU with strong CYP3A4 inducers including, but not limited to: phenytoin, rifampicin, carbamazepine and St John's Wort (Hypericum perforatum) should be avoided. An alternative concomitant medicinal product with no or minimal potential to induce CYP3A4 should be considered. If the strong CYP3A4 inducer cannot be avoided, ORSERDU dose adjustment should be applied (see sections 4.2 and 4.5).

Concomitant administration of ORSERDU with moderate CYP3A4 inducers including, but not limited to: bosentan, cenobamate, dabrafenib, efavirenz, etravirine, lorlatinib, phenobarbital, primidone and sotorasib should be avoided. An alternative concomitant medicinal product with no or minimal potential to induce CYP3A4 should be considered. If the moderate CYP3A4 inducer cannot be avoided, ORSERDU dose adjustment should be applied (see sections 4.2 and 4.5).

Thromboembolic events
Thromboembolic events are commonly observed in patients with advanced breast cancer and have been observed in clinical studies with ORSERDU (see section 4.8). This should be taken into consideration when prescribing ORSERDU to patients at risk.

4.5 Interaction with other medicinal products and other forms of interaction

ORSERDU is primarily metabolised by CYP3A4 and is a substrate of the Organic Anion Transporting Polypeptide 2B1 (OATP2B1). ORSERDU is an inhibitor of P-glycoprotein (P-gp) and Breast Cancer Resistance Protein (BCRP) efflux transporters.

<u>Effect of other medicinal products on ORSERDU</u>

CYP3A4 Inhibitors
Co-administration of the strong CYP3A4 inhibitor itraconazole (200 mg once daily for 7 days) with ORSERDU (172 mg once daily for 7 days) increased elacestrant plasma exposure (AUC_{inf}) and the peak concentration (C_{max}) in healthy subjects 5.3 and 4.4-fold, respectively.

Physiologically based pharmacokinetic (PBPK) simulations in cancer patients suggested that the concomitant administration of multiple daily doses of elacestrant 345 mg and itraconazole 200 mg may increase elacestrant steady-state AUC and C_{max} 5.5- and 3.9-fold, respectively, which may increase the risk of adverse reactions.

PBPK simulations in cancer patients suggested that concomitant administration of multiple daily doses of elacestrant 345 mg with moderate CYP3A4 inhibitors may increase elacestrant steady-state AUC and C_{max} by 2.3- and 1.9-folds, respectively, with fluconazole (200 mg once daily), and by 3.9- and 3.0-folds, respectively, with erythromycin (500 mg four times a day), which may increase the risk of adverse reaction.

CYP3A4 Inducers
Co-administration of the strong CYP3A4 inducer rifampicin (600 mg once daily for 7 days) with a single dose of ORSERDU 345 mg decreased elacestrant plasma exposure (AUC_{inf}) and the peak concentration (C_{max}) in healthy subjects by 86% and 73%, respectively, which may decrease elacestrant activity.

PBPK simulations in cancer patients suggested that the concomitant administration of multiple daily doses of elacestrant 345 mg and rifampicin 600 mg may decrease elacestrant steady-state AUC and C_{max} by 84% and 77%, respectively, which may decrease elacestrant activity.

PBPK simulations in cancer patients suggested that the concomitant administration of multiple daily doses of elacestrant 345 mg and the moderate CYP3A4 inducer efavirenz (600 mg) may decrease elacestrant steady-state AUC and C_{max} by 57% and 52%, respectively, which may decrease elacestrant activity.

OATP2B1 inhibitors
Elacestrant is a substrate of OATP2B1 *in vitro*. As it cannot be excluded that the coadministration of OATP2B1 inhibitors may increase the exposure of elacestrant, which may increase the risk of adverse reactions, caution is recommended in case of concomitant use of ORSERDU with OATP2B1 inhibitors.

Effect of ORSERDU on other medicinal products

P-gp substrates
Co-administration of ORSERDU (345 mg, single dose) with digoxin (0.5 mg, single dose) increased digoxin exposure by 27% for C_{max} and 13% for AUC. Digoxin administration should be monitored and its dose reduced as necessary.

Concomitant use of ORSERDU with other P-gp substrates may increase their concentrations, which may increase the adverse reactions associated with the P-gp substrates. The dose of coadministered P-gp substrates should be reduced according to their Summary of Product Characteristics.

BCRP substrates
Co-administration of ORSERDU (345 mg, single dose) with rosuvastatin (20 mg, single dose) increased rosuvastatin exposure by 45% for C_{max} and 23% for AUC. Rosuvastatin administration should be monitored and its dose reduced as necessary.

Concomitant use of ORSERDU with other BCRP substrates may increase their concentrations, which may increase the adverse reactions associated with the BCRP substrates. The dose of coadministered BCRP substrates should be reduced according to their Summary of Product Characteristics.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential/Contraception in males and females

ORSERDU should not be used during pregnancy or in women of childbearing potential not using contraception. Based on the mechanism of action of elacestrant and findings from reproductive toxicity studies in animals, ORSERDU can cause foetal harm when administered to pregnant women. Females of reproductive potential should be advised to use effective contraception during treatment with ORSERDU and one week after the last dose.

Pregnancy

There are no data from the use of elacestrant in pregnant women. Studies in animals have shown reproductive toxicity (see section 5.3). ORSERDU should not be used during pregnancy or in women of childbearing potential not using contraception. The pregnancy status of females of reproductive potential should be verified prior to starting treatment with ORSERDU. If pregnancy occurs while taking ORSERDU, the patient must be informed of the potential hazard to the foetus and potential risk of miscarriage.

Breast-feeding

It is unknown whether elacestrant/metabolites are excreted in human milk. Because of the potential for serious adverse reactions in the breast-fed infant, it is recommended that lactating women should not breast-feed during treatment with ORSERDU and one week after the last dose of ORSERDU.

Fertility

Based on findings from animal studies (see section 5.3) and its mechanism of action, ORSERDU may impair fertility in females and males of reproductive potential.

4.7 Effects on ability to drive and use machines

ORSERDU has no or negligible influence on the ability to drive and use machines. However, since fatigue, asthenia, and insomnia have been reported in some patients taking elacestrant (see section 4.8), caution should be observed by patients who experience those adverse reactions when driving or operating machinery.

4.8 Undesirable effects

Summary of the safety profile

The most common (≥ 10%) adverse reactions with ORSERDU were nausea, triglycerides increased, cholesterol increased, vomiting, fatigue, dyspepsia, diarrhoea, calcium decreased, back pain, creatinine increased, arthralgia, sodium decreased, constipation, headache, hot flush, abdominal pain, anaemia, potassium decreased, and alanine aminotransferase increased. The most common Grade ≥3 (≥2%) adverse reactions of elacestrant were nausea (2.7%), AST increased (2.7%), ALT increased (2.3%), anaemia (2%), back pain (2%), and bone pain (2%).

Serious adverse reactions reported in ≥ 1% of patients included nausea, dyspnoea, and thromboembolism (venous).

Adverse reactions leading to discontinuation in ≥ 1% of patients included nausea and decreased appetite.

Adverse reactions leading to dose reduction in ≥ 1% of patients included nausea.

Adverse reactions leading to dose interruption in ≥ 1% of patients were nausea, abdominal pain, alanine aminotransferase increased, vomiting, rash, bone pain, decreased appetite, aspartate aminotransferase increased, and diarrhoea.

Tabulated list of adverse reactions

Adverse reactions described in the list below reflect exposure to elacestrant in 301 patients with breast cancer in three open label studies (RAD1901-105, RAD1901-106, and RAD1901-308) in which patients received elacestrant 400 mg once daily as a single agent. The frequencies of adverse reactions are based on all-cause adverse event frequencies identified in patients exposed to elacestrant at the recommended dose in the target indication, whereas frequencies for changes in laboratory parameters are based on worsening from baseline by at least 1 grade and shifts to ≥ grade 3. The median duration of treatment was 85 days (range 5 to 1288).

The adverse reaction frequencies from clinical trials are based on all-cause adverse event frequencies, where a proportion of the events for an adverse reaction may have other causes than the drug, such as the disease, other medication or unrelated causes.

The following convention is used for the classification of the frequency of an adverse drug reaction (ADR) and is based on the Council for International Organizations of Medical Sciences (CIOMS) guidelines: 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); not known (cannot be estimated from the available data).

Table 3. Adverse reactions in patients treated with elacestrant monotherapy 345 mg in metastatic breast cancer

	Elacestrant N= 301	
Infections and infestations	Common	Urinary tract infection
Blood and lymphatic system disorders	Very common	Anaemia
	Common	Lymphocyte count decreased
Metabolism and nutrition disorders	Very common	Decreased appetite
Psychiatric disorders	Common	Insomnia
Nervous system disorder	Very common	Headache
	Common	Dizziness, Syncope
Vascular disorders	Very common	Hot flush*
	Uncommon	Thromboembolism (venous)*
Respiratory, thoracic and mediastinal disorders	Common	Dyspnoea, Cough*
Gastrointestinal disorders	Very common	Nausea, Vomiting, Diarrhoea, Constipation, Abdominal pain*, Dyspepsia*
	Common	Stomatitis
Hepatobiliary disorders	Uncommon	Acute hepatic failure
Skin and subcutaneous tissue disorders	Common	Rash*
Musculoskeletal and connective tissues disorders	Very common	Arthralgia, Back pain
	Common	Pain in extremity, Musculoskeletal chest pain *, Bone pain
General disorders and administration site conditions	Very common	Fatigue
	Common	Asthenia

	Elacestrant N= 301	
Investigations	Very common	Aspartate aminotransferase increased, Triglycerides increased, Cholesterol increased, Alanine aminotransferase increased, Calcium decreased, Creatinine increased, Sodium decreased, Potassium decreased
	Common	Blood alkaline phosphatase increased

*Incidence represents a grouping of similar terms.
ADRs listed by system organ class and by decreasing frequency..

Description of selected adverse reactions

Nausea
Nausea was reported in 35% of patients. Grade 3-4 nausea events were reported in 2.5% of patients. Nausea was generally reported early, with a median time to the first onset 14 days (range: 1 to 490 days). Nausea occurred more frequently in the first cycle and from Cycle 2 onward, the incidence of nausea was generally lower in subsequent cycles (i.e., over time). Prophylactic treatment for nausea was prescribed for 12 (5%) subjects in the elacestrant arm and 28 (11.8%) received an antiemetic for the treatment of nausea during the on-treatment period.

Elderly
In the RAD1901-308 study, 104 patients who received elacestrant were ≥ 65 years and 40 patients were ≥ 75 years. Gastrointestinal disorders were reported more frequently in patients aged ≥ 75 years. Monitoring of treatment emergent adverse reactions by the treating physician, should include consideration of the patient's age and comorbidities, when selecting personalised interventions.

Reporting of suspected adverse reactions
Reporting 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 national reporting system listed in Appendix V.

4.9 Overdose

The highest dose of ORSERDU administered in clinical studies was 1000 mg per day. The adverse drug reactions reported in association with doses higher than the recommended dose were consistent with the established safety profile (see section 4.8). The frequency and severity of gastrointestinal disorders (abdominal pain, nausea, dyspepsia and vomiting) appeared to be dose-related. There is no known antidote for an overdose of ORSERDU. Patients should be closely monitored and treatment of overdose should consist of supportive treatment.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Endocrine therapy, anti estrogen, ATC code: L02BA04

Mechanism of action

Elacestrant, a tetrahydronaphthalene compound, is a potent, selective and orally active estrogen receptor-α (ERα) antagonist and degrader.

Pharmacodynamic effects

Elacestrant inhibits the estradiol-dependent and independent growth of ERα-positive breast cancer cells, including models harbouring estrogen receptor 1 (*ESR1*) gene mutations. Elacestrant displayed potent antitumor activity in patient derived xenograft models previously exposed to multiple endocrine therapies, harbouring wild type *ESR1* or *ESR1* gene mutations in the ligand binding domain.

In patients with ER+ advanced breast cancer with a median of 2.5 prior lines of endocrine therapy, dosed with elacestrant dihydrochloride 400 mg (345 mg of elacestrant) daily, median reduction in tumour 16α-18F-fluoro-17β-estradiol (FES) uptake from baseline to Day 14 was 88.7% demonstrating reduced ER availability and antitumor activity measured by FES-PET/CT in patients with prior endocrine therapies.

Clinical efficacy and safety

The efficacy and safety of ORSERDU in patients with ER+/HER2- advanced breast cancer following prior endocrine therapy in combination with a CDK4/6 inhibitor was evaluated in RAD1901-308, a randomised, open-label, active-controlled, multicenter trial which compared ORSERDU with standard of care (SOC) (fulvestrant for patients who received prior aromatase inhibitors in the metastatic setting or aromatase inhibitors for patients who received fulvestrant in the metastatic setting). Eligible patients included post-menopausal women and men whose disease had relapsed or progressed on at least 1 and no more than 2 prior lines of endocrine therapy. All patients were required to have Eastern Cooperative Oncology Group (ECOG)performance status of 0 or 1, and evaluable lesions per Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1, i.e., measurable disease or bone only disease with evaluable lesions. Prior endocrine therapy must have included a combination with CDK4/6 inhibitor therapy and no more than 1 prior line of cytotoxic chemotherapy for metastatic breast cancer. Patients were required to be appropriate candidates for endocrine monotherapy. Patients with presence of symptomatic metastatic visceral disease, patients with cardiac comorbidity, and patients with severe hepatic impairment were excluded.

A total of 478 patients were randomised 1:1 to daily oral administration of 400 mg of elacestrant dihydrochloride (345 mg of elacestrant) or standard of care (SOC) (239 on elacestrant and 239 on SOC), including a total of 228 patients (47.7%) with ESR1 mutations at baseline (115 patients on elacestrant and 113 patients on SOC). Among the 239 patients randomised to the SOC arm, 166 received fulvestrant, and 73 received an aromatase inhibitor that included anastrozole, letrozole or exemestane. Randomisation was stratified by *ESR1* mutations status (ESR1-mut vs ESR1-mut-nd [no ESR1 mutations detected]), prior treatment with fulvestrant (yes vs no), and visceral metastasis (yes vs no). *ESR1* mutational status was determined by blood circulating tumor deoxyribonucleic acid (ctDNA) using the Guardant360 CDx assay and was limited to *ESR1* missense mutations in the ligand binding domain (between codons 310 to 547).

The median age of patients (ORSERDU vs standard of care) at baseline was 63.0 years (range of 24-89) vs 63.0 (range of 32-83) and 45.0% were over 65 (43.5 vs 46.4). Most patients were women (97.5% vs 99.6%) and most patients were white (88.4% vs 87.2%), followed by Asian (8.4% vs 8.2%), Black or African American (2.6% vs 4.1%), and Other/Unknown (0.5% vs 0.5%). Baseline ECOG performance status was 0 (59.8% vs 56.5%), 1 (40.2% vs 43.1%) or > 1 (0% vs 0.4%). Patient demographics for those with *ESR1*-mutated tumors were generally representative of the broader study population. The median duration of exposure to ORSERDU was 2.8 months (range: 0.4 to 24.8).

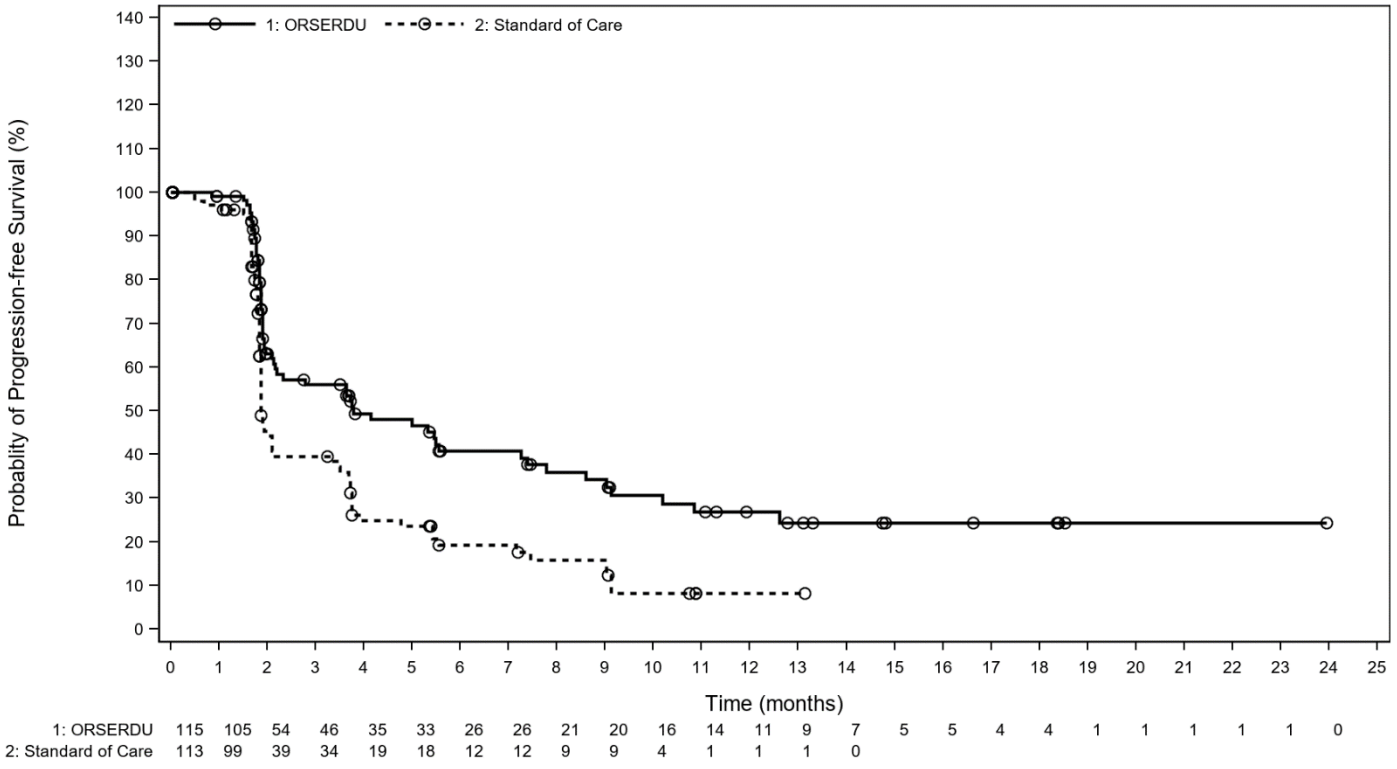
The primary efficacy endpoint was progression-free survival (PFS) as assessed by IRC (Independent Review Committee) in all patients, i.e., including patients with an *ESR1* mutation, and in patients with *ESR1* mutations. A statistically significant PFS benefit was observed in all patients with a median PFS of 2.79 months in the Orserdu arm as compared with 1.91 months in the standard of care arm (HR= 0.70, 95% CI: 0.55, 0.88). Efficacy results are presented in Table 4 and Figure 1 for patients with *ESR1* mutations.

Table 4: Efficacy results among patients with *ESR1* mutations (evaluated by a blinded imaging review committee)

	ORSERDU	**Standard of care**
Progression-free survival (PFS)	**N = 115**	**N = 113**
Number of PFS events, n (%)	62 (53.9)	78 (69.0)
Median PFS months* (95% CI)	3.78 (2.17, 7.26)	1.87 (1.87, 2.14)
Hazard ratio** (95% CI)	0.546 (0.387, 0.768)	
p-value (stratified log-rank)	0.0005	
Overall survival (OS)	**N = 115**	**N = 113**
Number of OS events, n (%)	61 (53)	60 (53.1)
Median OS months* (95% CI)	24.18 (20.53, 28.71)	23.49 (15.64, 29.90)
Hazard ratio** (95% CI)	0.903 (0.629, 1.298)	

CI=confidence interval; *ESR1*=estrogen receptor 1; PFS=progression-free survival.
*Kaplan-Meir estimate; 95% CI based on the Brookmeyer-Crowley method using a linear transformation.
**From a Cox proportional hazards model stratified by prior treatment with fulvestrant (yes vs no), and visceral metastasis (yes vs no).
Data cut-off dates are 06 September 2021 for PFS and 02 September 2022 for OS.

Figure 1: PFS in patients with an *ESR1* mutation (evaluated by a blinded imaging review committee)



Paediatric population

The European Medicines Agency has waived the obligation to submit the results of studies with ORSERDU in all subsets of the paediatric population in breast cancer (see section 4.2).

5.2 Pharmacokinetic properties

The elacestrant oral bioavailability is approximately 10%. Steady state is reached by Day 6 following once daily dosing. C_{max} and AUC increase slightly more than proportional to dose for doses ≥ 50 mg (salt form).

Absorption

Following oral administration, elacestrant was rapidly absorbed, reaching C_{max} within 1-4 hours. The geometric mean C_{max} was 52.86 ng/mL (35.2% coefficient of variation [CV%]) and AUC_{inf} was 1566 ng*h/mL (38.4% CV) after single dose administration of 345 mg of elacestrant in fed conditions. At steady state, the median [min, max] plasma concentration at 4h post-dose (C_{4h}) and AUC are predicted to be 108 ng/mL [27.5 – 351] and 2190 ng*h/mL [461 – 8470], respectively.

Effect of food
Administration of elacestrant 345 mg tablet with a high-fat high-calorie meal increased C_{max} and AUC by 40% and 20%, respectively, as compared to fasted administration. When the tablet was co-administered with a light meal, C_{max} and AUC increased in a similar fashion, i.e., by 30 and 20%, respectively. Ingestion with food may reduce gastrointestinal adverse effects.

Distribution

Plasma protein binding of elacestrant is > 99% and independent of concentration and hepatic impairment status. Elacestrant penetrates the blood brain barrier in a dose-dependent manner. Following once daily administration of elacestrant for 7 consecutive days, median concentrations of elacestrant in the cerebrospinal fluid were 0.0966 ng/mL and 0.155 ng/mL at the doses of 200 and 500 mg, respectively.

Based on population pharmacokinetic analysis, elacestrant is extensively distributed in the tissues with an apparent peripheral volume of distribution of 5411 L. The apparent central volume of distribution of elacestrant at steady state is 422 L.

Biotransformation

Elacestrant was a minor (< 10% of plasma radioactivity) component in human plasma. 4-[2-(Ethylamino)ethyl]benzoic acid (EAEBA) glucuronide was a major human plasma metabolite (about 41% of plasma radioactivity). Elacestrant is primarily metabolised by CYP3A4 with a potential small contribution by CYP2A6 and CYP2C9.

Elimination

The half-life of elacestrant is predicted to be approximately 30 hours. After a single dose, the mean (% CV) clearance of elacestrant was 220.3 L/hr (38.4%). At steady state, the mean (% CV) clearance of elacestrant is predicted to be 186 L/hr (43.5%).

Following a single oral dose of 345 mg radiolabeled elacestrant, 81.5% (majority as unchanged) was recovered in feces and 7.53% (trace as unchanged) was recovered in urine. Elacestrant renal clearance is very low (≤ 2.3 mL/min) and it was eliminated by oxidative metabolism and fecal excretion.

Special populations

Effect of age, weight and gender
From analyses of population pharmacokinetic data in cancer patients, no dose adjustment is warranted based on body weight, age, and gender.

Hepatic impairment
The C_{max} and AUC values were similar between subjects in the mild hepatic impairment group (Child-Pugh A) and the normal hepatic function group upon single dose administration of elacestrant 176 mg. There were significant increases in AUC_{0-t} (76%) and $AUC_{0-\infty}$ (83%) in the moderate hepatic impairment group (Child-Pugh B) compared to the normal hepatic function group. The C_{max} values were similar between the normal and moderate impairment groups.

The geometric mean elimination half-life ($t_{1/2}$) tended to increase with increasing severity of hepatic impairment. Elacestrant has not been studied in subjects with severe hepatic impairment (Child-Pugh C).

In PBPK modeling simulation of elacestrant at 345 mg, the steady state AUC and C_{max} were predicted to increase by 2.14- and 1.92-fold, respectively, in subjects with moderate hepatic impairment compared to patients with normal hepatic function.

5.3 Preclinical safety data

Elacestrant displayed low acute toxicity. In repeated dose toxicity studies in rats and monkeys, the antiestrogenic activity of elacestrant was responsible for the effects seen, particularly in the female reproductive system, but also in other organs sensitive to hormones such as mammary gland, pituitary and testes. Sporadic emesis and diarrhoea were recorded in monkeys. In addition, in long-term studies (26 weeks in rats and 39 weeks in cynomolgus monkeys), increased vacuolation of the mucosal epithelium of the non-glandular stomach were observed in rats and vacuolated macrophage infiltrates in the small intestine were recorded in both rats and monkeys. In monkeys this effect occurred at a level of systemic exposure of about 70% of the human exposure.

Elacestrant showed no genotoxic potential in the Ames test, chromosomal aberrations in human lymphocytes and in the micronucleus assay in rats.

Fertility studies in animals have not been conducted. In repeated-dose toxicity studies effects related to fertility were observed in rat and monkey female reproductive tract; these effects occurred below human exposures at MRHD (maximum recommended dose). Decreased cellularity of Leydig cells in rat testes was also observed at exposure levels 2.7-fold higher than in humans.

In embryo-foetal development studies in rats, oral administration of elacestrant resulted in maternal toxicity (body weight loss, low food consumption, red vulvar discharge) and increased resorptions, increased post-implantation loss, and reduced number of live foetuses and foetal variations and malformations below human exposures at MHRD.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core

Microcrystalline cellulose [E460]
Silicified microcrystalline cellulose
Crospovidone [E1202]
Magnesium stearate [E470b]
Colloidal silicon dioxide [E551]

Film-coating

Opadry II 85F105080 Blue containing polyvinyl alcohol [E1203], titanium dioxide [E171], macrogol [E1521], talc [E553b] and brilliant blue FCF aluminium lake [E133]

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

ORSERDU is packaged in aluminium-aluminium blisters packed into a cardboard box.

ORSERDU 86 mg film-coated tablets

Packs containing 28 film-coated tablets: 4 blisters with 7 tablets each

ORSERDU 345 mg film-coated tablets

Packs containing 28 film-coated tablets: 4 blisters with 7 tablets each

6.6 Special precautions for disposal

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

7. MARKETING AUTHORISATION HOLDER

Stemline Therapeutics B.V.
Basisweg 10
1043 AP Amsterdam
The Netherlands

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/23/1757/001
EU/1/23/1757/002

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation:15 September 2023

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu

ANNEX II

A. MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturers responsible for batch release

Stemline Therapeutics B.V.
Basisweg 10
1043 AP Amsterdam
The Netherlands

Berlin Chemie AG
Glienicker Weg 125
12489 Berlin
Germany

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

The marketing authorisation holder (MAH) shall submit the first PSUR for this product within 6 months following authorisation.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

ORSERDU 86 mg film-coated tablets
elacestrant

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains 86.3 mg elacestrant (as dihydrochloride).

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Film-coated tablet
28 film-coated tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Stemline Therapeutics B.V.
Basisweg 10
1043 AP Amsterdam
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/23/1757/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

ORSERDU 86 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER

1. NAME OF THE MEDICINAL PRODUCT

ORSERDU 86 mg film-coated tablets
elacestrant

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Stemline Therapeutics B.V.

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

ORSERDU 345 mg film-coated tablets
elacestrant

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains 345 mg elacestrant (as dihydrochloride).

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Film-coated tablet
28 film-coated tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Stemline Therapeutics B.V.
Basisweg 10
1043 AP Amsterdam
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/23/1757/002

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

ORSERDU 345 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER

1. NAME OF THE MEDICINAL PRODUCT

ORSERDU 345 mg film-coated tablets.
elacestrant

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Stemline Therapeutics B.V.

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

ORSERDU 86 mg film-coated tablets
ORSERDU 345 mg film-coated tablets
elacestrant

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What ORSERDU is and what it is used for

What ORSERDU is

ORSERDU contains the active substance elacestrant which belongs to a group of medicines called selective estrogen receptor degraders.

What ORSERDU is used for

This medicine is used to treat postmenopausal women and adult men who have a specific type of breast cancer that is advanced or has spread to other parts of the body (metastatic). It can be used to treat breast cancer that is estrogen receptor (ER)-positive, meaning that the cancer cells have receptors for the hormone oestrogen on their surface, and that is human epidermal growth factor receptor 2 (HER2)-negative, meaning that cancer cells have no or only a small amount of this receptor on their surface. ORSERDU is used as monotherapy (used on its own) in patients whose cancer has not responded to or progressed further following at least one line of hormonal treatment including a CDK 4/6 inhibitor and who have certain changes (mutations) in a gene called *ESR1*.

Your doctor will take a sample of your blood, which will be tested for these *ESR1* mutations. A positive result is required for initiation of treatment with ORSERDU.

How ORSERDU works

Oestrogen receptors are a group of proteins found inside the cells. They are activated when the hormone oestrogen binds to them. By binding to these receptors, oestrogen can in some cases stimulate cancer cells to grow and multiply. ORSERDU contains the active substance elacestrant that binds to the oestrogen receptors in the cancer cells and stops them from working. By blocking and

destroying oestrogen receptors, ORSERDU can reduce the growth and spread of breast cancer and help to kill cancer cells.

If you have any questions about how ORSERDU works or why this medicine has been prescribed for you, ask your doctor, pharmacist, or nurse.

2. What you need to know before you take ORSERDU

Do not use ORSERDU if:
- you are allergic to elacestrant or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor or pharmacist before taking ORSERDU

- if you have any liver disease (examples of liver disease include cirrhosis (scarring of the liver), liver impairment or cholestatic jaundice (yellowing of the skin and eyes due to a reduced flow of bile from the liver)). Your doctor will monitor you regularly and closely for adverse reactions.

By having advanced breast cancer you may have an increased risk of developing blood clots in your veins (a type of blood vessel). It is unknown if ORSERDU also increases this risk.

Children and adolescents
ORSERDU should not be given to children and adolescents under 18 years of age.

Other medicines and ORSERDU
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This is because ORSERDU can affect the way some other medicines work. Also, some other medicines can affect the way ORSERDU works.

Tell your doctor if you take any of the following medicines:
- antibiotics to treat bacterial infections (such as ciprofloxacin, clarithromycin, erythromycin, rifampicin, telithromycin)
- medicine for low blood sodium (such as conivaptan)
- medicines to treat depression (such as nefazodone or fluvoxamine)
- medicine to treat anxiety and alcohol withdrawal (such as tofisopam).
- medicines for the treatment of other cancers (such as crizotinib, dabrafenib, imatinib, lorlatinib, or sotorasib)
- medicines for high blood pressure or chest pain (such as bosentan, diltiazem or verapamil)
- medicines for fungal infections (such as fluconazole, isavuconazole, itraconazole, ketoconazole, posaconazole, or voriconazole)
- medicines for HIV infection (such as efavirenz, etravirine, indinavir, lopinavir, ritonavir, nelfinavir, saquinavir, or telaprevir)
- medicines to treat irregular heartbeats (such as digoxin, dronedarone, or quinidine)
- medicines used in organ transplantation to prevent rejection (such as cyclosporine)
- medicines to prevent cardiovascular events and to treat high levels of cholesterol (such as rosuvastatin)
- medicines used to prevent seizures (such as carbamazepine, cenobamate, phenobarbital, phenytoin, or primidone)
- medicines to treat vomiting (such as aprepitant)
- herbal medicines used to treat depression containing St. John’s wort

ORSERDU with food and drink
Do not drink grapefruit juice or eat grapefruit while on treatment with ORSERDU as it may change the amount of ORSERDU in your body and increase the side effects of ORSERDU (see Section 3 “How to take ORSERDU”.

Pregnancy, breast-feeding and fertility
This medicine should only be used in postmenopausal women and in men.

Pregnancy
ORSERDU may harm an unborn baby. You must not take ORSERDU if you are pregnant, think you may be pregnant or are planning to have a baby. If you think you may be pregnant or planning to have a baby, ask your doctor, or pharmacist for advice before using this medicine.

If you are a woman who could become pregnant, you should use effective contraception while you are being treated with ORSERDU and for one week after stopping treatment with ORSERDU. Ask your doctor for suitable methods. If you are a woman who could become pregnant, your doctor will rule out an existing pregnancy before starting you on treatment with ORSERDU. This may include having a pregnancy test.

Breast-feeding
You must not breast-feed while on treatment with ORSERDU and for one week after the last dose of ORSERDU. During treatment, your doctor will discuss the potential risks of taking ORSERDU during pregnancy or breast-feeding.

Fertility
ORSERDU may impair fertility in women and men.

Driving and using machines
ORSERDU has no or negligible influence on the ability to drive and use machines. However, since fatigue, weakness, and difficulty sleeping have been reported in some patients taking elacestrant, caution should be observed by patients who experience those adverse reactions when driving or operating machinery.

3. How to take ORSERDU

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

ORSERDU should be taken with food, just avoid grapefruit and grapefruit juice during treatment with ORSERDU (see section 2 “ORSERDU with food and drink”). Taking ORSERDU with food may reduce nausea and vomiting.

Take your dose of this medicine at approximately the same time each day. This will help you to remember to take your medicine.

ORSERDU tablets should be swallowed whole. They should not be chewed, crushed or split prior to swallowing. Do not take a tablet that is broken, cracked or otherwise damaged.

The recommended dose of ORSERDU is 345 mg (one 345 mg film-coated tablet) once daily. Your doctor will tell you exactly how many tablets to take. In certain situations (i.e. in case of liver problems, side effects, or if you are also using certain other medicines your doctor may instruct you to take a lower dose of ORSERDU, e.g. 258 mg (3 tablets of 86 mg) once daily, 172 mg (2 tablets of 86 mg) once daily, or 86 mg (1 tablet of 86 mg) once daily.

If you take more ORSERDU than you should
Tell your doctor or pharmacist if you think you have accidentally taken more ORSERDU than you should. He or she will decide what to do.

If you forget to take ORSERDU
If you forget to take a dose of ORSERDU, take it as soon as you remember. You may still take a forgotten dose up to 6 hours after the time you should have taken it. If more than 6 hours have passed or if you vomit after taking the dose, skip the dose for that day and take the next dose at your usual time the next day. Do not take a double dose to make up for the one that you missed.

If you stop taking ORSERDU
Do not stop using this medicine without talking to your doctor or pharmacist. If treatment with ORSERDU is stopped, your condition may worsen.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.
Tell your doctor or nurse if you notice any of the following side effects:

Very common (may affect more than 1 in 10 people)
- Decreased appetite
- Feeling sick (nausea)
- Increased triglycerides and cholesterol levels in your blood
- Vomiting
- Tiredness (fatigue)
- Indigestion (dyspepsia)
- Diarrhoea
- Decreased calcium levels in your blood
- Back pain
- Increased creatinine levels in your blood
- Joint pain (arthralgia)
- Decreased sodium levels in your blood
- Constipation
- Headache
- Hot flushes
- Abdominal pain
- Low levels of red blood cells, as measured in blood tests (anaemia)
- Decreased potassium levels in your blood
- Elevated liver function, as measured in blood tests (alanine aminotransferase increased, aspartate aminotransferase increased)

Common (may affect up to 1 in every 10 people)
- Pain in hands or legs (pain in extremity)
- Weakness (asthenia)
- Infection of the parts of the body that collect and pass out urine (urinary tract infection)
- Cough
- Shortness of breath (dyspnoea)
- Difficulty falling and staying asleep (insomnia)
- Elevated liver function, as measured in blood tests (Blood alkaline phosphatase increased)
- Rash
- Low levels of lymphocytes (a type of white blood cell), as measured in blood tests (Lymphocyte count decreased)

- Bone pain
- Dizziness
- Chest pain relating to the muscles and bones in the chest (Musculoskeletal chest pain)
- Inflammation of the mouth and lips (stomatitis)
- Fainting (syncope)

Uncommon (may affect up to 1 in every 100 people)
- Increased risk of blood clots (thromboembolism)
- Liver failure (acute hepatic failure)

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store ORSERDU

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and blister pack after EXP. The expiry date refers to the last day of that month.

This medicine does not require any special storage conditions.

Do not use this medicine if you notice any damage to the packaging or if there are any signs of tampering.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What ORSERDU contains
- The active substance is elacestrant.
  * Each 86 mg ORSERDU film-coated tablet contains 86.3 mg of elacestrant.
  * Each 345 mg ORSERDU film-coated tablet contains 345 mg of elacestrant

* The other ingredients are:

Tablet core
Microcrystalline cellulose [E460]
Silicified microcrystalline cellulose
Crospovidone [E1202]
Magnesium stearate [E470b]
Colloidal silicon dioxide [E551]

Film-coating
Opadry II 85F105080 Blue containing polyvinyl alcohol [E1203], titanium dioxide [E171], macrogol [E1521], talc [E553b] and brilliant blue FCF aluminium lake [E133]

What ORSERDU looks like and contents of the pack

ORSERDU is supplied as film-coated tablets in aluminium blisters.

ORSERDU 86 mg film-coated tablets
Blue to light blue, biconvex round shaped film-coated tablet with “ME” debossed on one side and plain face on the opposite side. Approximate diameter: 8.8 mm.

ORSERDU 345 mg film-coated tablets
Blue to light blue, biconvex, oval shaped film-coated tablet with “MH” debossed on one side and plain face on the opposite side. Approximate size: 19.2 mm (length), 10.8 mm (width).

Each pack contains 28 film-coated tablets (4 blisters with 7 tablets each).

Marketing Authorisation Holder
Stemline Therapeutics B.V.
Basisweg 10
1043 AP Amsterdam
The Netherlands

Manufacturer
Stemline Therapeutics B.V.
Basisweg 10
1043 AP Amsterdam
The Netherlands

or

Berlin Chemie AG
Glienicker Weg 125
12489 Berlin
Germany

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

België/Belgique/Belgien; България; Česká republika; Danmark; Eesti; Ελλάδα; Hrvatska; Ireland; Ísland; Κύπρος; Latvija; Lietuva; Luxembourg/Luxemburg; Magyarország; Malta; Nederland; Norge; Polska; Portugal; România; Slovenija; Slovenská republika; Suomi/Finland; Sverige
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Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.