swissmedic

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Swiss Public Assessment Report

Extension of therapeutic indication

Lynkuet

International non-proprietary name:	elinzanetant
Pharmaceutical form:	capsule, soft
Dosage strength(s):	60 mg
Route(s) of administration:	oral
Marketing authorisation holder:	Bayer (Schweiz) AG
Marketing authorisation no.:	69917
Decision and decision date:	extension of therapeutic indication approved on 29 July 2026

Note:

This assessment report is as adopted by Swissmedic with all information of a commercially confidential nature deleted.

SwissPARs are final documents that provide information on submissions at a particular point in time. They are not updated after publication.

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1 Terms, definitions, abbreviations

ADA	Anti-drug antibody
ADME	Absorption, distribution, metabolism, elimination
AE	Adverse event
ALT	Alanine aminotransferase
API	Active pharmaceutical ingredient
AST	Aspartate aminotransferase
ATC	Anatomical Therapeutic Chemical Classification System
AUC	Area under the plasma concentration-time curve
$AUC_{0\text{-}24h}$	Area under the plasma concentration-time curve for the 24-hour dosing interval
CI	Confidence interval
C_{max}	Maximum observed plasma/serum concentration of drug
CYP	Cytochrome P450
DDI	Drug-drug interaction
EMA	European Medicines Agency
ERA	Environmental risk assessment
ET	Endocrine therapy
FFA	Free fatty acids
FDA	Food and Drug Administration (USA)
GI	Gastrointestinal
GLP	Good Laboratory Practice
HF	Hot flushes
HPLC	High-performance liquid chromatography
HRT	Hormone replacement therapy
IC/EC_{50}	Half-maximal inhibitory/effective concentration
ICH	International Council for Harmonisation
Ig	Immunoglobulin
INN	International non-proprietary name
ITT	Intention-to-treat
LoQ	List of Questions
MAH	Marketing authorisation holder
Max	Maximum
Min	Minimum
MRHD	Maximum recommended human dose
N/A	Not applicable
NO(A)EL	No observed (adverse) effect level
PBPK	Physiology-based pharmacokinetics
PD	Pharmacodynamics
PIP	Paediatric investigation plan (EMA)
PK	Pharmacokinetics
PopPK	Population pharmacokinetics
PSP	Pediatric study plan (US FDA)
RMP	Risk management plan
SAE	Serious adverse event
SwissPAR	Swiss Public Assessment Report
TEAE	Treatment-emergent adverse event
TPA	Federal Act of 15 December 2000 on Medicinal Products and Medical Devices (SR 812.21)
TPO	Ordinance of 21 September 2018 on Therapeutic Products (SR 812.212.21)
VMS	Vasomotor symptoms

2 Background information on the procedure

2.1 Applicant's request(s) and information regarding procedure

Extension(s) of the therapeutic indication(s)
The applicant requested the addition of a new therapeutic indication or modification of an approved indication in accordance with Article 23 TPO.

Work-sharing procedure
The applicant requested a work-sharing procedure with Australia, Canada, the UK and Switzerland.
The Access NAS (new active substance) work-sharing initiative is a collaboration between regulatory authorities – specifically Australia's Therapeutic Goods Administration (TGA), Health Canada (HC), Singapore's Health Sciences Authority (HSA), the UK Medicines & Healthcare products Regulatory Agency (MHRA) and Swissmedic – and the pharmaceutical industry.
The work-sharing initiative involves the coordinated assessment of applications that have been filed in at least two jurisdictions.

2.2 Indication and dosage

2.2.1 Requested indication

Treatment of moderate-to-severe vasomotor symptoms (VMS) caused by adjuvant endocrine therapy.

2.2.2 Approved indication

Treatment of moderate-to-severe vasomotor symptoms (VMS) caused by adjuvant endocrine therapy related to breast cancer in adult female patients.

2.2.3 Requested dosage

Summary of the requested standard dosage:

No change to the dosage recommendation was requested with the application for extension of indication.

2.2.4 Approved dosage

(See appendix)

2.3 Regulatory history (milestones)

Application	24 September 2025
Formal control completed	23 October 2025
List of Questions (LoQ)	20 February 2026
Response to LoQ	21 April 2026 and 27 May 2026
Preliminary decision	5 June 2026
Response to preliminary decision	22 June 2026
Labelling corrections and/or other aspects	30 June 2026
Response to labelling corrections and/or other aspects	6 July 2026
Final decision	29 July 2026
Decision	approval

3 Medical context

Vasomotor symptoms (VMS) such as hot flushes (HF) and night sweats are hallmark symptoms of menopause that are reported by up to 80% of menopausal women for a median duration of 7 years. VMS are episodes of sudden sensation of extreme heat, originating from the upper chest and face, spreading to the rest of the body and lasting for several minutes. They may be followed by profuse sweating and accompanied by palpitations and anxiety. Annoying nocturnal HF and sweating can lead to significant sleep disturbance [1].

Hypogonadism due to cancer therapy is also frequently associated with VMS. The incidence of VMS is particularly high in breast cancer patients on endocrine therapy (ET), including ovarian suppression or ablation, tamoxifen, and aromatase inhibitors, with reported VMS rates of up to >90% [1]. Even though the increase in VMS is more rapid and almost concomitant with the initiation of the ET, symptoms are similar in type and intensity to those experienced by women with symptomatic menopause [2].

Besides reduced QoL, VMS is also an important risk factor for decreased anticancer therapy adherence. Treatment interruption and discontinuation rates for breast cancer patients have been reported to be greater than 20%, with side effects such as VMS cited as a key contributing factor [1].

Although HT is the most effective treatment for VMS, it is often contraindicated in patients with hormone-sensitive cancers [1]. Non-hormonal pharmacologic and non-pharmacologic options for the treatment of VMS are often used off-label, have limited efficacy and safety data, and may be associated with significant side effects [3]. Hence, there is a medical need for new therapies for patients who suffer from ET-related VMS.

Lynkuet (elinzanetant) is a NK-1/3 receptor antagonist that was previously authorised for the treatment of moderate to severe VMS in postmenopausal patients.

Based on the results of the OASIS 4 double-blind (up to week 12), randomised, placebo-controlled phase 3 study, which investigated the efficacy and safety of elinzanetant for the treatment of VMS caused by adjuvant ET in female breast cancer patients, the applicant proposed the addition of a new indication to Lynkuet for the treatment of moderate to severe VMS caused by adjuvant ET.

References

1. Zhu L et al. Management of vasomotor symptoms in cancer patients. The Oncologist 2025;30:oyaf002. https://doi.org/10.1093/oncolo/oyaf002.
2. Asinaro G et al. Menopausal symptoms in breast cancer survivors on adjuvant endocrine therapy compared with those of menopausal women. Maturitas 2025;191:108143.
3. NCCN Guidelines Survivorship. Version 2.2025 – May 23, 2025. www.NCCN.org.

4 Nonclinical aspects

The applicant did not submit new nonclinical studies to support the requested indication extension. This was considered acceptable. Based on the ERA, the extension of the indication will not be associated with a significant risk for the environment.

5 Clinical aspects

5.1 Clinical pharmacology

Sufficient plasma samples were drawn during the OASIS 4 study to assess the pharmacokinetics in the newly studied patient population. The pharmacokinetics of elinzanetant and metabolites M30/34, M27 and M18/21 were adequately described using the legacy PopPK model of the initial submission.

The demographics of the OASIS 4 population were observed to be comparable with those of the OASIS 1-3 population, with the difference that the minimal age is lower in the OASIS 4 population due to the drug-induced menopause affecting potentially younger patients. No clinically relevant age-dependent effect on the exposure of elinzanetant or metabolites was found.

The drug-drug interaction potential of elinzanetant is sufficiently well described to adequately assess the impact of adjuvant endocrine therapies as perpetrators, and/or victims. In addition, OASIS 4 data shows that elinzanetant has no clinically relevant impact on the exposure of anastrozole and tamoxifen.

5.2 Dose finding and dose recommendation

No dedicated dose finding was conducted for the proposed new indication. Instead, reference was made to the initial application for the treatment of VMS in postmenopausal women, for which the proposed dosage of 120 mg once daily had been previously approved. Because the new and authorised indications are similar, and given the acceptable safety profile found for the proposed dosage in OASIS 4, the dose selection is appropriate.

5.3 Efficacy

The efficacy of elinzanetant was investigated in the OASIS 4 randomised, double-blind, placebo-controlled, multicentre study in patients with hormone receptor-positive breast cancer. A total of 474 patients were randomised in a 2:1 ratio to receive either elinzanetant or placebo once daily at bedtime for 12 weeks, followed by elinzanetant for a further 40 weeks, resulting in a total treatment duration of up to 52 weeks. Patients experiencing at least 35 moderate to severe hot flushes per week, including nocturnal hot flushes, were enrolled in OASIS 4. All patients received concomitant adjuvant endocrine therapy with either tamoxifen (56% overall, of whom 27% also received GnRH therapy) or aromatase inhibitors (44% overall, of whom 31% also received GnRH therapy).

The median age of the enrolled patients was 51 years (range 28 to 70 years). Of the patients, 88.2% were White, 1.5% were Black or African American, 0.4% were Asian, and 2.5% were of Hispanic or Latin American ethnicity. The study population included patients with a prior hysterectomy (12.4%) or prior unilateral or bilateral oophorectomy (12.2%).

The primary endpoints were the mean change in the frequency of moderate to severe hot flushes from baseline to weeks 4 and 12, including both daytime and nocturnal hot flushes, as recorded in an electronic diary.

Key secondary endpoints were the mean change from baseline to week 12 in patient-reported outcomes (PROs), assessed using the PROMIS Sleep Disturbance Short Form 8b (PROMIS SD SF 8b) total T-score for sleep disturbance and the Menopause-Specific Quality of Life (MENQOL) total score for menopause-related quality of life.

The elinzanetant treatment group demonstrated a statistically significant reduction in the frequency of moderate to severe hot flushes from baseline to weeks 4 and 12 compared with placebo.

The daily number of moderate to severe vasomotor symptoms (VMS) decreased by 7.5 from a baseline value of 11.4 by week 12 in the elinzanetant group. In the placebo group, the decrease over the same period was 4.2 from a baseline value of 11.5. After 4 weeks, a significant difference was observed between elinzanetant (reduction of 6.5 VMS per day) and placebo (reduction of 3.0 VMS per day).

In patients receiving adjuvant endocrine therapy with tamoxifen or aromatase inhibitors, the mean (standard deviation) reduction from baseline in the average daily number of moderate to severe VMS at week 12 was as follows:

- Tamoxifen subgroup: −8.07 (7.15) in the elinzanetant arm (N=160) versus −3.01 (4.90) in the placebo arm (N=85);
- Aromatase inhibitor subgroup: −7.39 (4.72) in the elinzanetant arm (N=132) versus −5.84 (7.07) in the placebo arm (N=62).

For the key secondary endpoints, elinzanetant demonstrated statistically significant superiority over placebo in improving both the PROMIS SD SF 8b total T-score (sleep disturbance) and the MENQOL total score (menopause-related quality of life) from baseline to week 12.

The PROMIS SD SF 8b score at baseline was approximately 60.6 and 60.5 in the elinzanetant and placebo groups, respectively. By week 12, the score had decreased by 10.0 points with elinzanetant and by 3.9 points with placebo. The baseline MENQOL total score was approximately 4.8 in both the elinzanetant and placebo groups. By Week 12, the score had decreased by 1.2 points with elinzanetant and by 0.55 points with placebo.

5.4 Safety

The safety profile of elinzanetant as observed in the pivotal OASIS 4 study was characterised by fatigue (including asthenia, somnolence, and hypersomnia), gastrointestinal adverse effects (such as diarrhoea), dizziness (including vertigo), and depression-related treatment-emergent adverse events (TEAEs). A warning regarding potential central nervous effects under therapy with elinzanetant was requested and added to the Information for healthcare professionals. In its response to Swissmedic's Preliminary Decision, the applicant reported additional post-marketing cases of seizures, in addition to one patient who had been previously reported in the OASIS 2 study. The applicant has categorised seizures as an Important Identified Risk, and a warning regarding potential seizures under therapy with elinzanetant was requested and added to the Information for healthcare professionals.

Additional unfavourable effects that were reported more frequently for elinzanetant than for placebo included peripheral oedema, urinary tract infection, decreased appetite, pruritus, and pyrexia. Overall, the observed safety profile of elinzanetant in the new indication appeared similar to the indication of VMS associated with menopause. Notable differences between the two indications included depression-related TEAEs reported in the OASIS 4 study, whereas rash was reported as a common unfavourable effect in patients treated for VMS associated with menopause.

The proportions of patients in the OASIS 4 study who experienced severe, serious or treatment-emergent adverse events leading to discontinuation of elinzanetant were low.

Despite less than 5% of patients reporting liver events after exposure to elinzanetant, a potential for liver toxicity, which is known for NK receptor antagonists, cannot be excluded. For instance, more patients in the elinzanetant arm than in the placebo arm were reported with liver events, including hepatic steatosis, during the randomised week 1-12 study period. Liver safety has been labelled as a warning in the Information for healthcare professionals.

Endometrial biopsies, transvaginal ultrasound, and mammogram/ultrasound imaging did not reveal concerning safety signals. However, endometrial biopsies were only conducted on demand, while on-treatment results for transvaginal ultrasound and mammogram/ultrasound imaging were only available at week 52. Because randomised placebo treatment was limited to week 1-12, no comparison to placebo was possible for week 52 results. In this context, it is noteworthy that a higher

postmenopausal uterine bleeding rate was reported in the elinzanetant arm during week 1-12: 1.8% (5) patients vs no cases in the placebo arm. However, given elinzanetant's different mechanism of action compared to HT, specific adverse effects on the breast and uterus would not necessarily be expected. Endometrial safety has been labelled in the Information for healthcare professionals.

5.5 Final clinical benefit risk assessment

Since the potential benefits were considered to exceed the potential risks, the benefit-risk ratio of Lynkuet (elinzanetant) was deemed to be positive for the treatment of moderate to severe VMS caused by adjuvant ET related to breast cancer in adult female patients.

6 Risk management plan summary

The RMP summaries contain information on the medicinal products′ safety profiles and explain the measures that are taken to further investigate and monitor the risks, as well as to prevent or minimise them.
The RMP summaries are published separately on the Swissmedic website. It is the responsibility of the marketing authorisation holder to ensure that the content of the published RMP summaries is accurate and correct. As the RMPs are international documents, their summaries might differ from the content in the Information for healthcare professionals / product information approved and published in Switzerland, e.g. by mentioning risks that occur in populations or indications not included in the Swiss authorisations.

7 Appendix

Approved Information for healthcare professionals

Please be aware that the following version of the Information for healthcare professionals for Lynkuet was approved with the submission described in the SwissPAR. This Information for healthcare professionals may have been updated since the SwissPAR was published.

Please note that the valid and relevant reference document for the effective and safe use of medicinal products in Switzerland is the Information for healthcare professionals currently authorised by Swissmedic (see www.swissmedicinfo-pro.ch).

Note:
The following Information for healthcare professionals has been translated by the MAH. It is the responsibility of the authorisation holder to ensure the translation is correct. The only binding and legally valid text is the Information for healthcare professionals approved in one of the official Swiss languages.

▼ 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 new or serious adverse reactions. See the “Undesirable effects” section for advice on the reporting of adverse reactions.

Lynkuet®

Composition

Active substances

Elinzanetant.

Excipients

All-rac-alpha-tocopherol, caprylocaproyl macrogolglycerides, glycerol monocaprylocaprate, glycerol mono-oleate, polysorbate 80 (E 433).
Capsule shell: Gelatin, sorbitol 75 mg (E 420) and glycerol (E 422), red iron oxide, yellow iron oxide, titanium dioxide (E 171).
Printing ink: Ammonia solution concentrated, isopropyl alcohol, macrogol 400, polyvinyl acetate phthalate, propylene glycol (E 1520), purified water, ethanol, ethyl acetate, titanium dioxide (E 171).

Pharmaceutical form and active substance quantity per unit

Soft capsule with 60 mg elinzanetant.
Appearance
Opaque red, oblong soft capsules, with white imprint “EZN60”.

Indications/Uses

Treatment of moderate-to-severe vasomotor symptoms (VMS)

- in postmenopausal female patients.
- caused by adjuvant endocrine therapy related to breast cancer in adult female patients.

Dosage/Administration

The recommended daily dose is 120 mg elinzanetant (two 60 mg capsules) once daily at bedtime.
To date, no data are available for treatment durations of more than 12 months. Hence, the benefit-risk balance should be reviewed regularly after the first year of treatment.

Forgotten dose
If a dose has been forgotten, the next dose should be taken as scheduled on the following day at bedtime. Two doses should not be taken on the same day to make up for a forgotten dose.

Mode of administration

Oral use.
The capsules should be swallowed whole with water. The capsules must not be chewed, crushed or otherwise broken.
The capsules can be taken with or without food.

Special dosage instructions
Elderly patients
The safety and efficacy of elinzanetant have not been established in women over 65 years. No dose recommendation can be made for this population.

Children and adolescents
The safety and efficacy of elinzanetant have not been studied in children and adolescents under 18 years. Lynkuet has no indication in this age group.

Patients with impaired hepatic function
No dose adjustment is required for patients with mild chronic hepatic impairment (Child-Pugh A).
Elinzanetant is not recommended for use in patients with moderate (Child-Pugh B) chronic hepatic impairment (see “Warnings and precautions”, as well as “Pharmacokinetics”, section “Kinetics in specific patient groups”).
In patients with severe hepatic impairment (Child-Pugh C), elinzanetant is contraindicated.

Patients with impaired renal function
No dose adjustment is required for patients with mild or moderate renal impairment (eGFR 30 to 89 mL/min/1.73 m^2).
Elinzanetant is not recommended for use in patients with severe renal impairment (eGFR < 30 mL/min/1.73 m^2) (see “Pharmacokinetics”, section “Kinetics in specific patient groups”).

Co-administration with CYP3A4 inhibitors
Concomitant use of elinzanetant together with strong CYP3A4 inhibitors is contraindicated.
When moderate CYP3A4 inhibitors are used concomitantly, the recommended daily dose is 60 mg elinzanetant (one 60 mg capsule), taken once daily in the evening at bedtime (see “Interactions”).
After discontinuation of the moderate inhibitor, Lynkuet can be used again after 3 to 5 of its half-lives at the usual dose of 120 mg once daily. This dose adjustment is based on modeling and has not been studied in clinical trials.
No dose adjustment is required when weak CYP3A4 inhibitors are used concomitantly.

Contraindications

- Severe hepatic impairment

- Concomitant use of strong CYP3A4 inhibitors (see “Warnings and precautions” and “Interactions”)
- Hypersensitivity to the active substance or any of the excipients (see “Composition”)
- Known or suspected pregnancy

Warnings and precautions

Seizures

Seizures have been reported in patients taking elinzanetant during clinical studies and in post-marketing experience (see “Undesirable effects”).
Patients must be informed of the potential risk of seizures. Elinzanetant treatment in patients with a prior history of seizures or with clinical conditions that can lower the seizure threshold, including co-medications associated with this risk, requires an individual benefit-risk assessment.

Central nervous system effects

Patients should be advised that central nervous system effects, including fatigue, sleepiness and dizziness, may occur during treatment with elinzanetant (see “Effects on ability to drive and use machines” and “Undesirable effects”).
Patients with VMS caused by adjuvant endocrine therapy should be advised that treatment with elinzanetant may lead to depressed mood and depression (see “Undesirable effects”).

Clinically relevant interactions

Cytochrome P450 isoform 3A4 (CYP3A4) inhibitors reduce the clearance of elinzanetant, leading to greater exposure. Concomitant use of elinzanetant with strong CYP3A4 inhibitors is contraindicated. When used concomitantly with moderate CYP3A4 inhibitors, the elinzanetant dose must be adjusted (see “Dosage/Administration” and “Interactions”).
Strong or moderate CYP3A4 inducers reduce elinzanetant exposure. In the event of concomitant use of a strong or moderate CYP3A4 inducer, the patient should be informed that the efficacy of elinzanetant may be reduced. No data are available for a possible dose adjustment. Such a dose adjustment is not recommended, partly because elinzanetant exhibits non-linear absorption kinetics (see "Pharmacokinetics").

Hepatic safety

Clinical studies with elinzanetant have so far revealed no clear indications of any hepatotoxicity. However, transaminase elevations have been reported in association with elinzanetant treatment (see “Undesirable effects”). Du to the limited number of patients treated with elinzanetant in clinical studies to date, possible rare hepatic adverse reactions cannot be completely excluded, based on observations within this class of drugs.

Patients with impaired hepatic function

Use is not recommended in patients with moderate hepatic impairment. If such patients should nevertheless be treated with Lynkuet, liver function tests must be closely monitored (see “Dosage/Administration”).

Hormone replacement therapy (HRT)

Concomitant use of elinzanetant together with HRT has not been investigated. Hence, Lynkuet is not recommended for use together with systemic HRT.

Elinzanetant in combination with other breast cancer treatments

The use of elinzanetant has been studied in combination with AET (adjuvant endocrine therapy) consisting of aromatase inhibitors or tamoxifen, with or without GnRH agonists. The decision to treat women with elinzanetant who are receiving medication other than those evaluated in the clinical studies should be based on an individual benefit-risk assessment.

Excipients of particular interest

This medicinal product contains 75 mg sorbitol (E 420) per soft capsule. The additive effect of co-administered medicinal products containing sorbitol (or fructose) and dietary intake of sorbitol (or fructose) must be taken into account. The content of sorbitol in medicinal products for oral use may affect the bioavailability of other concomitantly administered medicinal products for oral use.

Interactions

Pharmacokinetic interactions

Effect of other medicinal products on the pharmacokinetics of elinzanetant
Elinzanetant is mainly metabolized via the cytochrome P450 isoform 3A4 (CYP3A4) and is a substrate for the P-glycoprotein (P-gp) transporter protein. Hence, medicinal products that induce or inhibit CYP3A may affect the clearance of elinzanetant.
In patients taking moderate CYP3A4 inhibitors (e.g. erythromycin, ciprofloxacin, fluconazole, verapamil), the recommended daily dose of Lynkuet is 60 mg (see “Dosage/Administration” and “Warnings and precautions”).
Concomitant use of Lynkuet with grapefruit juice is not recommended.

No clinically relevant interactions with P-gp inhibitors are expected due to high permeability of elinzanetant through membranes and its main elimination through metabolism.

Table 1 shows the geometric mean ratio (GMR) of the pharmacokinetic parameters of elinzanetant when taken with/without concomitant medication with 90% confidence intervals (CI).

Table 1: Interactions between elinzanetant and other medicinal products with regard to the influence of other medicinal products on the pharmacokinetics of elinzanetant

Active substance (dosage regimen)	*Effects on drug concentration. GMR (90% CI) elinzanetant*	*Recommendation*
Itraconazole 200 mg (a strong CYP3A4 and P-gp inhibitor) Elinzanetant 120 mg	C_{max}: 3.31 (2.74-4.00) AUC: 6.32 (5.36; 7.44)	Elinzanetant must not be used together with strong CYP3A4 inhibitors (e.g. itraconazole, clarithromycin, ritonavir or cobicistat) (see "Contraindications"). In patients taking moderate CYP3A4 inhibitors (e.g. erythromycin, ciprofloxacin, fluconazole, verapamil), a daily dose of 60 mg elinzanetant is recommended based on predictions from physiologically-based pharmacokinetic (PBPK) models. No dose adjustment is required when weak CYP3A4 inhibitors are co-administered.
Carbamazepine 600 mg (a strong CYP3A4 and P-gp inducer) Elinzanetant 120 mg	C_{max}: 0.56 (0.50; 0.62) AUC: 0.36 (0.31; 0.41)	Strong or moderate CYP3A4 inducers may lead to a reduction in efficacy (see "Warnings and precautions").
Esomeprazole 40 mg Elinzanetant 120 mg	C_{max}: 1.01 (0.87; 1.18)	No dose adjustment is required when proton pump inhibitors are taken together with elinzanetant.

Effect of elinzanetant on the pharmacokinetics of other medicinal products

Elinzanetant is both an inhibitor and inducer of human CYP3A4 *in vitro*. In addition, elinzanetant is an inhibitor of the transporters BCRP, P-gp and OATP1B3 *in vitro*. Hence, elinzanetant may affect exposure to medicinal products eliminated primarily by CYP3A4 or the transporters BCRP, P-gp and

OATP1B3. Clinical interaction studies with midazolam, a sensitive CYP3A4 substrate, showed that elinzanetant is a weak inhibitor of CYP3A4 at therapeutic doses in humans. This is not clinically relevant.
A slight increase in exposure was observed when elinzanetant was co-administered with rosuvastatin, a BCRP and OATP substrate; however, this increase is not clinically relevant.
No clinically relevant effect on exposure to dabigatran, a P-gp substrate, was observed after co-administration with elinzanetant.
Table 2 shows the geometric mean ratio (GMR) of the pharmacokinetic parameters of co-medication when taken with/without elinzanetant with 90% confidence intervals (CI).

Table 2: Interactions between elinzanetant and other medicinal products with regard to the effect of elinzanetant on other medicinal products

Active substance (dosage regimen)	*Effects on drug concentration. GMR (90% CI) elinzanetant*	*Recommendation*
Elinzanetant, multiple daily doses of 120 mg Midazolam 1 mg (a sensitive CYP3A4 substrate)	C_{max}: 1.49 (1.36; 1.64) AUC: 1.80 (1.61; 2.00)	Caution is required when elinzanetant is co-administered with CYP3A4 substrates with a narrow therapeutic window (e.g. ciclosporin, fentanyl or tacrolimus). The information in the Information for healthcare professionals for these CYP3A4 substrates must also be observed.
Elinzanetant 120 mg Rosuvastatin 5 mg	C_{max}: 1.28 (1.11; 1.48) AUC: 1.23 (1.07; 1.40)	Elinzanetant can be used together with BCRP substrates.
Elinzanetant, multiple daily doses of 120 mg Tamoxifen, multiple daily doses of 20 mg	Tamoxifen: 1.06 (0.97; 1.15), 4-hydroxytamoxifen: 1.10 (1.02; 1.19), N-desmethyltamoxifen: 0.99 (0.93; 1.05), Endoxifen: 0.97 (0.92; 1.04)	Elinzanetant can be used together with tamoxifen.
Elinzanetant 120 mg	C_{max}: 1.15 (0.75; 1.76) AUC: 1.19 (0.79; 1.81)	Elinzanetant can be used together with P-gp substrates.

Dabigatran 75 mg		
Elinzanetant, multiple daily doses of 120 mg Anastrozole, multiple daily doses of 1 mg	Anastrozole: 1.00 (0.94 – 1.06)	Elinzanetant can be used together with anastrozole.

Pregnancy, lactation

Pregnancy

There are no available data on the use of elinzanetant in pregnant woman. If pregnancy occurs during treatment with Lynkuet, treatment must be discontinued. Studies in animals have shown reproductive toxicity (see “Preclinical data”).

Lynkuet is contraindicated during pregnancy (see “Contraindications”). Women of childbearing potential must use effective contraception during treatment and for 2 weeks after stopping treatment. Non-hormonal contraceptives are recommended for this patient group.

Lactation

There are no human data on the possible excretion of elinzanetant or its metabolites in human milk, and it is not known whether elinzanetant might have an effect on milk production or the breastfed infant.

In animals, elinzanetant and its metabolites are excreted in milk (see “Preclinical data”). Concentrations of elinzanetant in milk were higher than in plasma. Lynkuet is not recommended for use in breast-feeding women.

Fertility

No human data are available on the possible influence of elinzanetant on fertility.

In female rats, impairment of fertility was observed at exposures markedly exceeding human exposure at the therapeutic dose (see “Preclinical data”).

Effects on ability to drive and use machines

Driving ability after administration of elinzanetant was assessed in a clinical study using computer-based driving simulation. Compared with placebo, minor impairment of driving ability was observed after the first dose, but not after multiple doses. However, the predefined, validated threshold for impaired driving ability was not exceeded.

Nevertheless, users should be advised to be careful when driving a vehicle or using machines if fatigue, dizziness or sleepiness occur during treatment with Lynkuet (see “Warnings and precautions”, “Undesirable effects” and “Properties/Effects”).

Undesirable effects

Treatment of moderate-to-severe VMS in postmenopausal female patients
The safety profile data are based on data from 4 phase II and III studies (SWITCH-1, OASIS 1/2/3), in which a total of n=1113 postmenopausal patients with VMS received at least one dose of elinzanetant 120 mg, and from the post-marketing phase. For this indication, the most frequently observed adverse reactions (≥ 5%) with elinzanetant were headache and fatigue.

Treatment of moderate-to-severe VMS caused by adjuvant endocrine therapy
The safety profile data are based on data from a phase III study (OASIS 4), in which n=465 female patients with VMS caused by adjuvant endocrine therapy received at least one dose of elinzanetant 120 mg, and from the post-marketing phase.
For this indication, the most commonly observed adverse reactions (≥ 5%) with elinzanetant were fatigue, sleepiness, diarrhea, depression and muscle cramps.

The adverse reactions observed in clinical studies are listed below by system organ class (according to MedDRA) and frequency, with frequency categories defined as follows: very common: ≥1/10, common: ≥1/100, <1/10, uncommon: ≥1/1000, <1/100, rare: ≥1/10'000, <1/1000, very rare: <1/10’000.

Table 3: Adverse reactions observed with elinzanetant

	Elinzanetant in female patients with postmenopausal VMS	Elinzanetant in female patients with VMS caused by adjuvant endocrine therapy
Infections and infestations		
Common		Urinary tract infection
Metabolism and nutrition disorders		
Common		Decreased appetite
Psychiatric disorders		
Common		Depression Depressed mood
Nervous system disorders		
Common	Headache Sleepiness Dizziness	Sleepiness Dizziness Vertigo
Rare	Seizure *	Seizure *
Gastrointestinal disorders		

Common	Upper abdominal pain Diarrhea	Diarrhea
Hepatobiliary disorders		
Common		Alanine aminotransferase (ALT) increased *
Uncommon	Alanine aminotransferase (ALT) increased * Aspartate aminotransferase (AST) increased *	Aspartate aminotransferase (AST) increased *
Skin and subcutaneous tissue disorders		
Common	Rash (including maculopapular, papular and pruritic rash)	Alopecia Pruritus
Uncommon	Photosensitivity reaction *	Photosensitivity reaction *
Musculoskeletal and connective tissue disorders		
Common	Muscle cramps/muscle tightness	Muscle cramps/muscle tightness
General disorders		
Very common		Fatigue/asthenia
Common	Fatigue/asthenia	Oedema peripheral Fever

* see “Description of selected undesirable effects”

Description of selected undesirable effects

Seizure

As part of clinical studies, only a few patients with a prior history of seizures were treated with elinzanetant. In one of these patients with a pre-existing seizure disorder, a seizure occurred after initiation of treatment with elinzanetant, following a period of many years without seizures. There have been post-marketing reports of seizures in patients, some of whom had a prior history of seizures and/or were receiving co-medications that can lower the seizure threshold.

Photosensitivity reaction

In the pooled safety data (SWITCH-1, OASIS 1/2/3) up to 52 weeks, photosensitivity reactions were reported in 0.4% of patients treated with elinzanetant and in 0.1% of patients treated with placebo.
In OASIS 4 up to 52 weeks, photosensitivity reactions were reported in 0.9% of patients treated with elinzanetant and in 0.6% of patients treated with placebo.

ALT and AST increased
In the pooled safety data (SWITCH-1, OASIS 1/2/3) up to 52 weeks, the event “ALT increased” was reported in 0.6% of patients treated with elinzanetant and in 0.5% of patients treated with placebo. The event “AST increased” was reported in 0.4% of patients treated with elinzanetant and in 0.5% of patients treated with placebo. In OASIS 4 up to 52 weeks, the event “ALT increased” was reported in 1.1% of patients treated with elinzanetant and in 0.6% of patients treated with placebo. The event “AST increased” was reported in 0.6% of patients treated with elinzanetant and in none of the patients treated with placebo.

Reporting suspected adverse reactions after authorization of the medicinal product is very important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions online via the ElViS portal (Electronic Vigilance System). You can obtain information about this at www.swissmedic.ch.

Overdose

No cases of overdose have been reported.

Symptoms
In clinical studies with healthy subjects, single doses of up to 600 mg elinzanetant were investigated. The adverse reactions at higher doses were comparable with those at the therapeutic dose, but occurred slightly more frequently and with moderately higher intensity. No additional adverse reactions were observed with use of daily doses up to 240 mg for 5 days. No dose-limiting toxic effects were observed within the dose range investigated.

Therapy
There is no specific antidote.
In the event of overdose, the patient should be closely monitored. Depending on the symptoms, supportive treatment should be considered.

Properties/Effects

ATC code

G02CX07

Mechanism of action

Elinzanetant is a non-hormonal, selective neurokinin 1 (NK-1) and 3 (NK-3) receptor antagonist that blocks NK-1 and NK-3 receptor signaling on kisspeptin/neurokinin B/dynorphin (KNDy) neurons, thereby modulating neuronal activity involved in thermo- and sleep regulation. The decrease in

estrogen levels during menopause, or the blockade of estrogen activity by adjuvant endocrine therapy, is accompanied by hyperactivation of KNDy neurons in the hypothalamus, leading to altered activity of the thermo- and sleep-regulatory center. This results in so-called vasomotor symptoms (VMS).
Elinzanetant has high affinity for human NK-1 receptors (pK_i values of 8.7 to 10.2) and NK-3 receptors (pK_i values of 8.0 to 8.8), but not for human NK-2 receptors (pK_i just 6.0). Elinzanetant is more than 100-fold more selective for the human NK-3 receptor and more than 300-fold for the human NK-1 receptor than for numerous other non-NK receptors and off-targets.

Pharmacodynamics

Safety pharmacodynamics
After administration of a single oral dose of elinzanetant at doses up to 5 times the recommended dose, no clinically relevant prolongation of the QTc interval was observed.

Clinical efficacy

Treatment of moderate-to-severe vasomotor symptoms (VMS) in postmenopausal female patients
The efficacy of elinzanetant was investigated in two randomized, double-blind, placebo-controlled, multicenter studies (OASIS 1 and 2) in a total of n=796 postmenopausal female patients. Patients aged 40-65 years experiencing at least 50 moderate-to-severe hot flashes over a period of 7 consecutive days during a screening phase were eligible for inclusion. Female patients were treated with 120 mg elinzanetant or placebo in a double-blind manner for 12 weeks. All patients then received 120 mg elinzanetant for a further 14 weeks.
The mean age of enrolled patients was 54.6 years. 80.4% of the patients were white, 17.1% were black or African American and 0.5% were of Asian origin.
The study population included patients with natural menopause, as well as those post-hysterectomy (39%) or post-oophorectomy (21%). 31% of the patients had already received hormone replacement therapy (HRT).

The studies each had four primary endpoints, viz. the mean change in frequency and severity of moderate-to-severe VMS from baseline to weeks 4 and 12, taking into account both daytime and night-time VMS, with hot flashes recorded in an electronic diary. The key secondary endpoints were the mean change in frequency of moderate-to-severe hot flashes from baseline to week 1 as per diary, the mean change in patient self-assessment (Patient-Reported Outcome, PRO) using PROMIS SD SF 8b total T-score to assess sleep disturbances and MENQOL total score to assess menopause-related quality of life from baseline to week 12.

In both studies, elinzanetant showed statistically significant superiority versus placebo across all four primary endpoints. In the pooled data from both studies, the daily number of moderate-to-severe VMS decreased with elinzanetant by 9.2 from a baseline of 14.0 by week 12. With placebo, the decrease during this period was 6.0, compared to a baseline value of 15.2. After as little as 4 weeks, a significant and clinically relevant difference was observed between elinzanetant (a decrease of 8.05 VMS per day) and placebo (a decrease of 4.9).
The baseline severity score was approximately 2.5 in both treatment groups. By week 12, it decreased by 0.9 with elinzanetant and by 0.6 with placebo. Once again, a significant difference was observed between the two groups after as little as 4 weeks. Findings for the secondary endpoints investigated (including PROMIS SD SF 8b total T-score to assess sleep disturbances and MENQOL total score to assess menopause-related quality of life) were consistent.

A clinically relevant reduction in frequency and severity of moderate-to-severe VMS was observed as early as during the first week of treatment. Efficacy was maintained throughout the entire 26-week treatment period.

In another randomized, double-blind, placebo-controlled, multicenter phase III study (OASIS 3) in n=628 postmenopausal women, the efficacy of elinzanetant was investigated over a duration of up to 12 months; efficacy of elinzanetant was maintained up to the end of treatment.

Treatment of moderate-to-severe vasomotor symptoms (VMS) caused by adjuvant endocrine therapy
The efficacy of elinzanetant was investigated in a randomised, double-blind, placebo-controlled, multicentre study (OASIS 4) in female patients with hormone receptor-positive breast cancer. A total of n=474 female patients were randomised at a 2:1 ratio to receive either elinzanetant or placebo once daily at bedtime for a period of 12 weeks, followed by elinzanetant for 40 weeks, resulting in a total treatment duration of up to 52 weeks. Patients experiencing at least 35 moderate-to-severe hot flushes per week, including nighttime hot flushes, were enrolled in OASIS 4. All patients were concurrently receiving adjuvant endocrine therapy with either tamoxifen (56% in total; 27% of whom were receiving concomitant GnRH) or aromatase inhibitors (44% in total; 31% of whom were receiving concomitant GnRH).
The mean age of enrolled female patients was 51 years (age range: 28-70). 88.2% of patients were White, 1.5% Black or Afro-American, 0.4% Asian and 2.5% of Hispanic or Latin American descent. The study population included female patients with previous hysterectomy (12.4%) or previous unilateral/bilateral oophorectomy (12.2%).
The primary endpoint was the mean change in frequency of moderate-to-severe hot flushes from baseline up to weeks 4 and 12, including daytime and nighttime hot flushes measured using an electronic diary.

Key secondary endpoints included the mean change in patient-reported outcomes (PROs), assessed via the PROMIS SD SF 8b total T-score for sleep disturbance and the MENQOL total score for menopause-related quality of life in the menopause, from baseline up to week 12.
The elinzanetant treatment group showed a statistically significant reduction in frequency of moderate-to-severe hot flushes from baseline up to weeks 4 and 12, compared to placebo.
The daily number of moderate-to-severe VMS decreased by 7.5 from a baseline of 11.4 by week 12 in the elinzanetant group. In the placebo group, the decrease over this period was 4.2, from a baseline of 11.5. After 4 weeks, a significant difference was found between elinzanetant (a decrease of 6.5 VMS per day) and placebo (a decrease of 3). In female patients receiving adjuvant endocrine therapy with tamoxifen or aromatase inhibitors, the mean (standard deviation) reduction in the average daily number of moderate-to-severe VMS from baseline to week 12 was as follows:

- Tamoxifen subgroup: -8.07 (7.15) in the elinzanetant arm [N=160] vs. -3.01 (4.90) in the placebo arm [N=85];
- Aromatase inhibitor subgroup: -7.39 (4.72) [N=132] in the elinzanetant arm vs. -5.84 (7.07) [N=62] in the placebo arm.

For elinzanetant, statistically significant superiority over placebo was shown for the key secondary endpoints, viz. improvement in the PROMIS SD SF 8b total T-score (sleep disturbance) and the MENQOL total score (quality of life in the menopause), from baseline to week 12.
The PROMIS SD SF 8b score at baseline was approximately 60.6 and 60.5 for the elinzanetant group and placebo group, respectively. By week 12, it had decreased by 10 with elinzanetant and by 3.9 with placebo. The baseline MENQOL total score was approximately 4.8 for both the elinzanetant and placebo groups. By week 12, it had decreased by 1.2 with elinzanetant and by 0.55 with placebo.

Endometrial safety
The endometrial safety of elinzanetant was investigated in the OASIS 1 and 2 studies (each lasting 6 months) and OASIS 3 (lasting 12 months) using transvaginal ultrasound and endometrial biopsies; after 12 months of treatment with elinzanetant, evaluable biopsies were available from 116 patients. Transvaginal ultrasound revealed no indications of any increase in endometrial thickness. No cases of endometrial hyperplasia or endometrial malignancies were identified in the endometrial biopsies.

Bone safety
In the OASIS 3 study, a subgroup of n=343 patients underwent DEXA scans to measure bone mineral density (BMD) at baseline and after 12 months of treatment. Mean percentage changes in BMD vs. baseline with elinzanetant were comparable to those with placebo and were within the expected age-related changes per year.

Pharmacokinetics

The steady-state exposure variables of elinzanetant in women with VMS taking 120 mg elinzanetant daily are as follows: The $AUC_{(0-24)ss}$ is 8572.0 h·µg/L with a geometric coefficient of variation (CV) of 46.7%. The peak steady-state plasma concentration ($C_{max,ss}$) is 1422.7 µg/L with a geometric CV of 34.8%.
Elinzanetant is practically insoluble in water and readily soluble under acidic conditions.

Absorption

C_{max} and AUC of elinzanetant increased disproportionately over the dose range of 40 to 160 mg once daily.
Steady-state plasma concentrations of elinzanetant were reached 5 to 7 days after daily dosing, whereupon modest accumulation (< 2-fold) was observed.
The median time to reach C_{max} of elinzanetant was 1.0 (1 to 4) hours. The absolute bioavailability of elinzanetant is 52%.
After food intake, a prolongation of T_{max} to 2.5 – 3.5 hours post-dose, as well as a reduction in C_{max} by approximately 70% and AUC by 30 – 40%, were observed. The minimum plasma concentration C_{trough} remained unchanged regardless of food intake.

Distribution

After intravenous administration, the mean steady-state volume of distribution (V_{ss}) of elinzanetant was 137 L, indicating extensive extravascular distribution. Plasma protein binding of elinzanetant is high (99.7%) and is influenced by circadian fluctuations. The blood-to-plasma ratio is between 0.6 and 0.7.
Exposure of elinzanetant in the human brain was demonstrated in clinical positron emission tomography (PET) studies.

Metabolism

Elinzanetant is primarily metabolized by CYP3A4 into three active metabolites. These metabolites have similar potency on human NK-1 and NK-3 receptors as elinzanetant.
At steady state, the geometric mean plasma AUC_{ss} for the three major metabolites corresponded to 53%, 29% and 27% of the parent compound AUC_{ss} respectively (based on the PopPK model).

Elimination

The clearance of elinzanetant after a single intravenous dose was 8.77 L/h.
After oral administration of elinzanetant, approximately 90% of the dose was excreted via feces (mainly as metabolites) and less than 1% via the urine. The half-life of elinzanetant in women with vasomotor symptoms was approximately 45 hours.

Kinetics in specific patient groups

Patients with impaired hepatic function

In patients with Child-Pugh Class A (mild) chronic hepatic impairment, a 1.2-fold increase in C_{max} and a 1.5-fold increase in $AUC_{(0-24)}$ was observed after multiple-dose administration of 120 mg elinzanetant, compared to subjects with normal hepatic function. In patients with Child-Pugh Class B (moderate) chronic hepatic impairment, mean C_{max} and $AUC_{(0-24)}$ of elinzanetant increased by 2.3-fold. Elinzanetant has not been studied in patients with Child-Pugh Class C (severe) chronic hepatic impairment.

Patients with impaired renal function

In patients with moderate renal impairment (eGFR 30 to 59 mL/min/1.73 m^2), a 2.3-fold increase in $C_{max,unbound}$ and a 2.2-fold increase in $AUC_{unbound}$ were observed after administration of a single dose of 120 mg elinzanetant. In patients with severe renal impairment (eGFR less than 30 mL/min/1.73 m^2), a 1.9-fold increase in $C_{max,\ unbound}$ and $AUC_{unbound}$ was observed.

In patients with mild or moderate renal impairment, population pharmacokinetic analyses of clinical study data showed similar exposure (AUC) and peak plasma concentration (C_{max}) of elinzanetant as in patients with normal renal function.

Elinzanetant has not been studied in patients with end-stage renal failure (eGFR < 15 mL/min/1.73 m^2).

Age, BMI, race (white, black or African American) and ethnicity had no clinically relevant effect on the pharmacokinetics of elinzanetant.

Preclinical data

Systemic toxicity

Repeat-dose toxicity studies were conducted in rats and cynomolgus monkeys. In female rats, daily administration of elinzanetant for 4 weeks at doses of 100 mg/kg (40-fold the $AUC_{(0-24)}$ at the human therapeutic dose) showed mucification of the vaginal epithelium, uterine atrophy and persistent corpora lutea.

In a 13-week study on rats with twice-daily administration, treatment with elinzanetant at doses of ≥ 50 mg/kg/day in male and ≥ 20 mg/kg/day in female animals (4- and 7-fold, respectively, the $AUC_{(0–24\ h)}$ compared to the human therapeutic dose) resulted in tremor and muscle contractions (first observed on day 24) and convulsions (from day 34 onwards) in 10 out of 106 animals.

In the same study, daily administration of elinzanetant at doses from 100 mg/kg/day (16-fold the $AUC_{(0-24)}$ at the human therapeutic dose) showed skeletal muscle degeneration and necrosis. Convulsions were also observed in a 2-year rat study at doses from 60 mg/kg/day (20-fold the $AUC_{(0-24)}$ at the human therapeutic dose).

In cynomolgus monkeys, daily administration of elinzanetant for 39 weeks with twice-daily administration of doses from 60 mg/kg/day showed reduced cyclical ovarian activity.

Furthermore, diarrhea was observed in female animals at a dose of 80 mg/kg/day and in male animals at both 30 mg/kg/day and 80 mg/kg/day. Exposure ($AUC_{(0-24h)}$) at these doses was comparable to that at the recommended human dose.

Reproductive toxicity

In the embryofetal development studies with elinzanetant, there was no evidence of embryofetal lethality or teratogenicity at high doses up to 100 mg/kg/day in rats and up to 140 mg/kg/day in rabbits (23-fold and 1-fold the $AUC_{(0-24)}$ at the human therapeutic dose, respectively).

In the female rat fertility and early embryonic development study, there was a higher proportion of pre-implantation and post-implantation embryo losses, leading to reduced litter size and lower fetal body weights, at the dose of 100 mg/kg/day (16-fold the $AUC_{(0-24)}$ at the human therapeutic dose). These effects were not observed after doses of 25 mg/kg/day (4-fold the $AUC_{(0-24)}$ at the human therapeutic dose).

In the pre- and post-natal development studies in rats, F_0 females showed post-implantation losses, prolonged gestation length, delayed parturition and dystocia, as well as lower pup weights, at doses of 100 mg/kg/day (23-fold the $AUC_{(0-24)}$ at the human therapeutic dose). Increased total litter loss and a corresponding decrease in pup viability on postnatal day 5 was observed in the range of human therapeutic exposure.

After administration of radiolabelled elinzanetant to lactating rats, approximately 6% of the elinzanetant dose was excreted in milk.

Genotoxicity

Elinzanetant showed no genotoxic potential in a series of *in vitro* and *in vivo* genotoxicity tests including a bacterial mutation assay (Ames test), a mouse lymphoma assay and an *in vivo* bone marrow micronucleus test in rats. Additionally, the principal human metabolites of elinzanetant were negative for *in vitro* genotoxicity in the Ames test and micronucleus test.

Carcinogenicity

In a 2-year carcinogenicity study with elinzanetant in rats, an increase in uterine neoplasms and lymphomas was reported. The findings were seen at a dose from 60 mg/kg/day, representing at least 29-fold the total $AUC_{(0-24)}$ at the human therapeutic dose, and are thus not considered clinically relevant. These effects were not observed at a dose representing 7-fold the total $AUC_{(0-24)}$ at the human therapeutic dose. The increased incidence of uterine neoplasms in aged rats undergoing reproductive senescence, with pronounced reduction in body weight, resembles effects observed in

dietary restriction studies in rats and chronic, drug-induced hypoprolactinemia, a rat-specific mode of action, which is not relevant for humans.

In the 26-week carcinogenicity study with elinzanetant in transgenic mice, no drug-related neoplasms were observed up to the highest dose of 85 and 70 mg/kg/day in male and female animals, respectively (3 and 2 times the $AUC_{(0-24)}$ at the human therapeutic dose, respectively).

Safety pharmacology

Overall, non-clinical data reveal no special hazard for humans based on conventional studies of secondary pharmacodynamics, safety pharmacology and abuse potential.

In a core battery of safety pharmacology studies, elinzanetant caused no acute respiratory or neurobehavioral effects in rats at doses up to 100 mg/kg; at this dose, mean $C_{max, unbound}$ at steady state was 28-fold higher than the human C_{max} of 1423 ng/mL (= 7.1 nM free) at 120 mg/day. A cardiovascular study on monkeys showed a slight, reversible increase in heart rate (by up to 15%) and a minor reduction in body temperature (by up to 0.63°C) at single doses of 20 and 60 mg/kg; no changes were found at the low dose of 6 mg/kg. Mean maximal unbound drug plasma concentrations at 6 mg/kg were comparable with concentrations after the therapeutic dose of 120 mg/day in patients and, at 60 mg/kg, were up to 15-fold higher at steady state.

Elinzanetant has no proarrhythmic potential *in vitro* at concentrations of up to 1.91 micromolar (equivalent to 300 times the human therapeutic dose based on $C_{max, unbound}$) and *in vivo* (monkey) at 60 mg/kg (equivalent to 15 times the human therapeutic dose based on $C_{max, unbound}$).

Other information

Shelf life

Do not use this medicinal product after the expiry date (“EXP”) stated on the container.

Special precautions for storage

Keep out of the reach of children.
Do not store above 25°C.
Do not freeze.
Store in the original packaging.

Authorization number

69917 (Swissmedic).

Packs

Packs of 24, 60 or 180 (3 x 60) soft capsules. (B)

Marketing authorization holder

Bayer (Schweiz) AG, Zurich.

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