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

Zurzuvae 20 mg hard capsules
Zurzuvae 25 mg hard capsules
Zurzuvae 30 mg hard capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Zurzuvae 20 mg hard capsules

Each hard capsule contains 20 mg zuranolone.

Zurzuvae 25 mg hard capsules

Each hard capsule contains 25 mg zuranolone.

Zurzuvae 30 mg hard capsules

Each hard capsule contains 30 mg zuranolone.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Hard capsule.

Zurzuvae 20 mg hard capsules

Size 1 (approximately 19 mm in length) hard capsules with a light-orange cap and an ivory to light-yellow body, printed with “S-217 20mg” in black ink.

Zurzuvae 25 mg hard capsules

Size 1 (approximately 19 mm in length) hard capsules with a light-orange cap and a light-orange body, printed with “S-217 25mg” in black ink.

Zurzuvae 30 mg hard capsules

Size 1 (approximately 19 mm in length) hard capsules with an orange cap and a light-orange body, printed with “S-217 30mg” in black ink.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Zurzuvae is indicated for the treatment of postpartum depression (PPD) in adults following childbirth (see section 5.1).

4.2 Posology and method of administration

Posology

The recommended dose is 50 mg zuranolone (two 25 mg capsules) taken orally once daily for 14 days as a single course of treatment. No data on additional treatment in case of a relapse or an insufficient response to zuranolone are available.

The dose may be reduced to 40 mg (two 20 mg capsules) taken orally once daily for 14 days if the patient does not tolerate 50 mg (see section 4.4). If required, dosing may be stopped without down-titration.

Zuranolone may be used alone or with stable background oral antidepressant therapy (see sections 4.4, 4.5 and 5.1).

Zuranolone should be taken in the evening. If an evening dose is missed, the patient should be instructed to take the next dose at their regular time in the evening of the next day. The patient should not take additional capsules on the same day to make up for the missed dose. The patient should continue taking zuranolone once daily until the full treatment course (14 days) is completed.

Concomitant use with strong CYP3A inhibitors
The recommended dose is 30 mg taken orally once daily during the 14 day treatment period when used with strong CYP3A inhibitors.

Special populations

Renal impairment
The recommended dose in patients with moderate (estimated glomerular filtration rate [eGFR] 30 to 59 mL/min) or severe renal impairment (eGFR < 30 mL/min not requiring dialysis) is 30 mg taken orally once daily during the 14 day treatment period. No dose adjustment is necessary in patients with mild renal impairment (eGFR 60 to 89 mL/min) (see section 5.2).

Hepatic impairment
The recommended dose in patients with severe hepatic impairment (Child-Pugh class C) is 30 mg taken orally once daily during the 14 day treatment period. No dose adjustment is necessary in patients with mild (Child-Pugh class A) or moderate hepatic impairment (Child-Pugh class B) (see section 5.2).

Paediatric population
The safety and efficacy of Zurzuvae in postpubertal females less than 18 years old have not been established. No data are available.

There is no relevant use of Zurzuvae in prepubertal females.

Method of administration

Zurzuvae should be taken orally once daily in the evening with fat-containing food as either a meal or snack (e.g. fat-containing dairy products, meats and oily fish, avocado, hummus, soy-based products, nuts, peanut butter, chocolate, or fat-containing nutritional bars or drinks) (see section 5.2).

Zurzuvae capsules are swallowed whole.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Pregnancy (see section 4.6).

4.4 Special warnings and precautions for use

Impaired ability to drive or engage in potentially hazardous activities

Zuranolone impairs the ability to drive due to central nervous system (CNS) depressant effects. Patients should be counselled not to drive or engage in other potentially hazardous activities until at least 12 hours after taking each dose of zuranolone. Patients should be advised that they may not be able to assess their own ability to perform these activities (see section 4.7).

Central nervous system depressant effects

Zuranolone can cause CNS depressant effects such as somnolence and sedation (see section 4.8). Alcohol and other CNS depressants may increase CNS depressant effects or impairment of psychomotor performance (see section 4.5).

The zuranolone dose should be reduced or permanently discontinued based on the severity of the adverse reaction and the individual sensitivity of the patient to these effects (see section 4.2 or 4.5).

Drug interactions

Concomitant use of zuranolone with CYP3A inducers should be avoided (see section 4.5).

Abuse potential and dependence

Zuranolone has potential for abuse. In a human abuse potential study in recreational CNS depressant users (N = 60), zuranolone (30, 60 and 90 mg) had dose dependent abuse potential when compared to alprazolam (1.5 mg and 3 mg) on positive subjective measures of “drug liking”, “overall drug liking”, “take drug again”, “high”, and “good drug effects”.

Based on data from clinical trials, zuranolone has low physical dependence potential.

Caution should be used in individuals with a history of abuse or addiction to alcohol or other substances.

Excipients

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

4.5 Interaction with other medicinal products and other forms of interaction

CNS depressant medicinal products and alcohol

Co-administration of repeated 50 mg daily doses of zuranolone with alcohol or alprazolam led to increased impairment in psychomotor performance. If use with another CNS depressant medicinal product (such as opioids, benzodiazepines, non-benzodiazepine hypnotics, gabapentinoids and sedating antidepressants) is unavoidable, dose reduction should be considered (see section 4.4).

Effect of other medicinal products on the pharmacokinetics of zuranolone

In vitro studies showed that zuranolone is metabolised primarily by CYP3A.

CYP3A inducers
Systemic exposure (area under the curve to infinity [AUC_{inf}]) to zuranolone is reduced by 85% in the presence of rifampin (strong CYP3A inducer) (see section 5.2). Concomitant use of zuranolone with a CYP3A inducer decreases the exposure of zuranolone which may reduce the efficacy of zuranolone. Concomitant use of zuranolone with CYP3A inducers (e.g. carbamazepine, phenobarbitol, phenytoin, primidone, rifampicin, St John's Wort, and efavirenz) should be avoided.

Strong CYP3A inhibitors
Concomitant use of zuranolone with a strong CYP3A inhibitor increases the exposure of zuranolone. Systemic exposure (AUC_{inf}) to zuranolone is increased 62% when administered in combination with itraconazole. The dose of zuranolone should be reduced to 30 mg when used with a strong CYP3A inhibitor (e.g. protease inhibitors, azole antifungals, some macrolides such as clarithromycin or telithromycin) (see section 4.2).

Grapefruit products are inhibitors of CYP3A and should be avoided while taking zuranolone.

Paediatric population

Interaction studies have only been performed in adults.

4.6 Fertility, pregnancy and lactation

Pregnancy

Zuranolone is contraindicated during pregnancy (see section 4.3). There are no or limited data from the use of zuranolone in pregnant women. Studies in animals have shown reproductive toxicity (see section 5.3).

Women of childbearing potential have to use effective contraception during treatment and for 7 days following discontinuation of treatment. Patients should be advised on the use of effective contraception.

Breast-feeding

Data from a clinical lactation study indicate that zuranolone is present in low levels in human breast milk. The calculated maximum relative infant dose (RID) was < 1%. In most subjects, concentrations of zuranolone in breast milk were below the level of quantification limit by 6 days after the last dose (see section 5.2). The effect of zuranolone on breastfed newborns/infants is unknown and there are limited data on the effect on milk production (see section 5.3).

Breast-feeding should be discontinued during treatment with zuranolone, unless in the judgement of the healthcare professional, the benefits of breast-feeding outweigh the possible risks for the child.

Fertility

There are no human data on the effects of zuranolone on human fertility. Data from male and female animal studies showed no zuranolone-related effects on fertility or reproduction function at clinically relevant doses (see section 5.3).

4.7 Effects on ability to drive and use machines

Zuranolone has a major influence on the ability to drive and use machines. Zuranolone has been reported to cause somnolence, dizziness, sedation and confusional state (see section 4.8).

Two computer-based driving simulation studies evaluated the effects of bedtime zuranolone 30 mg and 50 mg administration on next-morning driving performance, 9 hours after dosing. The driving

ability of healthy adults was impaired in a dose-dependent manner following single and repeat nightly administration. Exposure-response modelling of the standard deviation of lateral position (SDLP) data from the two driving simulation studies found that median placebo corrected SDLP falls below the threshold associated with a blood alcohol concentration (BAC) of 0.05% by 12 hours after a single dose and after 7 evening doses of zuranolone.

Patients should be counselled not to engage in potentially hazardous activities, such as driving a vehicle or operating machinery, for at least 12 hours after each zuranolone dose. Patients should be advised that they may not be able to assess their own ability to perform these activities (see section 4.4).

4.8 Undesirable effects

Summary of the safety profile

The most frequently reported adverse drug reactions (ADRs) were somnolence (27.6%), dizziness (13.3%), and sedation (11.2%). The serious adverse reaction was confusional state (1.3%).

The frequency of zuranolone-treated subjects who discontinued treatment due to ADRs was 2%. These ADRs were somnolence (2%) and sedation (1%). The frequency of zuranolone-treated subjects who had a dose reduction or interruption due to ADRs was 14.3%. The most frequently reported ADRs leading to dose reduction or interruption were somnolence (8.2%), dizziness (6.1%) and sedation (3.1%).

Tabulated list of adverse reactions

ADRs are presented in the Table 1. The ADRs are listed by system organ class (SOC) and frequency. Frequency categories were defined according to 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).

Table 1. Adverse drug reactions occurring in patients with PPD treated with zuranolone

System organ class (SOC)	Adverse drug reaction	Frequency
Psychiatric disorders	Memory impairment	Common
	Confusional state	Common
Nervous system disorders	Somnolence	Very common
	Dizziness	Very common
	Sedation	Very common
	Tremor	Common
Gastrointestinal disorders	Diarrhoea	Common
General disorders and administration site conditions	Fatigue	Common

Description of selected adverse reactions

Somnolence and sedation
Among subjects treated with zuranolone 50 mg, somnolence occurred in 26.5% of subjects and sedation in 11.2% of subjects. All events were assessed as mild or moderate in severity, with 69.7% of somnolence events and 58.3% of sedation events occurring within the first 2 days of treatment.

Confusional state
Confusional state was reported in 1 subject who received zuranolone 50 mg and resulted in dose reduction. Serious confusional state occurred in 1 subject who received 30 mg and resolved the same day following interruption of treatment, with treatment resuming at a reduced dose.

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

One case of intentional overdose with zuranolone was reported during premarketing clinical trials. The patient took 330 mg (6.5 times the MRHD) of zuranolone and was reported to be in an altered state of consciousness. The event resolved the next day following treatment with intravenous fluids.

Overdose with zuranolone may result in excessive CNS depressant effects (see sections 4.4 and 4.8).

There is no specific antidote for zuranolone overdose. Appropriate supportive measures should be provided as dictated by the patient's clinical status.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Psychoanaleptics, other antidepressants, ATC code: N06AX31

Mechanism of action

Zuranolone is a synthetic neuroactive steroid (NAS) that exhibits potent positive allosteric modulation of the gamma-aminobutyric acid-A ($GABA_A$) receptor. Zuranolone enhances GABAergic activity at synaptic and extrasynaptic $GABA_A$ receptors and has also been shown to increase cell surface expression of $GABA_A$ receptors in *in vitro* studies. Zuranolone may exert antidepressant effects by enhancing GABAergic inhibition.

Pharmacodynamic effects

Cardiac electrophysiology
At a dose up to 2 times the MRHD, zuranolone does not cause clinically significant QTc interval prolongation nor any other clinically significant effect on other electrocardiography (ECG) parameters.

Clinical efficacy and safety

The efficacy of zuranolone for the treatment of women with PPD was studied in a randomised, double-blind, parallel-group, placebo-controlled, multi-centre study (217-PPD-301 [NCT04442503]). Female subjects aged 18 to 45 were randomized 1:1 to receive either zuranolone 50 mg or placebo, orally once daily. Subjects enrolled were to have a total score ≥ 26 at baseline in the 17-item Hamilton Depression Rating (HAMD-17) scale. Subjects also met criteria for MDE per DSM-5 (Diagnostic and Statistical Manual of Mental Disorders – 5th edition) criteria. The criteria were limited to onset of symptoms in the third trimester or within 4 weeks of delivery. Subjects started treatment up to 12 months following childbirth. Subjects were followed for 4 weeks after the 14 day treatment course.

Table 2. Population characteristics

Parameter		**217-PPD-301† (SKYLARK)**
Age (years) – mean (min, max)		30 (19, 44)
Taking a stable dose of oral antidepressants* for at least 30 days before baseline		15%
Race	White	70%
	Black or African American	22%
	Asian	1%
	Other/Mixed	7%
Ethnicity	Hispanic or Latino	39%
Body mass index (kg/m^2) - mean (min, max)		30 (19, 45)
Subjects with PPD onset following, and within the first 4 weeks of, childbirth		67%
HAMD-17 total score at baseline – mean (min, max)		28.7 (21, 36)
MADRS total score at baseline – mean (min, max)		35.3 (22, 49)

HAMD-17 = Hamilton depression rating scale; MADRS = Montgomery–Åsberg Depression Rating Scale; min = minimum; max = maximum

* Subjects taking stably dosed (≥ 30 days) antidepressant therapies (ADTs), with the exception of nefazodone, trazodone, or brexanolone, were eligible to enter the studies. The most common ADT used was sertraline.

† Full Analysis Set (FAS)

The study showed statistical superiority for the primary endpoint, change from baseline at Day 15 in depressive symptoms as measured by the HAMD-17 total score, compared to placebo. A summary of the efficacy results in Study 217-PPD-301 are presented in Table 3.

Table 3. Summary of efficacy results in study 217-PPD-301

Efficacy endpoint	**Placebo (N = 97)**	**Zuranolone 50 mg (N = 98)**	**p-value ***
Primary endpoint: Day 15 (EOT) LS mean change (SE) from baseline in HAMD-17 total score	(n = 90) -11.6 (0.823)	(n = 93) -15.6 (0.817)	0.0007
LS mean treatment difference (95% CI)	-4.0 (-6.3, -1.7)		
Secondary endpoints			
Day 3 LS mean change (SE) from baseline in HAMD-17 total score	(n = 96) -6.1 (0.710)	(n = 98) -9.5 (0.704)	0.0008
LS mean treatment difference (95% CI)	-3.4 (-5.4, -1.4)		
Day 28 LS mean change (SE) from baseline in HAMD-17 total score	(n = 85) -13.4 (0.875)	(n = 77) -16.3 (0.884)	0.0203
LS mean treatment difference (95% CI)	-2.9 (-5.4, -0.5)		
Day 45 LS mean change (SE) from baseline in HAMD-17 total score	(n = 85) -14.4 (0.902)	(n = 84) -17.9 (0.903)	0.0067
LS mean treatment difference (95% CI)	-3.5 (-6.0, -1.0)		
Day 15 Number of subjects (%) with HAMD-17 response** †	(n = 90) 35 (38.9)	(n = 93) 53 (57.0)	
Relative Risk (95% CI) Risk Difference (95% CI)	1.409 (1.038, 1.912) 0.164 (0.022, 0.307)		0.0278 0.0239
Day 15	(n = 90)	(n = 93)	

Efficacy endpoint	Placebo (N = 97)	Zuranolone 50 mg (N = 98)	p-value *
Number of subjects (%) with CGI-I response ‡	42 (46.7)	62 (66.7)	
Relative Risk (95% CI)	1.422 (1.097, 1.843)		0.0078
Risk Difference (95% CI)	0.195 (0.055, 0.336)		0.0065

CGI-I = Clinical Global Impression Improvement scale; EOT = End of treatment; HAMD-17 = Hamilton depression rating scale; N = number of subjects in the FAS; n = number of subjects at the visit; CI = confidence interval; LS = least squares; SE = standard error

* LS means and corresponding p-values and CIs are from mixed model for repeated measures (MMRM) analysis. Relative risks, risk differences and corresponding p-values and CIs are from model-based generalized estimation equation (GEE) analysis.

** HAMD-17 response is defined as ≥ 50% reduction from baseline in HAMD-17 total score.

† Among participants with HAMD-17 response at Day 15, three (5.7%) subjects in the 50 mg zuranolone group experienced relapse (defined as at least 2 consecutive HAMD-17 total scores ≥ 20 after Day 15), and none experienced rebound (defined as any HAMD-17 total score greater than or equal to baseline after Day 15).

‡ CGI-I response is defined as a CGI-I score of very much improved or much improved.

Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with Zurzuvae in one or more subsets of the paediatric population in the treatment of postpartum depression (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Absorption

Once-daily administration of zuranolone 50 mg resulted in accumulation of approximately 1.5-fold in systemic exposures and steady state was achieved in 3 to 5 days.

Following oral administration, peak zuranolone concentrations occur at 5 to 6 hours post-dose.

Effect of food
Following administration of zuranolone 30 mg to healthy volunteers, the maximum serum concentration (C_{max}) increased 228% and the AUC increased 55% with a low-fat meal (400 to 500 calories, 25% fat) compared to fasted conditions. The C_{max} increased 334% and the AUC increased 90% with a high-fat meal (800 to 1000 calories, 50% fat) compared to fasted conditions. The time at maximum concentration (t_{max}) was not impacted by food. Exposure at doses up to 90 mg remained approximately dose linear with consumption of a moderate-fat meal (700 calories; 30% fat).

Distribution

The volume of distribution of zuranolone following oral administration is high (> 500 L) and was independent of dose. Zuranolone did not distribute preferentially into red blood cells.

Zuranolone is highly protein bound (> 99.5%) to plasma proteins.

Distribution into breast milk
The distribution of zuranolone into human breast milk was studied in a group of 14 healthy lactating women treated with daily oral administration of zuranolone 30 mg for 5 days. At steady state (Day 5), the calculated daily infant dose was low (approximately 0.00135 mg/kg/day), reflecting a mean RID of 0.357% compared to the maternal dose. From a simulation, the expected mean RID associated with a 50 mg maternal dose was 0.738% for an infant with a milk intake of 150 mL/kg/day and 0.984% for an infant with a milk intake of 200 mL/kg/day.

Biotransformation

Zuranolone undergoes extensive metabolism, with CYP3A identified as a primary enzyme involved. There were no human metabolites circulating at > 10% of total drug-related material and none are considered to contribute to the therapeutic effects of zuranolone.
Zuranolone is not an inhibitor of CYP1A2, CYP2B6 or CYP2C19 and is not expected to be an inhibitor of CYP2B6, CYP2C8, CYP2C9, CYP2D6 or CYP3A4 at clinically relevant concentrations. Zuranolone is not expected to be an inhibitor of BSEP, BCRP, MDR1, MATE1, MATE2-K, OAT1, OAT3, OATP1B1, OATP1B3, OCT1, or OCT2 at clinically relevant concentrations. Zuranolone is not a substrate of P-glycoprotein.
Clinical DDI studies indicate that repeated administration of zuranolone prior to administration of simvastatin (CYP3A substrate) or bupropion (CYP2B6 substrate) did not alter the exposure of simvastatin or bupropion. Zuranolone is not expected to cause a drug interaction through CYP450 enzyme induction.

Elimination

The terminal half-life of zuranolone ($t_{1/2}$) is approximately 19.7 to 24.6 hours in an adult population. The clearance of zuranolone was independent of dose. The mean apparent clearance (CL/F) of zuranolone is 32.7 L/h.

Excretion

Following oral administration of radiolabelled zuranolone, 45% of the dose was recovered in urine as metabolites with negligible unchanged zuranolone and 41% in faeces as metabolites with less than 2% as unchanged zuranolone.

Pharmacokinetics in special patient groups

Weight, race, or age
The pharmacokinetics (PK) of zuranolone was similar between healthy subjects and subjects with PPD.

Black or African American subjects had a 14% higher CL/F compared to subjects of other races (Asian, White, or other) but this increase was not clinically meaningful.

No dose adjustments are necessary based on weight, race, or age.

Renal impairment
Exposure to zuranolone was increased in patients with moderate (eGFR 30 to 59 mL/min) and severe (eGFR 15 to 29 mL/min) renal impairment (see section 4.2). Zuranolone has not been studied in patients with eGFR of < 15 mL/min requiring dialysis (see section 4.2).

Hepatic impairment
C_{max} and AUC_{inf} for zuranolone were unchanged in patients with mild (Child-Pugh class A) or moderate (Child-Pugh class B) hepatic impairment compared to matched healthy subjects. C_{max} was 24% lower and AUC_{inf} was 56% higher in patients with severe (Child-Pugh class C) hepatic impairment (see section 4.2).

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and carcinogenic potential.

Reproductive toxicity

In the pivotal rat embryo-foetal development study, a low incidence of foetal malformations was noted from the mid-dose and higher. The developmental no adverse effect level (NOAEL) was 2.5 mg/kg/day. Exposures at this dose are approximately 3-fold above the expected exposures in humans. In mice, an increase in cleft palate was noted from the mid-dose and higher, which could be related to lower foetal body weight. The exposure margin at the NOAEL was 1.9-fold above the expected exposures in humans. In rabbits no malformations were seen, however, all doses tested resulted in exposures below those expected in humans.

In a pre-/postnatal development study in rats, total litter loss and increased pup mortality due to lack of nursing occurred at the mid-dose and higher. The NOAEL for pre and postnatal development was the low dose, resulting in a 2-fold exposure margin as compared to expected human exposure.

At zuranolone exposures 5.6-fold greater than MRHD, a relative elevation in neuronal death was observed in rats exposed to a single dose of zuranolone on postnatal Day 7, which corresponds in humans to a period of brain development beginning during the third trimester of pregnancy and continuing up to a few years after birth.

Toxicity in juvenile animals

In juvenile toxicity studies in rats, zuranolone treatment-related findings were consistent with those noted in adult animals.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule contents

Croscarmellose sodium (E468)
Mannitol (E421)
Microcrystalline cellulose (E460)
Silica, colloidal anhydrous (E551)
Sodium stearyl fumarate

Capsule shell

Gelatin (E441)
Red iron oxide (E172)
Titanium dioxide (E171)
Yellow iron oxide (E172)

Capsule print (black ink)

Ammonium hydroxide (E527)
Black iron oxide (E172)
Propylene glycol (E1520)
Shellac glaze (E904)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

4 years

6.4 Special precautions for storage

Store below 25 °C.

6.5 Nature and contents of container

Zurzuvae 20 mg hard capsules

High-density polyethylene (HDPE) bottles with child resistant, foil induction-sealed polypropylene closures. Pack sizes of 14 or 28 hard capsules.

Polyvinyl chloride (PVC) laminated polychlorotrifluoroethylene (PCTFE) aluminium blister. Pack size of 28 capsules in 1 carton.

Zurzuvae 25 mg hard capsules

HDPE bottles with child resistant, foil induction-sealed polypropylene closures. Pack sizes of 14 or 28 hard capsules.

PVC laminated PCTFE aluminium blister. Pack size of 28 capsules in 1 carton.

Zurzuvae 30 mg hard capsules

HDPE bottles with child resistant, foil induction-sealed polypropylene closures. Pack size of 14 capsules.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

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

7. MARKETING AUTHORISATION HOLDER

Biogen Netherlands B.V.
Prins Mauritslaan 13
1171 LP Badhoevedorp
The Netherlands

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/25/1977/001
EU/1/25/1977/002
EU/1/25/1977/003
EU/1/25/1977/004
EU/1/25/1977/005
EU/1/25/1977/006
EU/1/25/1977/007

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation:

10. DATE OF REVISION OF THE TEXT

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

ANNEX II

A. MANUFACTURER 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. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

Biogen Netherlands B.V.
Prins Mauritslaan 13
1171 LP Badhoevedorp
The Netherlands

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

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

OUTER CARTON BOTTLE – 20 mg CAPSULES

1. NAME OF THE MEDICINAL PRODUCT

Zurzuvae 20 mg hard capsules
zuranolone

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each capsule contains 20 mg zuranolone.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

14 hard capsules
28 hard capsules

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

Oral 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

Store below 25 °C.

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

Biogen Netherlands B.V.
Prins Mauritslaan 13
1171 LP Badhoevedorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/25/1977/001 14 capsules
EU/1/25/1977/002 28 capsules

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

zurzuvae 20 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING

BOTTLE LABEL – 20 mg CAPSULES

1. NAME OF THE MEDICINAL PRODUCT

Zurzuvae 20 mg hard capsules
zuranolone

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each capsule contains 20 mg of zuranolone.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

14 hard capsules
28 hard capsules

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

Oral 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

Store below 25 °C.

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

Biogen Netherlands B.V.

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/25/1977/001 14 capsules
EU/1/25/1977/002 28 capsules

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON BOTTLE – 25 mg CAPSULES

1. NAME OF THE MEDICINAL PRODUCT

Zurzuvae 25 mg hard capsules
zuranolone

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each capsule contains 25 mg of zuranolone.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

14 hard capsules
28 hard capsules

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

Oral 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

Store below 25 °C.

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

Biogen Netherlands B.V.
Prins Mauritslaan 13
1171 LP Badhoevedorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/25/1977/004 14 capsules
EU/1/25/1977/005 28 capsules

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

zurzuvae 25 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING

BOTTLE LABEL – 25 mg CAPSULES

1. NAME OF THE MEDICINAL PRODUCT

Zurzuvae 25 mg hard capsules
zuranolone

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each capsule contains 25 mg of zuranolone.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

14 hard capsules
28 hard capsules

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

Oral 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

Store below 25 °C.

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

Biogen Netherlands B.V.

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/25/1977/004 14 capsules
EU/1/25/1977/005 28 capsules

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON BOTTLE – 30 mg CAPSULES

1. NAME OF THE MEDICINAL PRODUCT

Zurzuvae 30 mg hard capsules
zuranolone

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each capsule contains 30 mg of zuranolone.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

14 hard capsules

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

Oral 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

Store below 25 °C.

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

Biogen Netherlands B.V.
Prins Mauritslaan 13
1171 LP Badhoevedorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/25/1977/007

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

zurzuvae 30 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING

BOTTLE LABEL – 30 mg CAPSULES

1. NAME OF THE MEDICINAL PRODUCT

Zurzuvae 30 mg hard capsules
zuranolone

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each capsule contains 30 mg of zuranolone.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

14 hard capsules

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

Oral 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

Store below 25 °C.

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

Biogen Netherlands B.V.

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/25/1977/007

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON BLISTER – 20 mg CAPSULES

1. NAME OF THE MEDICINAL PRODUCT

Zurzuvae 20 mg hard capsules
zuranolone

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each capsule contains 20 mg of zuranolone.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

28 hard capsules

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

Oral 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

Store below 25 °C.

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

Biogen Netherlands B.V.
Prins Mauritslaan 13
1171 LP Badhoevedorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/25/1977/003

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

zurzuvae 20 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INNER CARTON BLISTER – 20 mg CAPSULES

1. NAME OF THE MEDICINAL PRODUCT

Zurzuvae 20 mg hard capsules
zuranolone

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each capsule contains 20 mg of zuranolone.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

28 hard capsules

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

Oral use.

1. Press and hold
2. Pull

1. Press and hold down the tip of the button on the left.
2. While holding the button down, pull out insert from the right.

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

Store below 25 °C.

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

Biogen Netherlands B.V.

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/25/1977/003

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTERS – 20 mg CAPSULES

1. NAME OF THE MEDICINAL PRODUCT

Zurzuvae 20 mg hard capsules
zuranolone

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Biogen Netherlands B.V.

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON BLISTER – 25 mg CAPSULES

1. NAME OF THE MEDICINAL PRODUCT

Zurzuvae 25 mg hard capsules
zuranolone

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each capsule contains 25 mg of zuranolone.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

28 hard capsules

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

Oral 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

Store below 25 °C.

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

Biogen Netherlands B.V.
Prins Mauritslaan 13
1171 LP Badhoevedorp
The Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/25/1977/006

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

zurzuvae 25 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INNER CARTON BLISTER – 25 mg CAPSULES

1. NAME OF THE MEDICINAL PRODUCT

Zurzuvae 25 mg hard capsules
zuranolone

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each capsule contains 25 mg of zuranolone.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

28 hard capsules

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

Oral use.

1. Press and hold
2. Pull

1. Press and hold down the tip of the button on the left.
2. While holding the button down, pull out insert from the right.

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

Store below 25 °C.

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

Biogen Netherlands B.V.

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/25/1977/006

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTERS – 25 mg CAPSULES

1. NAME OF THE MEDICINAL PRODUCT

Zurzuvae 25 mg hard capsules
zuranolone

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Biogen Netherlands B.V.

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Zurzuvae 20 mg hard capsules
Zurzuvae 25 mg hard capsules
Zurzuvae 30 mg hard capsules
zuranolone

▼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. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Zurzuvae is and what it is used for

What Zurzuvae is
Zurzuvae is an antidepressant medicine used to treat postpartum depression (PPD). It should be taken after giving birth by adults aged 18 years or older.

What Zurzuvae is used for
Postpartum depression is depression that begins during pregnancy or soon after giving birth.

Symptoms can include low mood or sadness, sleep disturbances, changes in weight, difficulty in concentrating, feelings of worthlessness, loss of interest in favourite activities, and feelings of being slowed down or anxiety.

How Zurzuvae works
Zurzuvae increases the activity of GABA (gamma-aminobutyric acid) on receptors in the brain. GABA is involved in the regulation of mood. By increasing the activity of GABA, Zurzuvae may help the parts of the brain affected by depression. Typically, **symptoms start to improve by the third day of the 14 day Zurzuvae treatment course.**

2. What you need to know before you take Zurzuvae

Do not take Zurzuvae
- if you are allergic to zuranolone or any of the other ingredients of this medicine (listed in section 6).
- if you are pregnant.

Warnings and precautions

Zurzuvae can **reduce awareness and alertness**. It is important to **discuss these possible effects with your doctor or pharmacist before taking Zurzuvae.**
- Do not drive for at least 12 hours after taking each Zurzuvae dose. You may not be able to tell on your own how much Zurzuvae is affecting you and whether you are safe to drive.
- Zurzuvae may also cause sleepiness, slow thinking, trouble remembering, confusion, and dizziness during the day. These effects may interfere with your daily activities, including taking care of your child. Do not perform potentially dangerous activities if you feel any of these effects.
  Tell your doctor if you notice any of these signs.

Talk to your doctor before taking Zurzuvae if you think any of these apply:
- if you have abused or been addicted to **alcohol, illegal drugs** or **prescribed medicines**
- if you have had **depression, mood problems or suicidal thoughts** or behaviour.

Ask your doctor if other medicines you are taking prevent you from taking Zurzuvae.

Children and adolescents
This medicine is not for children and adolescents under 18 years of age. Zurzuvae has not been tested in this age group.

Other medicines and Zurzuvae
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This is because Zurzuvae can affect the way some medicines work and some medicines can have an effect on Zurzuvae. Only take other medicines while you are on Zurzuvae if your doctor tells you that you can.

In particular, tell your doctor or pharmacist if you are taking any of the following medicines as your dose of Zurzuvae may need to be adjusted. See section 3, How to take Zurzuvae:
- medicines that may increase the level of Zurzuvae in your blood. These include those used to treat:
  - **fungal infections,** such as ketoconazole, posaconazole, voriconazole, itraconazole
  - **bacterial infections,** such as the antibiotics clarithromycin, josamycin, telithromycin, troleandomycin
  - **HIV infection,** such as ritonavir, elvitegravir, indinavir, saquinavir, telaprevir, danoprevir, lopinavir, nelfinavir, boceprevir
  - **cancer,** such as ceritinib, idelalisib, ribociclib, tucatinib.

- medicines that can affect the nervous system, such as:
  - **painkillers like opioids** (such as methadone, tramadol, morphine, oxycodone, codeine)
  - **sleep aids** like benzodiazepines (such as diazepam, lorazepam), and nonbenzodiazepine hypnotics (such as zolpidem, zopiclone)
  - **antidepressants causing drowsiness** (such as amitriptyline, clomipramine, dosulepin, doxepin, mianserin, mirtazapine, trazodone, trimipramine)
  - **medicines used to treat seizures, nerve pain or anxiety** (such as gabapentin and pregabalin).

- medicines that may reduce how well Zurzuvae works, such as:
  - **rifampin** (antibiotic)
  - **St. John's Wort** (herbal remedy taken for depression)
  - **phenobarbital** (also known as barbiturates, used for epilepsy or sleep problems)
  - **efavirenz** (used for HIV infection)
  - **carbamazepine, phenytoin, and primidone** (used to treat seizures).

Talk to your doctor or pharmacist before taking Zurzuvae, if any of the above apply to you (or you are not sure).

Zurzuvae with alcohol
Do not drink alcohol or take products containing alcohol while taking Zurzuvae without talking to your doctor. Taking alcohol while on this medicine may make side effects such as drowsiness and sleepiness worse.

Zurzuvae with food and drink
Avoid grapefruit or grapefruit juice while taking Zurzuvae.

Pregnancy
Zurzuvae may cause harm to an unborn baby. Do not take Zurzuvae if you are pregnant.

Use reliable contraception during treatment and for 7 days afterwards. Speak to your nurse or doctor about suitable methods of contraception for you.

Tell your doctor straight away if, during treatment with Zurzuvae **you become pregnant or think you are pregnant.**

Breast-feeding
Zurzuvae passes into breast milk. You should not breast-feed unless your doctor tells you you can.

Tell your doctor straight away if you are breast-feeding or plan to breast-feed.

Driving and using machines
Do not drive or take part in any potentially dangerous activities such as operating machinery for at least 12 hours after taking Zurzuvae (see above section warnings and precautions).

Zurzuvae contains a negligible amount of sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium free'.

3. How to take Zurzuvae

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

Recommended dose
The recommended dose is 50 mg (two 25 mg capsules) taken once daily in the evening. Take it every day for 14 days. Zurzuvae is only prescribed for a single 14 day course of treatment.

Do not stop taking Zurzuvae until you finish your 14 day treatment course, even if you feel better. Typically, symptoms start to improve by the third day of Zurzuvae treatment.

Your doctor may reduce your dose to 40 mg (two 20 mg capsules) taken once daily in the evening if you have trouble with side effects.

Some medicines may cause side effects when taken at the same time as Zurzuvae. If your doctor prescribes one of these medicines while you are taking Zurzuvae, your doctor may reduce the dose of Zurzuvae to prevent side effects when taking both medicines at the same time.

If you have any moderate or severe kidney-related problems or severe liver problems, your doctor will prescribe a dose of 30 mg (one capsule) taken once daily in the evening.

How to take Zurzuvae capsules
- Swallow Zurzuvae capsules whole without chewing or opening them.

- **Take Zurzuvae with food containing fat.** This will help to increase the absorption of Zurzuvae into your body so it can be effective to treat your PPD. Typical fat-containing foods include:
  - Cheese, whole milk, whole milk dairy products and yoghurt
  - Meats, oily fish
  - Avocado, hummus, soy-based products (tofu)
  - Nuts, peanut butter, chocolate, fat-containing nutritional bars or drinks.

  These can be taken as either a meal or a snack.

If you take more Zurzuvae than you should
If you take more Zurzuvae than you should, seek medical help immediately, either by calling your doctor or going to the nearest hospital emergency (A&E) department. Do not drive yourself because you may start to feel sleepy. Always take the labelled medicine container with you to show the doctor, even if there are no capsules left.

If you forget to take Zurzuvae
If you forget to take Zurzuvae, skip the missed dose and take the next dose at your regular time in the evening the next day. **Do not take a double dose to make up for forgetting a dose**. Continue taking Zurzuvae once daily until the remainder of the prescription is completed.

If you stop taking Zurzuvae
Treatment with Zurzuvae can be stopped without needing to gradually reduce the dose.

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. The following side effects may happen with this medicine.

Very common (may affect more than 1 in 10 people)
- drowsiness or sleepiness
- dizziness.

Common (may affect up to 1 in 10 people)
- loose stools (diarrhoea)
- lack of energy
- trouble remembering information
- trembling or shaking
- feeling confused.

Tell your doctor, or pharmacist if you notice any of the side effects above.

Reporting of side effects
If you get any side effects, talk to your doctor, or pharmacist. 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 Zurzuvae

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 bottle or blister after EXP.

The expiry date refers to the last day of that month.

Store below 25 ºC.

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 to protect the environment.

6. Contents of the pack and other information

What Zurzuvae contains

The active substance is zuranolone.

Each hard capsule of Zurzuvae 20 mg contains 20 mg of zuranolone.

Each hard capsule of Zurzuvae 25 mg contains 25 mg of zuranolone.

Each hard capsule of Zurzuvae 30 mg contains 30 mg of zuranolone.

The other ingredients are:

Capsule contents: croscarmellose sodium (E468), mannitol (E421); microcrystalline cellulose (E460); silica, colloidal anhydrous (E551); sodium stearyl fumarate.

Capsule shell: gelatin (E441); red iron oxide (E172); titanium dioxide (E171); yellow iron oxide (E172).

Capsule print (black ink): ammonium hydroxide (E527); black iron oxide (E172); propylene glycol (E1520); shellac glaze (E904).

What Zurzuvae looks like and contents of the pack

Zurzuvae 20 mg hard capsules are hard capsules with a light-orange cap and an ivory to light-yellow body, printed with “S-217 20mg” in black ink.

Zurzuvae 25 mg hard capsules are hard capsules with a light-orange cap and a light-orange body, printed with “S-217 25mg” in black ink.

Zurzuvae 30 mg hard capsules are hard capsules with an orange cap and a light-orange body, printed with “S-217 30mg” in black ink.

The capsules are provided in bottle packs containing:
- 14 or 28 hard capsules of Zurzuvae 20 mg, or
- 14 or 28 hard capsules of Zurzuvae 25 mg, or
- 14 hard capsules of Zurzuvae 30 mg

The capsules are provided in blister packs containing:
- 28 hard capsules of Zurzuvae 20 mg, or
- 28 hard capsules of Zurzuvae 25 mg.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Biogen Netherlands B.V.
Prins Mauritslaan 13
1171 LP Badhoevedorp
The Netherlands

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

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Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu.