swissmedic

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Swissmedic, Swiss Agency for Therapeutic Products

Swiss Public Assessment Report

Desveneurax

International non-proprietary name:	desvenlafaxine
Pharmaceutical form:	prolonged-release tablet
Dosage strength(s):	50 mg and 100 mg
Route(s) of administration:	oral
Marketing authorisation holder:	Neuraxpharm Switzerland AG
Marketing authorisation no.:	69469
Decision and decision date:	approved on 22 November 2024

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
FDA	Food and Drug Administration (USA)
GI	Gastrointestinal
GLP	Good Laboratory Practice
HPLC	High-performance liquid chromatography
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)

2 Background information on the procedure

2.1 Applicant's request(s)

New active substance status
The applicant requested new active substance status for desvenlafaxine in the above-mentioned medicinal product.

Authorisation in accordance with Article 14 paragraph 1 a^{bis} TPA
The applicant requested a simplified authorisation procedure in accordance with Article 14 paragraph 1 a^{bis} TPA.

2.2 Indication and dosage

2.2.1 Requested indication

Treatment of major depressive disorder (MDD) in adults.

2.2.2 Approved indication

Treatment of major depressive disorder (MDD) in adults.

2.2.3 Requested dosage

The recommended dose of desvenlafaxine is 50 mg administered once a day, with or without food. The therapeutic dose range is 50 to 200 mg once a day. The dose must only be increased after clinical assessment and must not exceed 200 mg. Because of dose-related side effects, the lowest effective dose must be maintained. If a dose increase is indicated, this must be done gradually, at intervals of at least 7 days.

2.2.4 Approved dosage

(see appendix)

2.3 Regulatory history (milestones)

Application	19 June 2023
Formal objection	14 July 2023
Response to formal objection	7 September 2023
Formal control completed	21 September 2023
List of Questions (LoQ)	16 January 2024
Response to LoQ	27 March 2024
Preliminary decision	25 June 2024
Response to preliminary decision	26 August 2024
Final decision	22 November 2024
Decision	approval

Swissmedic has reviewed the quality-related aspects of the application for the authorisation of the medicinal product Desveneurax, prolonged-release tablet, exclusively on the basis of primary data.

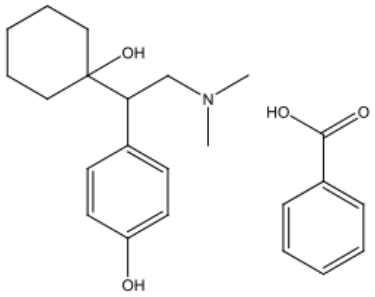
The authorisation of Desveneurax, prolonged-release tablet is based primarily on the medicinal product Pristiq, comprimidos de liberacion prolongada, which contains the same active substance and has been authorised in Spain for more than 10 years.

Apart from the quality-related aspects for which Swissmedic has conducted an independent scientific review, this SwissPAR refers to the authorisation of the foreign medicinal product Desveneurax, prolonged-release tablet (Austria).

3 Quality aspects

3.1 Drug substance

INN: Desvenlafaxine benzoate
Chemical name: 4-[1-(RS)-2-(Dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]phenol benzoate
Molecular formula: $C_{23}H_{31}NO_4$
Molecular mass: 385.50
Molecular structure:



Physicochemical properties:
Desvenlafaxine benzoate is a white, almost white, or slightly yellow powder. The non-hygroscopic compound is sparingly soluble in pH 4.5 and pH 6.8 buffer solutions and 0.9% NaCl solution.

Synthesis:
The synthesis of desvenlafaxine benzoate consists of several chemical transformation steps. Adequate information is provided regarding the manufacturing process, critical steps and intermediates.

Specification:
The drug substance specification includes tests for appearance, identity, water content, assay, related substances, residue on ignition, sulfated ash, residual solvents, and particle size distribution. The applied limits are justified and in line with the relevant guidelines and the European Pharmacopoeia, if applicable. The analytical methods are adequately described and validated in accordance with the ICH guidelines.

Stability:
The stability of desvenlafaxine benzoate was investigated using commercial scale batches which were manufactured by the proposed commercial manufacturing site. The stability samples were stored under long-term conditions (25°C/60% rh) and accelerated conditions (40°C/75% rh) as defined in the corresponding ICH guideline on stability studies. Based on these studies, an adequate retest period was defined for desvenlafaxine benzoate drug substance.

3.2 Drug product

Description and composition:
Desvenlafaxine 50 mg prolonged-release tablets are light pink, biconvex, round tablets. Desvenlafaxine 100 mg prolonged-release tablets are reddish-orange, biconvex, round tablets. The core tablets are composed of the well-known excipients hypromellose, microcrystalline cellulose, talc, stearic acid, magnesium stearate, and silica (colloidal, anhydrous). The film-coating consists of polyvinyl alcohol, titanium dioxide, talc, macrogol, and colourants.

Pharmaceutical development:
Suitable pharmaceutical development data have been provided for the finished product composition and manufacturing process, including principles of quality by design (QbD).

Manufacture:
Desvenlafaxine prolonged-release tablets are manufactured using a granulation process. Control of the manufacturing process is ensured through defined operating parameters based on results of the development studies. In addition, in-process controls with adequate acceptance criteria are established.

Specification:
The drug product specifications include tests for description, identification, assay, related substances, dissolution, uniformity of dosage units, water, dimensions, and microbial purity. The proposed acceptance criteria and analytical methods were considered appropriate for quality control of the drug product.

Container closure system:
The drug product is packed in aluminium-PVC/PE/PVdC blisters or aluminium-OPA/Alu/PVC blisters.

Stability:
Appropriate stability data are provided for desvenlafaxine prolonged-release tablets. The stability study was carried out according to ICH stability guidelines. Based on the results of this study, a shelf-life of 36 months was established. The product should not be stored above 30°C.

3.3 Quality conclusions

Satisfactory and consistent quality of the drug substance and drug product have been demonstrated.

4 Nonclinical aspects

In accordance with Art. 14 para. 1 a^{bis} TPA, Swissmedic has only reviewed the nonclinical overview or risk assessment for the authorisation of Desveneurax, prolonged-release tablet.

The approval of Desveneurax, prolonged-release tablet is based on the medicinal product Pristiq, comprimidos de liberacion prolongada, which contains the same active substance and has been authorised in the Spain for more than 10 years.

5 Clinical aspects

In accordance with Art. 14 para. 1 a^{bis} TPA, Swissmedic has conducted only a summary review of efficacy and safety for the authorisation of the medicinal product Desveneurax, prolonged-release tablet.

The authorisation of Desveneurax, prolonged-release tablet is based primarily on the medicinal product Pristiq, comprimidos de liberacion prolongada, which contains the same active substance and has been authorised in Spain for more than 10 years.

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 Desveneurax, prolonged-release tablet 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.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.

Desveneurax®

The efficacy and safety of Desveneurax prolonged-release tablets have only been summarily reviewed by Swissmedic. The marketing authorisation of Desveneurax prolonged-release tablets is based on Desveneurax, date of revision of the text May 2022, which contains the same active substance and is authorised in Austria.

Composition

Active substances

Desvenlafaxinum ut desvenlafaxini benzoas

Excipients

Tablet core

Hypromellosum, Cellulosum microcristallinum, Talcum, Acidum stearicum, Magnesii stearas, Silica colloidalis anhydrica.

Film coating

Poly(alcohol vinylicus), Titanii dioxidum (E171), Macrogolum 3350, Talcum, Ferrum oxydatum rubrum (E172) Ferrum oxydatum flavum (E172) (Desveneurax 50 mg prolonged-release tablets only), Sunset yellow FCF aluminum lake (E110) (Desveneurax 100 mg prolonged-release tablets only).

Pharmaceutical form and active substance quantity/quantities per unit

Prolonged-release tablets each containing 50 or 100 mg desvenlafaxine (as desvenlafaxine benzoate).

Desveneurax 50 mg prolonged-release tablets

Light pink, biconvex, round shaped tablet

Desveneurax 100 mg prolonged-release tablets

Red orange, biconvex, round shaped tablet

Indications/Uses

Treatment of major depressive disorder (MDD) in adults.

Dosage/Administration

Posology

The recommended dose of desvenlafaxine is 50 mg administered once a day, with or without food. The therapeutic dose range is 50 to 200 mg once a day. The dose must only be increased after clinical assessment and must not exceed 200 mg. Because of the risk of dose-related side effects, the

lowest effective dose must be maintained. If increasing the dose is indicated, it must be done gradually, at intervals of at least 7 days.
The general consensus is that acute episodes of major depressive disorder require ongoing pharmacological treatment over several months or more. Patients must maintain the same dose with which they showed a response. They must be reassessed periodically to determine the need to continue treatment.
It is recommended that desvenlafaxine prolonged-release tablets should be taken at about the same time every day. Tablets must be swallowed whole with fluid, not dividing, crushing, chewing or dissolving them.

Patients with impaired hepatic function

The dose does not need to be adjusted for patients with hepatic impairment (see “Pharmacokinetics”).

Patients with impaired renal function

For patients with severe renal impairment (24-hour creatinine clearance [CrCl] <30 ml/min) or terminal kidney disease (TKD), the recommended initial dose is 50 mg every other day.
Since a large inter-individual variability in clearance has been observed in these patients, it is recommended to establish the dose for each patient individually. No additional doses should be administered to patients after dialysis.

Elderly patients

The dose does not need to be adjusted merely according to age. However, when determining the dose in elderly patients, it must be remembered that there may be a reduction in renal desvenlafaxine clearance (see “Patients with impaired renal function”). Doses must be increased carefully to reduce the risk of orthostatic hypotension (see “Undesirable effects” and “Pharmacokinetics”).

Children and adolescents

The safety and efficacy of desvenlafaxine in children and adolescents below the age of 18 years have not been established (see “Warnings and precautions”).

Discontinuation of desvenlafaxine

Symptoms associated with discontinuation of desvenlafaxine, other SNRIs and SSRIs have been reported. Abrupt discontinuation should be avoided whenever possible. When stopping treatment with desvenlafaxine, the dose should be gradually reduced over a period of at least one to two weeks in order to reduce the risk of withdrawal reactions (2 weeks or more in patients who were treated for longer than 6 weeks) (see “Warnings and precautions” and “Undesirable effects”).
If intolerable withdrawal symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose should be considered. Subsequently, the physician may continue decreasing the dose, but at a more gradual rate.

Switching treatment from other antidepressants to desvenlafaxine

Withdrawal symptoms have been reported when treatment is switched from other antidepressants, including venlafaxine, to desvenlafaxine. To minimise withdrawal symptoms, it may be necessary to reduce the initial antidepressant gradually.

Using desvenlafaxine with reversible MAOIs such as linezolid or methylene blue

Do not start desvenlafaxine treatment in patients who are being treated with a reversible MAOI such as linezolid or in those who have been administered intravenous methylene blue, as this will increase the risk of serotonergic syndrome (see section “Contraindications”). In patients who require urgent treatment due to a psychiatric disorder, non-pharmacological treatment should be considered, including hospitalisation.
In some cases, patients on desvenlafaxine treatment require urgent treatment with linezolid or intravenous methylene blue. If there are no acceptable alternative treatments and it is considered that the potential benefits of linezolid or intravenous methylene blue treatment outweigh the risk of serotonergic syndrome in a given patient, desvenlafaxine treatment must be stopped immediately and linezolid or intravenous methylene blue may be administered. The patient should be monitored in case symptoms of serotonergic syndrome appear within two weeks or for up to 24 hours after the last dose of linezolid or intravenous methylene blue, whichever is first (see “Warnings and precautions”). Desvenlafaxine treatment may be resumed 24 hours after the last dose of linezolid or intravenous methylene blue.

Mode of administration

Oral use.

Contraindications

Hypersensitivity to the active substance, to venlafaxine, or to any of the excipients (see “Composition”).
Desvenlafaxine must not be administered concomitantly with monoamine oxidase inhibitors (MAOIs), or until 14 days have passed since the MAOI treatment was stopped. Considering the half-life of desvenlafaxine, MAOI treatment must not be started until at last 7 days have passed since the desvenlafaxine treatment was stopped (see “Interactions”). Starting desvenlafaxine treatment is also contraindicated in patients who are being treated with a reversible MAOI such as linezolid or in those who have been administered intravenous methylene blue, as this will increase the risk of serotonergic syndrome (see “Dosage/Administration” and “Warnings and precautions”).

Warnings and precautions

Suicide/suicidal thoughts or clinical worsening

Depression is associated with an increased risk of suicidal thoughts, self-harm and suicide (suicide-related events). This risk persists until significant remission occurs. As improvement may not occur during the first few weeks or more of treatment, patients should be closely monitored until such improvement occurs. It is general clinical experience that the risk of suicide may increase during initial treatment.

Patients with a history of suicide-related events, or those exhibiting a significant degree of suicidal ideation prior to commencement of treatment, are known to be at greater risk of suicidal thoughts or suicide attempts. They should receive particularly careful monitoring during treatment. A meta-analysis of placebo-controlled clinical trials of antidepressant drugs in adult patients with psychiatric disorders showed an increased risk of suicidal behaviour with antidepressants compared to placebo in patients less than 25 years old.

Close supervision of patients and in particular those at high suicidal risk should accompany drug therapy, especially in early treatment and following dose changes. Patients (and caregivers of patients) should be alerted about the need to monitor for any clinical worsening, suicidal behaviour or thoughts and unusual changes in behaviour and to seek medical advice immediately if these symptoms present.

Symptoms that can occur are e.g. anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggression, impulsiveness, akathisia (psychomotor restlessness), hypomania and mania, especially when starting treatment or whenever the dose or dose regimen is changed.

For patients at risk of suicide attempts, the smallest quantity of medicinal product should be provided to reduce the risk of overdose.

Sexual dysfunction

Selective serotonin - noradrenaline reuptake inhibitors (SNRIs) may cause symptoms of sexual dysfunction (see “Undesirable effects”). There have been reports of long-lasting sexual dysfunction where the symptoms have continued despite discontinuation of SNRIs.

Children and adolescents

Desvenlafaxine should not be used in the treatment of children and adolescents under the age of 18 years. Suicide-related behaviours (suicide attempt and suicidal thoughts), and hostility (predominantly aggression, oppositional behaviour and anger) were more frequently observed in clinical trials among children and adolescents treated with antidepressants compared to those treated with placebo. If, based on clinical need, a decision to treat is nevertheless taken, the patient should be carefully monitored for the appearance of suicidal symptoms. In addition, long-term safety data in children and adolescents concerning growth, maturation and cognitive and behavioural development are lacking.

Mania/hypomania

In clinical trials, cases of mania with desvenlafaxine have been described. Symptoms of mania/hypomania may be seen in a small proportion of patients with mood disorders who have received antidepressants, including desvenlafaxine. Desvenlafaxine must be used carefully in patients with a history or family history of mania or hypomania.

Serotonergic syndrome or reactions similar to Neuroleptic Malignant Syndrome (NMS)

As with other serotonergic medicines, during desvenlafaxine treatment, serotonergic syndrome or reactions similar to neuroleptic malignant syndrome (NMS), a potentially fatal life-threatening condition, may occur, especially during concomitant use with other serotonergic medicines (including triptans, SSRIs, other SNRIs, lithium, sibutramine, fentanyl and its analogues, tramadol, dextromethorphan, tapentadol, meperidine, methadone, pentazocine and St John's wort [Hypericum perforatum]), with medicines that affect serotonin metabolism (such as MAOIs, including linezolid (an antibiotic that is a non-selective reversible MAOI) and intravenous methylene blue), or with anti-psychotics or other dopamine agonists (see "Dosage/Administration", "Contraindications" and "Interactions"). Symptoms of serotonergic syndrome may include changes in mental state (e.g. agitation, hallucinations and coma), autonomic instability (e.g. tachycardia, labile hypertension and hyperthermia), neuromuscular aberrations (e.g. hyperreflexia and lack of coordination) and/or gastrointestinal symptoms (e.g. nausea, vomiting and diarrhoea). Serotonergic syndrome in its most severe form may appear to be NMS, which includes hyperthermia, muscle stiffness, autonomic instability with possible rapid fluctuation of vital signs and change in mental state (see "Interactions"). If concomitant treatment with desvenlafaxine and other agents that may affect serotonergic and/or dopaminergic neurotransmission systems is justified, it is recommendable to monitor the patient very closely, especially when they begin treatment or their dose is increased.
The concomitant use of desvenlafaxine and serotonin precursors (such as trytophan supplements) is not recommended.

Concomitant administration of medicines containing venlafaxine and/or desvenlafaxine

Desvenlafaxine is the primary active metabolite of venlafaxine, a medicine used to treat depression, generalised anxiety, social anxiety and panic disorder. Products containing desvenlafaxine must not be used concomitantly with products containing venlafaxine or other products containing desvenlafaxine.

Closed-angle glaucoma

Since cases of mydriasis associated with using desvenlafaxine have been reported, patients with high intraocular pressure or those at risk of acquiring acute closed-angle glaucoma must be carefully monitored.

Blood pressure

In clinical trials, blood pressure increases have been observed in some patients, especially in those treated with high doses. Pre-existing hypertension should be controlled prior to treatment with desvenlafaxine. The blood pressure of patients who are receiving desvenlafaxine treatment must be monitored regularly. During desvenlafaxine treatment, cases of high blood pressure requiring immediate treatment have been reported. Sustained blood pressure increases can cause side effects. In patients who experience a sustained blood pressure increase during desvenlafaxine treatment, reducing the dose or stopping the treatment must be considered. Special attention must be paid to patients whose health might be compromised by blood pressure increases (see “Undesirable effects”).

Cardiovascular/cerebrovascular disorders

Caution should be exercised when administering desvenlafaxine to patients with cardiovascular or cerebrovascular or lipid metabolism disorders (see “Undesirable effects”). In clinical trials with desvenlafaxine, dose-dependent increases in blood pressure and heart rate have been observed. Desvenlafaxine has not been systematically evaluated in patients with a history of a recent myocardial infarction, unstable heart disease, uncontrolled hypertension or cerebrovascular disease. Patients with a history of a recent myocardial infarction, unstable heart disease or uncontrolled arterial hypertension were excluded from all clinical trials.

Serum lipids

Dose-related elevations in fasting serum total cholesterol, LDL (low density lipoprotein) cholesterol, and triglycerides were observed in clinical studies. Measurement of serum lipids should be considered during treatment with desvenlafaxine.

Seizures

Cases of seizures have been reported in clinical trials with desvenlafaxine. Desvenlafaxine has not been systematically evaluated in patients with convulsive disorders. Patients with a history of seizures were excluded from the clinical trials. Caution should be exercised when prescribing desvenlafaxine in these patients. Treatment should be discontinued in any patient who develops seizures.

Aggressiveness

Aggressiveness may occur in a small number of patients who have received antidepressants, including desvenlafaxine. This was reported when starting, changing the dose and stopping treatment. As with other antidepressants, precautions must be taken when using desvenlafaxine in patients with a history of aggressiveness.

Abnormal bleeding

Selective serotonin reuptake inhibitors (SSRIs) and serotonin and noradrenaline reuptake inhibitors (SNRIs), including desvenlafaxine, may increase the risk of haemorrhagic events. Concomitant use of acetylsalicylic acid, non-steroidal anti-inflammatory drugs (NSAIDs), warfarin and other anticoagulants may increase this risk. Haemorrhagic events related to SSRIs and SNRIs range from ecchymosis, haematoma, epistaxis and petechiae to gastrointestinal and life-threatening bleeding. Patients must be warned of the risk of bleeding associated with concomitant use of desvenlafaxine and NSAIDs, acetylsalicylic acid and other medicines that may affect blood coagulation and increase the risk of bleeding.
SNRIs may increase the risk of postpartum haemorrhage (see “Pregnancy, lactation” and “Undesirable effects”).

Akathisia/psychomotor restlessness

Using selective serotonin reuptake inhibitors/serotonin and noradrenaline reuptake inhibitors (SSRIs/SNRIs) has been associated with the appearance of akathisia, which is characterised by subjectively anxious or unpleasant restlessness and the need to be moving, often accompanied by an inability to sit or stand still. It is most likely to be seen in the first few weeks of treatment. In patients who develop these symptoms, it may be harmful to increase the dose.

Hyponatraemia

During treatment with SSRIs or SNRIs (including desvenlafaxine) cases of hyponatraemia and/or syndrome of inappropriate antidiuretic hormone secretion (SIAHS) have been described. Caution should be exercised when using desvenlafaxine in patients at risk of hyponatraemia, such as patients with hypovolaemia or those who are dehydrated, including elderly patients and patients being treated with diuretics.

Withdrawal symptoms observed on stopping treatment with SSRIs/SNRIs

When treatment is stopped, it is common to see withdrawal symptoms, especially if it is stopped suddenly (see “Undesirable effects”).
During the marketing of SSRIs/SNRIs, there have been spontaneous reports of side effects caused by discontinuing this kind of medicine, especially if it is done suddenly. The symptoms most frequently reported include: mood swings, irritability, agitation, dizziness, sensory changes (e.g. paraesthesia, including electric shock sensations), anxiety, confusion, headache, lethargy, emotional lability, insomnia, hypomania, tinnitus and convulsions. Although these symptoms are generally self-limiting, cases of serious withdrawal symptoms have been reported.

Dry mouth

Dry mouth is reported in 18% of patients treated with desvenlafaxine. This may increase the risk of caries, and patients should be advised upon the importance of dental hygiene.

Warnings about excipients

Desveneurax 100 mg prolonged-release tablets contain Sunset yellow FCF aluminum lake (E110). Sunset yellow S (E110) may cause allergic reactions.

Interactions

Monoamine oxidase inhibitors (MAOIs)

Desvenlafaxine is contraindicated in patients who are taking MAOIs. Desvenlafaxine is a serotonin and noradrenaline reuptake inhibitor. Desvenlafaxine must not be administered in combination with monoamine oxidase inhibitors (including reversible MAOIs such as linezolid or intravenous methylene blue), or until 14 days have passed since the MAOI treatment was stopped. Considering the half-life of desvenlafaxine, MAOI treatment must not be started until at least 7 days have passed since the desvenlafaxine treatment was stopped (see “Contraindications”).

Medicines that act on the central nervous system (CNS)

The use of desvenlafaxine in combination with other medicines that act on the CNS has not been studied in detail, except in the cases described in this section. Therefore, caution should be exercised when administering desvenlafaxine in combination with other medicines that act on the CNS.

Serotonergic syndrome

As with other serotonergic medicines, this syndrome, a potentially life-threatening condition, may occur during desvenlafaxine treatment, especially during concomitant use with other medicines that may affect serotonergic neurotransmission systems (including triptans, SSRIs, other SNRIs, lithium, sibutramine, fentanyl and its analogues, tramadol, dextromethorphan, tapentadol, meperidine, methadone, pentazocine and St John’s wort [Hypericum perforatum]), with medicines which affect serotonin metabolism (such as MAOIs, including linezolid (an antibiotic that is a non-selective reversible MAOI) and methylene blue), or with serotonin precursors (such as tryptophan supplements) (see “Dosage/Administration”, “Contraindications” and “Warnings and precautions”).
If concomitant treatment with desvenlafaxine and an SSRI, SNRI or 5-hydroxytryptamine receptor agonist (triptan) is clinically justified, it is recommendable to monitor the patient very closely, especially when they begin treatment or their dose is increased. The concomitant use of desvenlafaxine and serotonin precursors (such as trytophan supplements) is not recommended (see “Warnings and precautions”).

Ethanol

In a clinical trial, it was demonstrated that desvenlafaxine does not significantly increase the impairment of mental and motor capacity caused by ethanol. However, as with all medicines that act on the CNS, patients must be told to avoid consuming alcohol during Desveneurax treatment.

Effect of other medicinal products on desvenlafaxine

CYP3A4 inhibitors

CYP3A4 is minimally involved in desvenlafaxine elimination. In a clinical trial, ketoconazole (200 mg, twice a day) increased the area under the concentration-time curve (AUC) of desvenlafaxine (400 mg, single dose) by approximately 43%, a weak interaction, and the Cmax by approximately 8%. Concomitant use of desvenlafaxine and potent CYP3A4 inhibitors may lead to higher desvenlafaxine concentrations. Therefore, caution should be exercised in patients whose treatment includes a CYP3A4 inhibitor and desvenlafaxine concomitantly.

Inhibitors of other CYP enzymes

Based on *in vitro* studies, medicines that inhibit the isoenzymes CYP1A1, 1A2, 2A6, 2D6, 2C8, 2C9, 2C19 and 2E1 are not expected to have a significant impact on the pharmacokinetics of desvenlafaxine.

Effect of desvenlafaxine on other medicinal products

Medicines metabolised by CYP2D6

When administering desvenlafaxine at a dose of 100 mg per day together with a single 50 mg dose of desipramine, a CYP2D6 substrate, the AUC of desipramine increased by 17%. When administering 400 mg, the AUC of desipramine increased by approximately 90%. Concomitant use of desvenlafaxine and a medicine metabolised by CYP2D6 may lead to higher concentrations of said medicine. However, clinical trials have demonstrated that desvenlafaxine has no clinically relevant effect on CYP2D6 metabolism at a dose of 100 mg per day.

Medicines metabolised by CYP3A4

In vitro, desvenlafaxine does not inhibit or induce CYP3A4 isoenzymes.
In a clinical trial, when administering 400 mg per day of desvenlafaxine with a single 4 mg dose of midazolam, a CYP3A4 substrate, the AUC of midazolam decreased by approximately 31%. In a second trial, in which desvenlafaxine 50 mg per day was administered with a single 4 mg dose of midazolam, the AUC and Cmax of midazolam decreased by approximately 29% and 14%, respectively.
Concomitant use of desvenlafaxine and CYP3A4 substrate medicines may lead to less exposure to said medicines.

Medicines metabolised by a combination of CYP2D6 and CYP3A4

A single 40 mg dose of tamoxifen was administered, initially metabolised to its active metabolites 4-hydroxy-tamoxifen and endoxifen by CYP2D6 with a small contribution of CYP3A4, together with desvenlafaxine (100 mg per day). The AUC of tamoxifen increased by 3% with concomitant

administration of desvenlafaxine. The AUC of 4-hydroxy-tamoxifen increased by 9% and that of endoxifen decreased by 12%.
When desvenlafaxine was administered at a dose of 100 mg per day together with a single 5 mg dose of aripiprazole, a CYP2D6 and CYP3A4 substrate, metabolised to the active metabolite dehydro-aripiprazole, the AUC of aripiprazole increased by 6% and that of dehydro-aripiprazole increased by 3%.
Clinical trials have shown that desvenlafaxine used at a dose of 100 mg per day has no relevant clinical effects on medicines metabolised by a combination of the enzymes CYP2D6 and CYP3A4.

Interactions with laboratory tests

False positives have been reported in immunoassays in urine for phencyclidine (PCP) and amphetamines in patients who are taking desvenlafaxine. This is due to lack of specificity in the tests conducted. False positives can be expected in tests for several days after discontinuing desvenlafaxine treatment. Confirmatory tests such as gas chromatography or mass spectrometry will distinguish desvenlafaxine from PCP and amphetamine.

Electroconvulsive therapy

There are no clinical data establishing the risks and/or benefits of electroconvulsive therapy combined with desvenlafaxine treatment.

Pregnancy, lactation

Pregnancy

There are no or limited amount of data from the use of desvenlafaxine in pregnant women. Studies in animals have shown reproductive toxicity (see “Preclinical data”). Desvenlafaxine must only be administered to pregnant women if the expected benefits outweigh the possible risks.
Epidemiological data has suggested that using SSRIs in pregnancy, especially towards the end of pregnancy, may increase the risk of persistent pulmonary hypertension of the newborn (PPHN). Although no study has investigated the association between PPHN and SNRI treatment, the possible risk with desvenlafaxine cannot be ruled out considering the related mechanism of action (serotonin reuptake inhibition).
If desvenlafaxine is used during pregnancy or just before childbirth, withdrawal symptoms may develop in the newborn. In neonates exposed to SSRIs or SNRIs, including venlafaxine, after the third trimester, complications have been described which required respiratory support, feeding through a tube or prolonged hospitalisation. These complications may occur immediately after childbirth.
Observational data indicate an increased risk (less than 2-fold) of postpartum haemorrhage following SSRI/SNRI exposure within the month prior to birth (see “Warnings and precautions” and “Undesirable effects”).

Lactation

Desvenlafaxine is excreted in human milk. Due to the potential for serious adverse reactions in breast-fed infants exposed to desvenlafaxine, a decision must be made whether to discontinue breast-feeding or to discontinue/abstain from Desveneurax therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Effects on ability to drive and use machines

Desvenlafaxine may cause sedation and dizziness. Consequently, patients must be told that if they experience sedation or dizziness, they must avoid performing potentially dangerous tasks, such as driving or using machinery.

Undesirable effects

Side effects in clinical trials on MDD

The safety of desvenlafaxine was evaluated in clinical trials on MDD with a total of 7,785 patients who were exposed to a dose of desvenlafaxine within the range of at least 10 to 400 mg/day. Long-term safety was assessed in more than 2,000 patients on MDD who were exposed to desvenlafaxine for at least 6 months and in more than 400 patients who were exposed for 1 year.
In most cases, side effects were most common during the first week of treatment, and were mild or moderate. In general, the frequency of the side effects was related to the dose.
The following table lists the side effects seen in all pre-marketing clinical trials on MDD conducted across the range of doses studied from 10 to 400 mg of desvenlafaxine.
Undesirable effects are arranged according to MedDRA system organ classes and frequency using the following convention:
Very common (≥1/10), Common (≥1/100 to <1/10), Uncommon (≥1/1,000 to <1/100), Rare (≥1/10,000 to <1/1,000), Very rare (<1/10,000), Not known (cannot be estimated from the available data).
The side effects are organised in decreasing order of severity within each frequency interval.

System organ class	**Side effects‡**
Immune system disorders	
Uncommon	hypersensitivity
Metabolism and nutrition disorders	
Common	reduced appetite
Rare	hyponatraemia
Psychiatric disorders	
Very common	insomnia
Common	anxiety, nervousness, anorgasmia, reduced libido, nightmares
Uncommon	depersonalisation, abnormal orgasm, withdrawal syndrome
Rare	hallucinations, hypomania, mania
Nervous system disorders	
Very common	dizziness, headache
Common	somnolence, tremor, attention deficit, paraesthesia, dysgeusia

Uncommon	syncope
Rare	seizures, dystonia
Not known	Serotonergic syndrome**
Eye disorders	
Common	mydriasis, blurred vision
Ear and labyrinth disorders	
Common	tinnitus, vertigo
Cardiac disorders	
Common	tachycardia, palpitations
Vascular disorders	
Common	hot flushes
Uncommon	peripheral coldness, orthostatic hypotension
Respiratory, thoracic and mediastinal disorders	
Common	yawning
Uncommon	epistaxis
Gastrointestinal disorders	
Very common	nausea, dry mouth, constipation
Common	vomiting, diarrhoea
Skin and subcutaneous tissue disorders	
Very common	hyperhidrosis
Common	cutaneous eruption
Uncommon	alopecia
Rare	angioedema**, photosensitivity reaction
Not known	Stevens-Johnson syndrome**
Musculoskeletal and connective tissue disorders	
Uncommon	musculoskeletal rigidity
Renal and urinary disorders	
Uncommon	proteinuria, urine retention, difficulty urinating
Reproductive system and breast disorders	
Common	erectile dysfunction*, delayed ejaculation*, ejaculatory insufficiency
Uncommon	sexual dysfunction, ejaculation disorder*
Not known	postpartum haemorrhage***
General disorders and administration site conditions	
Common	fatigue, asthenia, shivering, nervousness, irritability
Investigations	
Common	high blood pressure, weight gain, weight loss
Uncommon	changes in liver function tests, increased blood triglycerides, increased blood prolactin, hypercholesterolaemia

‡Side effects with a frequency of <1% were calculated manually; those ≥1% are shown directly in the table.

*Frequency calculated based on men only.

**Side effects identified during post-authorisation use.
***This event has been reported for the therapeutic class of SSRIs/SNRIs (see “Warnings and precautions” and “Pregnancy, lactation”).

Adverse ischaemic cardiac events

In clinical trials, uncommon cases of adverse cardiac ischaemic events were notified, such as myocardial ischaemia, myocardial infarction and coronary occlusion requiring revascularisation. These patients presented many underlying cardiac risk factors.
A higher number of patients experienced these events during desvenlafaxine treatment than with placebo (see “Warnings and precautions”).

Reactions after stopping treatment

Stopping treatment with SSRIs/SNRIs, including desvenlafaxine, (especially if sudden) is often associated with withdrawal symptoms. Side effects reported in association with stopping suddenly, dose reduction or reduction in treatment in clinical trials on MDD within a range of ≥2% included: dizziness, withdrawal syndrome, nausea and headache. In general, withdrawal symptoms were seen at higher doses and with longer-term treatment. These symptoms are mild to moderate, and self-limiting; however, in some patients, they may be serious and/or prolonged. Therefore, when desvenlafaxine treatment is no longer necessary, it is recommended that it should be stopped by gradually reducing the dose (see “Dosage/Administration” and “Warnings and precautions”).

Side effects reported as reasons for discontinuing treatment

In a combined analysis of placebo-controlled clinical trials lasting 8-12 weeks for major depressive disorder, 8% of the 3,335 patients who received desvenlafaxine (10 to 400 mg) discontinued the treatment due to side effects, compared with 4% of the 1,873 patients treated with placebo.
The most common side effect leading to discontinuation in at least 2% of the patients treated with desvenlafaxine in short-term trials (up to 12 weeks) was nausea (2%); whilst in the long-term trial (up to 11 months) discontinuation not due to side effects was at least 2% of patients and higher than with placebo in the double-blind phase.
For the 50 mg dose, the discontinuation rate due to side effects with desvenlafaxine (4%) was similar to the rate with placebo (4%). For the 100 mg and 200 mg doses of desvenlafaxine, discontinuation rates due to side effects were 8% and 15%, respectively.

Elderly patients

Of the 7,785 patients with MDD treated with desvenlafaxine in clinical trials, 5% were aged 65 or more. In general, no differences were observed in safety and efficacy between these patients and younger ones. However, in short-term placebo-controlled trials, a higher incidence of orthostatic systolic hypotension was observed and, in both the short-term and long-term trials, both of which

were placebo-controlled, higher systolic arterial pressure was observed in patients aged 65 or more than in those under 65 treated with desvenlafaxine.

Adverse reactions reported with other SNRIs

Although gastrointestinal bleeding is not considered an adverse reaction of desvenlafaxine itself, it is an adverse reaction of other SNRIs and may also occur with desvenlafaxine.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation 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 new or serious adverse reactions online via the ElViS portal (Electronic Vigilance System). You can obtain information about this at www.swissmedic.ch.

Overdose

There is little clinical experience of desvenlafaxine overdose in humans. In pre-marketing clinical trials, no cases of fatal desvenlafaxine overdose were reported. The lowest possible number of tablets must be prescribed to reduce the risk of overdose.
Of the patients included in the clinical trials on MDD, there were four adults who took doses greater than 800 mg of desvenlafaxine (4,000 mg [desvenlafaxine alone], 900, 1,800 and 5,200 mg [in combination with other medicines]); all of the patients recovered. Furthermore, the 11-month-old son of one of the patients accidentally ingested 600 mg of desvenlafaxine, was treated and recovered.
Treating an overdose must entail taking general measures used for overdose with any SSRI/SNRI. Adequate oxygenation and ventilation must be provided. Heart rate and vital signs must be monitored. General supportive and symptomatic measures are also recommended. If necessary, gastric lavage using a large-bore orogastric tube with adequate airway protection may be indicated if done immediately after ingestion or in symptomatic patients. Activated charcoal must also be administered. No desvenlafaxine-specific antidotes are known. Inducing vomiting is not recommended. Due to the moderate volume of distribution of the medicine, the benefit of forced diuresis, dialysis, haemoperfusion and exchange transfusion is questionable (see “Pharmacokinetics”).
In overdose treatment, the possibility that the patient may have ingested several medicines should always be considered. The doctor must decide whether it is necessary to contact a toxicology information service for further information on how to treat an overdose.

Properties/Effects

ATC code

N06AX23

Mechanism of action/Pharmacodynamics

Non-clinical trials have shown that desvenlafaxine is a selective serotonin and noradrenaline reuptake inhibitor (SNRI). It is believed that the efficacy of desvenlafaxine is related to promotion of the neurotransmitters serotonin and noradrenaline in the central nervous system.
In vitro, desvenlafaxine lacks significant affinity for many receptors, including muscarinic-cholinergic, histamine H1 and 1-adrenergic receptors. The same binding profile trial shows that desvenlafaxine also lacks significant affinity for several ion channels, including calcium, chlorine, potassium and sodium channels, as well as monoamine oxidase inhibitor (MAOI) activity.

Clinical efficacy

Trials on major depressive disorder

The efficacy of desvenlafaxine in MDD treatment was studied in patients who met DSM-IV (Diagnostic and Statistical Manual of Mental Disorders) diagnostic criteria for major depressive disorder. In general, doses of 50-400 mg/day showed efficacy in four randomised, double-blind, placebo-controlled, short-term (8-week) studies and two relapse prevention trials conducted in adult outpatients with major depressive disorder. Desvenlafaxine demonstrated superiority over placebo, measured through improvement in total score on the 17-item Hamilton Depression Rating Scale (HAM-D) and on the Clinical Global Impressions Scale – Improvement (CGI-I). The joint analysis of these studies showed an average difference compared with placebo in change in relation to the baseline score on the HAM-D17 scale of 1.5 (0.9, 2.1), 2.2 (1.4, 2.9) and 2.4 (1.2, 3.6) for doses of 50 mg/day, 100 mg/day and 200 mg/day, respectively.
The percentage of patients with CGI-I scores of 1 (very much improved) or 2 (much improved) varied from 55 to 61% for desvenlafaxine (dose of 50 to 200 mg/day) compared with 45% in the placebo group.
Of the 7,785 patients assessed in pre-marketing clinical trials with desvenlafaxine, 5% were aged 65 or more. In general, no differences were observed in efficacy between these patients and younger ones.
In a long-term trial (relapse prevention), adult outpatients who met DSM-IV criteria for major depressive disorder, who responded to 8 weeks' open, acute treatment with 50 mg/day of desvenlafaxine and who remained stable for 12 weeks with desvenlafaxine, were randomly assigned using a double-blind method to remain on active treatment or change to placebo for a maximum of 26 weeks to assess relapses.
Response to treatment during the open phase was defined as a total score of ≤11 on the HAM-D17 scale and ≤2 on the CGI-I scale in the assessment on day 56; not presenting a total score of ≥16 on the HAM-D17 scale in any of the visits was defined as a stable response. Relapse during the double-blind phase was defined as follows: (1) a total score of ≥16 on the HAM-D17 scale in any of the visits, (2) treatment discontinuation due to unsatisfactory response, (3) hospitalisation due to depression, (4)

suicide attempt, or (5) suicide. Patients who received continuous desvenlafaxine treatment went significantly longer without a relapse than those treated with placebo. At 26 weeks, Kaplan-Meier's estimated likelihood of relapse was 14% with desvenlafaxine treatment compared with 30% with placebo treatment.

In a second long-term randomised trial (relapse prevention), patients who responded after 12 weeks' acute treatment with desvenlafaxine 200-400 mg once a day in an open-label design were randomised to receive desvenlafaxine or placebo for a further 6 months. Response to treatment during the open phase was defined as a total score of ≤11 on the HAM-D17 scale in the assessment on day 84. Relapse during the double-blind phase was defined as follows: (1) a total score of ≥16 on the HAM-D17 scale in any of the visits, (2) a total score on the CGI-I scale of ≥6 (versus day 84) in any visit, or (3) withdrawal from the trial due to unsatisfactory response. Patients who received desvenlafaxine took significantly longer to see a MDD relapse than patients who received placebo during the double-blind phase of the trial ($p<0.0001$). Incidence of relapse in the 6-month double-blind follow-up period was 24% and 42% for desvenlafaxine and placebo, respectively.

Two studies comparing desvenlafaxine and venlafaxine retard versus placebo were conducted with flexible doses of desvenlafaxine in the range 200 to 400 mg per day. In one of them, neither desvenlafaxine (200-400 mg/day) nor venlafaxine (75-150 mg/day) was different to placebo. In the other study, venlafaxine retard (150-225 mg/day) was superior to placebo, whilst desvenlafaxine (200-400 mg/day) was no different to placebo.

Another study compared desvenlafaxine (50-100 mg/day) and duloxetine (60 mg/day) with placebo. In the non-adjusted analysis for multiple comparisons, desvenlafaxine 100 mg/day was superior to placebo with a magnitude of effect similar to duloxetine. In this study, desvenlafaxine 50 mg/day was no different to placebo.

Pharmacokinetics

Absorption

The pharmacokinetics after administering a single dose of desvenlafaxine are linear and proportional to the dose between 50 and 600 mg. The mean terminal half-life, t½, is approximately 11 hours. Administering a daily dose, steady-state plasma concentrations are reached after approximately 4-5 days. At steady state, accumulation after several doses of desvenlafaxine is linear and predictable from the single-dose pharmacokinetic profile.

Desvenlafaxine is absorbed well, with an absolute oral bioavailability of 80% (coefficient of variation [CV] of 20%). Maximum plasma concentrations (Cmax) are observed 7.5 hours after oral administration. After administering repeated 100 mg doses, an AUC and maximum plasma concentrations of 6,747 ng·h/ml (CV of 23%) and 376 ng/ml (CV of 23%) are observed, respectively. Administering it with food minimally influences absorption of the medicine. After administering with low-, medium- and high-fat foods, increases in the Cmax of approximately 16% are observed after

consuming high-fat foods. No changes in AUC values were recorded for any of the foods. Plasma protein binding of desvenlafaxine is low (30%) and independent of the concentration of the medicine.

Distribution

The volume of distribution of desvenlafaxine at steady state after intravenous administration is 3.4 l/kg, which indicates that it is distributed to non-vascular compartments.

Metabolism

Approximately 45% of desvenlafaxine is eliminated unchanged in the urine. Desvenlafaxine is primarily metabolised through conjugation with O-glucuronide and, to a lesser degree, through oxidative metabolism.

Elimination

Approximately 19% of the dose administered is eliminated in the form of a glucuronide metabolite and a quantity <5% as an oxidative metabolite (N,O-didesmethylvenlafaxine) in the urine. CYP3A4 is the isoenzyme of the predominant P450 cytochrome that mediates in the oxidative metabolism (N-demethylation) of desvenlafaxine. The metabolic route of CYP2D6 is unaffected, so after administering 100 mg, the pharmacokinetics of desvenlafaxine were similar in individuals with a slow and fast CYP2D6 metaboliser phenotype.
In vitro desvenlafaxine neither inhibits the isoenzymes CYP1A2, 2A6, 2C8, 2C9, 2C19 and 3A4 nor induces expression of CYP3A4 or other isoenzymes. Desvenlafaxine is neither a substrate nor an inhibitor of the glycoprotein P transporter, according to data obtained *in vitro*.

Kinetics in specific patient groups

Elderly patients

In a study in healthy volunteers who received a dose of up to 300 mg, an age-dependent reduction in desvenlafaxine clearance was observed, which led to a 32% increase in the Cmax and a 55% increase in AUC values in individuals aged over 75, compared with individuals aged 18 to 45. Individuals aged 65 to 75 presented no changes in the Cmax, but showed an increase of approximately 32% in the AUC compared with individuals aged 18 to 45 (see “Dosage/Administration”).

Children and adolescents

No pharmacokinetic data are available for children and adolescents.

Hepatic impairment

The pharmacokinetics of desvenlafaxine 100 mg was studied in individuals with mild (Child-Pugh A, n = 8), moderate (Child-Pugh B, n = 8) and severe (Child-Pugh C, n = 8) hepatic impairment and in healthy volunteers (n = 12).

The mean AUC increased by approximately 31% and 35% in patients with moderate and severe hepatic impairment, respectively, compared with healthy volunteers. The mean AUC values were comparable in individuals with mild hepatic impairment and in healthy volunteers (difference <5%). Systemic clearance (CL/F) decreased by approximately 20% and 36% in patients with moderate and severe hepatic impairment, respectively, compared with healthy volunteers. CL/F values in individuals with mild hepatic impairment were comparable with those of healthy volunteers (difference <5%). The mean t½ changed from approximately 10 hours in healthy volunteers and in individuals with mild hepatic impairment to 13 and 14 hours in those with moderate and severe hepatic impairment, respectively.

Renal impairment

The pharmacokinetics of desvenlafaxine 100 mg was studied in individuals with mild (n = 9), moderate (n = 8) and severe (n = 7) renal impairment, in individuals with terminal kidney disease (TKD) who required dialysis (n = 9) and in age-matched healthy volunteer controls (n = 8). Elimination presented a significant correlation with creatinine clearance (CrCl). Total bodily clearance was reduced by 29%, 39% and 51% in patients with mild, moderate and severe renal impairment (CrCl 24 h <30 ml/min), respectively, and by 58% in individuals with TKD, compared with healthy volunteers. This reduction in clearance led to increases in the AUC of 42%, 56% and 108% in patients with mild (24hCrCl=50-80 ml/min), moderate (24hCrCl=30-50 ml/min) and severe (24hCrCl<30 ml/min) renal impairment, respectively, and 116% in individuals with TKD.
The mean terminal half-life was prolonged from 11.1 hours in control individuals to 13.5, 15.5 and 17.6 hours in patients with mild, moderate and severe renal impairment, respectively, and 22.8 hours in individuals with TKD.
For patients with severe renal impairment (24h CrCl<30 ml/min) or TKD, it is recommended that the dose should be adjusted (see “Dosage/Administration”).
During a standard 4-hour haemodialysis procedure, less than 5% of the medicine was eliminated from the body. Therefore, no additional doses must be administered to patients after dialysis.

ECG changes

No clinically relevant differences were observed compared with placebo in terms of QT, QTc, PR and QRS intervals. In a specific study of the QTc interval using certain prospectively determined criteria, desvenlafaxine did not cause prolongation of the QT interval. No differences were observed between treatment with placebo and desvenlafaxine in terms of the QRS interval.

Preclinical data

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

Reduction in fertility was observed in a study in which male and female rats received desvenlafaxine. This effect was observed at oral doses approximately 30 times and 5 times the maximum human dose of 200 mg/day.
After oral administration of desvenlafaxine to pregnant female rats and rabbits at maternally toxic doses during the period of organogenesis, a reduction in foetal weight and survival of litters was observed in the first 4 days of lactation. The cause of the death which was seen with exposure 5 to 30 times greater than the maximum dose in humans of 200 mg/day is not known.
No evidence of teratogenicity was observed.

Other information

Shelf life

Do not use this medicine after the expiry date (“EXP”) stated on the package.

Special precautions for storage

Do not store above 30°C.
Keep out of the reach of children.

Authorisation number

69469 (Swissmedic)

Packs

Desveneurax 50 mg prolonged-release tablets

Packs of 20, 28, 50 or 100 prolonged-release tablets (B).

Desveneurax 100 mg prolonged-release tablets

Packs of 28, 50 or 100 prolonged-release tablets (B).

Marketing authorisation holder

Neuraxpharm Switzerland AG, Cham

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