1. NAME OF THE MEDICINAL PRODUCT

PRILIGY (dapoxetine hydrochloride)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each PRILIGY 30 mg film-coated tablet contains 30 mg of dapoxetine base (as a hydrochloride salt).
Each PRILIGY 60 mg film-coated tablet contains 60 mg of dapoxetine base (as a hydrochloride salt).
The chemical name is (+)-(S)-N, N-dimethyl-(α)-[2-(1-naphthalenyloxy) ethyl]-benzenemethanamine hydrochloride.
For excipients, see Section List of Excipients.

3. PHARMACEUTICAL FORM

PRILIGY Tablets are round, convex, film-coated tablets.
30 mg: light grey tablets debossed with "30" inside a triangle on one side
60 mg: grey tablets debossed with "60" inside a triangle on one side

4. CLINICAL PARTICULARS

4.1 Therapeutic indication

PRILIGY is indicated for the treatment of premature ejaculation (PE) in men 18 to 64 years of age, who have all of the following:
- Persistent or recurrent ejaculation with minimal sexual stimulation before, on, or shortly after penetration and before the patient wishes; and
- Marked personal distress or interpersonal difficulty as a consequence of PE; and
- Poor control over ejaculation.

PRILIGY IS NOT INDICATED for the treatment of erectile dysfunction (ED).

4.2 Posology and method of administration

For oral use. Tablets should be swallowed whole. It is recommended that tablets be taken with at least one full glass of water. Patients should be cautioned to avoid situations where injury could result should syncope or its prodromal symptoms such as dizziness or lightheadedness occur (see Sections Special Warnings and Special Precautions for Use and Section Effects on Ability to Drive and Use Machines).

Adult men (18 to 64 years of age)
The recommended starting dose for all patients is 30 mg, taken as needed approximately 1 to 3 hours prior to sexual activity. If the effect of 30 mg is insufficient and the side effects are acceptable, the dose may be increased to the maximum recommended dose of 60 mg. The maximum recommended dosing frequency is once every 24 hours.

PRILIGY may be taken with or without food (see Section Pharmacokinetic Properties.)

Before treatment is initiated, the physician should obtain a careful medical history focussing on past orthostatic events and also perform an orthostatictest (blood pressure and pulse rate, supine and standing). If the patients discloses a history suggestive of orthostatic reactions or an orthostatic test shows this kind reaction, treatment with Priligy should be avoided.

The physician who elects to use PRILIGY for the treatment of premature ejaculation should evaluate the risks and patient-reported benefits of the medicinal product after the first four weeks of treatment or after 6 doses to assess the patient risk-benefit balance and to determine whether continuing treatment with PRILIGY is appropriate.

Elderly (age 65 years and over)
Safety and efficacy of PRILIGY have not been established in patients age 65 years and over as limited data are available in this population (see Section Pharmacokinetic Properties.)

Children and adolescents
PRILIGY should not be used in individuals below 18 years of age.

Patients with renal impairment
No dose adjustment is required but caution is advised in patients with mild or moderate renal impairment. PRILIGY is not recommended for use in patients with severe renal impairment (see Section Pharmacokinetic Properties.)

Patients with hepatic impairment
No dose adjustment is required in patients with mild hepatic impairment. PRILIGY is contraindicated in patients with moderate and severe hepatic impairment (Child-Pugh Class B and C) (see Sections Contraindications, Section Pharmacokinetic Properties.)

Known CYP2D6 poor metabolizers or use with potent CYP2D6 inhibitors
Caution is advised if increasing the dose to 60 mg in a patient known to be a CYP2D6 poor metabolizer or if increasing the dose to 60 mg in a patient concomitantly treated with potent CYP2D6 inhibitors (see Sections Special Warnings and Special Precautions for Use, Section Interactions with Other Medicinal Products and Other Forms of Interaction and Section Pharmacokinetic Properties).

Patients treated with potent or moderate inhibitors of CYP3A4
Concomitant use of potent CYP3A4 inhibitors is contraindicated. The dose is restricted to 30 mg when used concomitantly with moderate CYP3A4 inhibitors (see Sections Contraindications, Section Special Warnings and Special Precautions for Use and Section Interactions with Other Medicinal Products and Other Forms of Interaction).

4.3 Contraindications

PRILIGY is contraindicated in patients with known hypersensitivity to dapoxetine hydrochloride or to any of the excipients.

PRILIGY is contraindicated in patients with significant pathological cardiac conditions [such as heart failure (NYHA class II-IV), conduction abnormalities (second- or third-degree AV block or sick sinus syndrome) not treated with a permanent pacemaker, significant ischemic heart disease or significant valvular disease].

PRILIGY is contraindicated for concomitant treatment with monoamine oxidase inhibitors (MAOIs), or within 14 days of discontinuing treatment with an MAOI. Similarly, an MAOI should not be administered within 7 days after PRILIGY has been discontinued (see Section Interactions with Other Medicinal Products and Other Forms of Interaction).

PRILIGY is contraindicated for concomitant treatment with thioridazine, or within 14 days of discontinuing treatment with thioridazine. Similarly, thioridazine should not be administered within 7 days after PRILIGY has been discontinued (see Section Interaction with Other Medicinal Products and Other Forms of Interaction).

PRILIGY is contraindicated for concomitant treatment with serotonin reuptake inhibitors [selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs)] or other medicinal/herbal products with serotonergic effects [e.g., L-tryptophan, triptans, tramadol, linezolid, lithium, St. John's Wort (*Hypericum perforatum*)] or within

14 days of discontinuing treatment with these medicinal/herbal products. Similarly these medicinal/herbal products should not be administered within 7 days after PRILIGY has been discontinued (see Section Interaction with Other Medicinal Products and Other Forms of Interaction).

PRILIGY is contraindicated for concomitant treatment with potent CYP3A4 inhibitors such as ketoconazole, itraconazole, ritonavir, saquinavir, telithromycin, nefazodone, nelfinavir, atazanavir, etc. (see Section Interactions with Other Medicinal Products and Other Forms of Interaction).

PRILIGY is contraindicated in patients with moderate and severe hepatic impairment.

4.4 Special warnings and precautions for use

General
PRILIGY is only indicated in men with PE. Safety has not been established and there are no data on the ejaculation-delaying effects in men without PE.

Use with recreational drugs
Patients should be advised not to use PRILIGY in combination with recreational drugs.
Recreational drugs with serotonergic activity such as ketamine, methylenedioxymethamphetamine (MDMA) and lysergic acid diethylamide (LSD) may lead to potentially serious reactions if combined with PRILIGY. These reactions include, but are not limited to, arrhythmia, hyperthermia, and serotonin syndrome. Use of PRILIGY with recreational drugs with sedative properties such as narcotics and benzodiazepines may further increase somnolence and dizziness.

Ethanol
Combining alcohol with PRILIGY may increase alcohol-related neurocognitive effects and may also enhance neurocardiogenic adverse events such as syncope, thereby increasing the risk of accidental injury; therefore, patients should be advised to avoid alcohol while taking PRILIGY (see Sections Interactions with Other Medicinal Products and Other Forms of Interaction and Section Effects on Ability to Drive and Use Machines).

Syncope
The frequency of syncope characterized as loss of consciousness in the PRILIGY clinical development program varied depending on the population studied and ranged from 0.06% (30 mg) to 0.23% (60 mg) for subjects enrolled in the Phase 3 placebo-controlled clinical trials to 0.64% (all doses combined) for Phase 1 non-PE healthy subject studies.

Possibly prodromal symptoms such as nausea, dizziness/lightheadedness, and diaphoresis were reported more frequently among patients treated with PRILIGY compared to placebo. In patients receiving 30 mg PRILIGY in Phase 3 clinical trials, nausea was reported in 11.0%, dizziness in 5.8% and hyperhidrosis/diaphoresis in 0.8%. In patients receiving 60 mg PRILIGY in Phase 3 clinical trials, nausea was reported in 21.2%, dizziness in 11.7% and hyperhidrosis/diaphoresis in 1.5%. In addition, the occurrence of syncope and possibly prodromal symptoms appears dose dependent as demonstrated by higher incidences among patients treated with doses higher than 60 mg, the recommended maximum daily dose.

Cases of syncope characterized as loss of consciousness observed in the clinical trials were considered vasovagal in etiology and the majority occurred during the first 3 hours after dosing, after the first dose, or associated with study-related procedures in the clinic setting (such as blood draw and orthostatic maneuvers and blood pressure measurements). Possibly prodromal symptoms, such as nausea, dizziness, lightheadedness, palpitations, asthenia, confusion and diaphoresis generally occurred within the first 3 hours following dosing and often preceded the syncope. Patients need to be made aware that they could experience syncope at any time with or without prodromal symptoms during their treatment with PRILIGY. Prescribers should counsel patients about the importance of maintaining adequate hydration and about how to recognize prodromal signs and symptoms to decrease the likelihood of serious injury associated with falls due to loss of consciousness. If the patient experiences possibly prodromal symptoms, the patient should immediately lie down so his head is lower than the rest of his body or sit down with his head between his knees until the symptoms

pass, and be cautioned to avoid situations where injury could result, including driving or operating hazardous machinery, should syncope or other CNS effects occur (see Section Effects on Ability to Drive and Use Machines.)

Combining alcohol with PRILIGY may enhance neurocardiogenic adverse events such as syncope, thereby increasing the risk of accidental injury; therefore, patients should be advised to avoid alcohol with taking PRILIGY.

Subjects with underlying cardiovascular disease were excluded from Phase 3 clinical trials. The risk of adverse cardiovascular outcomes from syncope (cardiac syncope and syncope from other causes) is increased in patients with underlying structural cardiovascular disease (e.g., documented outflow obstruction, valvular heart disease, carotid stenosis and coronary artery disease). There are insufficient data to determine whether this increased risk extends to vasovagal syncope in patients with underlying disease.

Orthostatic hypotension
Orthostatic hypotension has been reported in clinical trials. The prescriber should counsel the patient in advance that if he experiences possibly prodromal symptoms, such as lightheadedness soon after standing, he should immediately lie down so his head is lower than the rest of his body or sit down with his head between his knees until the symptoms pass. The prescriber should also inform the patient not to rise quickly after prolonged lying or sitting. In addition, PRILIGY should be prescribed with caution in patients taking medicinal products with vasodilatation properties (such as alpha adrenergic receptor antagonists, nitrates, PDE5 inhibitors) due to possible reduced orthostatic tolerance (see Section 4.5 Interactions with Other Medicinal Products and Other Forms of Interaction).

Moderate CYP3A4 inhibitors
The dose is restricted to 30 mg when used concomitantly with moderate CYP3A4 inhibitors such as erythromycin, clarithromycin, fluconazole, amprenavir, fosamprenavir, aprepitant, verapamil, and diltiazem, and caution is advised (see Sections Posology and Method of Administration and Section Interactions with Other Medicinal Products and Other Forms of Interaction).

Potent CYP2D6 inhibitors
Caution is advised if increasing the dose to 60 mg in a patient taking potent CYP2D6 inhibitors or if increasing the dose to 60 mg in a patient known to be a CYP2D6 poor metabolizer, as this may increase exposure levels, which may result in a higher incidence and severity of dose dependent adverse events (see Sections Posology and Method of Administration, Section Interactions with Other Medicinal Products and Other Forms of Interaction and Section Pharmacokinetic Properties).

Suicide/suicidal thoughts
Antidepressants, including SSRIs, increased the risk compared to placebo of suicidal thinking and suicidality in short-term studies in children and adolescents with Major Depressive Disorder and other psychiatric disorders. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24. In clinical trials with PRILIGY for the treatment of premature ejaculation, there was no clear indication of treatment-emergent suicidality.

Mania
PRILIGY should not be used in patients with a history of mania/hypomania or bipolar disorder and should be discontinued in any patient who develops symptoms of these disorders.

Seizure
Due to the potential of SSRIs to lower the seizure threshold, PRILIGY should be discontinued in any patient who develops seizures and avoided in patients with unstable epilepsy. Patients with controlled epilepsy should be carefully monitored.

Use in children and adolescents under age 18
PRILIGY should not be used in individuals below 18 years of age.

Co-morbid depression and psychiatric disorders
Men with underlying signs and symptoms of depression should be evaluated prior to treatment with PRILIGY to rule out undiagnosed depressive disorders. Concomitant treatment of PRILIGY with antidepressants, including SSRIs and SNRIs, is contraindicated (see Section Contraindications). Discontinuation of treatment for ongoing depression or anxiety in order to initiate PRILIGY for the treatment of PE is not recommended. PRILIGY is not indicated for psychiatric disorders and should not be used in men with these disorders, such as schizophrenia, or in those suffering with co-morbid depression, as worsening of symptoms associated with depression cannot be excluded. This could be the result of underlying psychiatric disorder or might be a result of medicinal product therapy. Physicians should encourage patients to report any distressing thoughts or feelings at any time and if signs and symptoms of depression develop during treatment, PRILIGY should be discontinued.

Haemorrhage
There have been reports of bleeding abnormalities with SSRIs. Caution is advised in patients taking PRILIGY, particularly in concomitant use with medicinal products known to affect platelet function (e.g., atypical antipsychotics and phenothiazines, acetylsalicylic acid, nonsteroidal anti-inflammatory drugs [NSAIDs], anti-platelet agents) or anticoagulants (e.g., warfarin), as well as in patients with a history of bleeding or coagulation disorders. (See Section Interactions with Other Medicinal Products and Other Forms of Interaction.)

Renal Impairment
PRILIGY is not recommended for use in patients with severe renal impairment and caution is advised in patients with mild or moderate renal impairment (see Sections Posology and Method of Administration and Section Pharmacokinetic Properties).

Withdrawal effects
Abrupt discontinuation of chronically administered SSRIs used to treat chronic depressive disorders has been reported to result in the following symptoms: dysphoric mood, irritability, agitation, dizziness, sensory disturbances (e.g., paresthesias such as electric shock sensations), anxiety, confusion, headache, lethargy, emotional lability, insomnia, and hypomania.

However, a double-blind clinical trial in subjects with PE designed to assess the withdrawal effects of 62 days of daily or as needed dosing with 60 mg PRILIGY showed no evidence of withdrawal syndrome and little evidence of withdrawal symptoms with only a slightly higher incidence of mild or moderate insomnia and dizziness reported in subjects switched to placebo after daily dosing. (See Section Pharmacodynamic Properties: Clinical Trials.) Consistent results were seen in a second double-blind clinical trial with a 24-week treatment phase of 30 and 60 mg doses as needed followed by a 1-week withdrawal assessment period.

4.5 Interaction with other medicinal products and other forms of interaction

Potential for interaction with monoamine oxidase inhibitors
In patients receiving an SSRI in combination with a monoamine oxidase inhibitor (MAOI), there have been reports of serious, sometimes fatal, reactions including hyperthermia, rigidity, myoclonus, autonomic instability with possible rapid fluctuations of vital signs, and mental status changes that include extreme agitation progressing to delirium and coma. These reactions have also been reported in patients who have recently discontinued an SSRI and have been started on an MAOI. Some cases presented with features resembling neuroleptic malignant syndrome. Animal data on the effects of combined use of an SSRI and MAOIs suggest that these medicinal products may act synergistically to elevate blood pressure and evoke behavioral excitation. Therefore, PRILIGY should not be used in combination with an MAOI, or within 14 days of discontinuing treatment with an MAOI. Similarly, an MAOI should not be administered within 7 days after PRILIGY has been discontinued. (See Section Contraindications.)

Potential for interaction with thioridazine
Thioridazine administration alone produces prolongation of the QTc interval, which is associated with serious ventricular arrhythmias. Medicinal products such as PRILIGY that inhibit the CYP2D6 isoenzyme appear to inhibit the metabolism of thioridazine and the resulting elevated levels of thioridazine are expected to augment the prolongation of the QTc interval. PRILIGY should not be used in combination with thioridazine or within 14 days of discontinuing treatment with thioridazine. Similarly, thioridazine should not be administered within 7 days after PRILIGY has been discontinued (see Section Contraindications).

Medicinal/herbal products with serotonergic effects
As with other SSRIs, co-administration with serotonergic medicinal/herbal products (including MAOIs, L-tryptophan, triptans, tramadol, linezolid, SSRIs, SNRIs, lithium and St. John's Wort (*Hypericum perforatum*) preparations) may lead to an incidence of serotonin associated effects. PRILIGY should not be used in combination with other SSRIs, MAOIs or other serotonergic medicinal/herbal products or within 14 days of discontinuing treatment with these medicinal/herbal products. Similarly, these medicinal/herbal products should not be administered within 7 days after PRILIGY has been discontinued (see Section Contraindications).

CNS active medicinal products
The use of PRILIGY in combination with CNS active medicinal products has not been systematically evaluated in patients with premature ejaculation. Consequently, caution is advised if the concomitant administration of PRILIGY and such medicinal products is required.

Effects of co-administered medicinal products on dapoxetine hydrochloride
In vitro studies in human liver, kidney, and intestinal microsomes indicate dapoxetine is metabolized primarily by CYP2D6, CYP3A4 and flavin monooxygenase 1 (FMO1). Therefore, inhibitors of these enzymes may reduce dapoxetine clearance.

CYP3A4 inhibitors
Potent CYP3A4 inhibitors
Administration of ketoconazole (200 mg twice daily for 7 days) increased the Cmax and AUCinf of dapoxetine (60 mg single dose) by 35% and 99%, respectively. Considering the contribution of both unbound dapoxetine and desmethyldapoxetine, the Cmax of the active fraction (the sum of the unbound exposure of dapoxetine and desmethyldapoxetine) may be increased by approximately 25% and the AUC of the active fraction may be doubled if taken with potent CYP3A4 inhibitors. These increases in the Cmax and AUC of the active fraction may be markedly increased in a part of the population which lack a functional CYP2D6 enzyme, i.e., CYP2D6 poor metabolizers, or in combination with potent inhibitors of CYP2D6.

Therefore, concomitant use of PRILIGY and potent CYP3A4 inhibitors, such as ketoconazole, itraconazole, ritonavir, saquinavir, telithromycin, nefazodone, nelfinavir and atazanavir, is contraindicated (see Section Contraindications).

Moderate CYP3A4 inhibitors
Concomitant treatment with moderate CYP3A4 inhibitors such as erythromycin, clarithromycin, fluconazole, amprenavir, fosamprenavir, aprepitant, verapamil and diltiazem may also give rise to significantly increased exposure of dapoxetine and desmethyldapoxetine, especially in CYP2D6 poor metabolizers. Therefore, the maximum dose of PRILIGY is 30 mg if combined with any of these drugs and caution is advised (see Sections 4.2 Posology and Method of Administration, 4.4 Special Warnings and Special Precautions for Use).

Potent CYP2D6 inhibitors
The Cmax and AUCinf of dapoxetine (60 mg single dose) increased by 50% and 88%, respectively, in the presence of fluoxetine (60 mg/day for 7 days). Considering the contribution of both unbound dapoxetine and desmethyldapoxetine, the Cmax of the active fraction may be increased by approximately 50% and the AUC of the active fraction may be doubled if taken with potent CYP2D6 inhibitors. These increases in the Cmax and AUC of the active fraction are similar to those expected

for CYP2D6 poor metabolizers and may result in a higher incidence and severity of dose dependent adverse events. Therefore, caution is advised if increasing the dose to 60 mg in a patient taking potent CYP2D6 inhibitors or if increasing the dose to 60 mg in a patient known to be a CYP2D6 poor metabolizer (see Sections Posology and Method of Administration and Section Special Warnings and Special Precautions for Use).

PDE5 inhibitors

The pharmacokinetics of dapoxetine (60 mg) in combination with tadalafil (20 mg) and sildenafil (100 mg) were evaluated in a single dose crossover study. Tadalafil did not affect the pharmacokinetics of dapoxetine. Sildenafil caused slight changes in dapoxetine pharmacokinetics (22% increase in AUCinf and 4% increase in Cmax), which are not expected to be clinically significant. However, PRILIGY should be prescribed with caution in patients who use PDE5 inhibitors due to possible reduced orthostatic tolerance (see Section Special Warnings and Special Precautions for Use).

Effects of dapoxetine hydrochloride on co-administered medicinal products

Tamsulosin

Concomitant administration of single or multiple doses of 30 mg or 60 mg PRILIGY to patients receiving daily doses of tamsulosin did not result in changes in the pharmacokinetics of tamsulosin. The addition of PRILIGY to tamsulosin did not result in a change in the orthostatic profile and there were no differences in orthostatic effects between tamsulosin combined with either 30 or 60 mg PRILIGY and tamsulosin alone; however, PRILIGY should be prescribed with caution in patients who use alpha adrenergic receptor antagonists due to possible reduced orthostatic tolerance (see Section Special Warnings and Special Precautions for Use).

Medicinal products metabolized by CYP2D6

Multiple doses of PRILIGY (60 mg/day for 6 days) followed by a single 50 mg dose of desipramine increased the mean Cmax and AUCinf of desipramine approximately 11% and 19%, respectively, compared to desipramine administered alone. Dapoxetine may give rise to a similar increase in the plasma concentrations of other drugs metabolized by CYP2D6. The clinical relevance is likely to be small.

Medicinal products metabolized by CYP3A

Multiple dosing of PRILIGY (60 mg/day for 6 days) decreased the AUCinf of midazolam (8 mg single dose) by approximately 20% (range –60 to +18%). The clinical relevance of the effect on midazolam is likely to be small in most patients. The increase in CYP3A activity may be of clinical relevance in some individuals concomitantly treated with a medicinal product mainly metabolized by CYP3A and with a narrow therapeutic window.

Medicinal products metabolized by CYP2C19

Multiple dosing of PRILIGY (60 mg/day for 6 days) did not affect the pharmacokinetics of a single 40 mg dose of omeprazole. Dapoxetine is unlikely to affect the pharmacokinetics of other CYP2C19 substrates.

Medicinal products metabolized by CYP2C9

Multiple dosing of PRILIGY (60 mg/day for 6 days) did not affect the pharmacokinetics or pharmacodynamics of a single 5 mg dose of glyburide. Dapoxetine is unlikely to affect the pharmacokinetics of other CYP2C9 substrates.

PDE5 inhibitors

In a single-dose crossover study, dapoxetine (60 mg) did not affect the pharmacokinetics of tadalafil (20 mg) or sildenafil (100 mg).

Warfarin

There are no data evaluating the effect of chronic use of warfarin with PRILIGY; therefore, caution is advised when PRILIGY is used in patients taking warfarin chronically. (See Section Special Warnings and Special Precautions for Use: Haemorrhage.) In a pharmacokinetic study, dapoxetine (60 mg/day

for 6 days) did not affect the pharmacokinetics or pharmacodynamics (PT or INR) of warfarin following a single 25 mg dose.

Ethanol
Coadministration of a single dose of ethanol, 0.5 g/kg (approximately 2 drinks), did not affect the pharmacokinetics of dapoxetine (60 mg single dose) or the pharmacokinetics of ethanol; however, PRILIGY in combination with ethanol increased somnolence and significantly decreased self-rated alertness. Pharmacodynamic measures of cognitive impairment (Digit Vigilance Speed, Digit Symbol Substitution Test) did not show a significant separation from placebo with either ethanol or PRILIGY alone but did show a statistically significant effect when PRILIGY was coadministered with ethanol versus ethanol alone. Concomitant use of alcohol and PRILIGY increases the chance or severity of adverse reactions such as dizziness, drowsiness, slow reflexes, or altered judgment. Combining alcohol with PRILIGY may also enhance neurocardiogenic adverse events such as syncope, thereby increasing the risk of accidental injury; therefore, patients should be advised to avoid alcohol while taking PRILIGY (see Sections Special Warnings and Special Precautions for Use and Section Effects on Ability to Drive and Use Machines).

4.6 Pregnancy and lactation

Category B2.
PRILIGY is not indicated for use by women.

Use during pregnancy
There is no evidence of teratogenicity, embryotoxicity, or fetotoxicity in rats or rabbits that received up to 100 mg/kg (rats) or 75 mg/kg (rabbits).

There is no evidence to suggest that dapoxetine exposure has an effect on a partner's pregnancy based on limited observational data from the clinical trial database. There are no adequate and well-controlled studies of dapoxetine in pregnant women.

Use during lactation
PRILIGY is not indicated for use by women.
It is not known if either dapoxetine or its metabolites are excreted in human breast milk.

4.7 Effects on ability to drive and use machines

Dizziness, disturbance in attention, syncope, blurred vision and somnolence have been reported in subjects receiving dapoxetine in clinical trials. Therefore, patients should be warned to avoid situations where injury could result, including driving or operating hazardous machinery.

Combining alcohol with PRILIGY may increase alcohol-related neurocognitive effects and may also enhance neurocardiogenic adverse events such as syncope, thereby increasing the risk of accidental injury; therefore, patients should be advised to avoid alcohol while taking PRILIGY (see Sections Special Warnings and Special Precautions for Use and Section Interactions with Other Medicinal Products and Other Forms of Interaction).

4.8 Undesirable effects

Clinical Trial Data
The safety of PRILIGY was evaluated in 6081 subjects with premature ejaculation who participated in five double-blind, placebo-controlled clinical trials. Of the subjects evaluated, 4222 received PRILIGY: 1615 received PRILIGY 30 mg as needed and 2607 received 60 mg, either as needed or once daily.

Syncope characterized as loss of consciousness has been reported in clinical trials and is considered medicinal product-related. The majority of cases occurred during the first 3 hours after dosing, after the first dose or associated with study-related procedures in the clinic setting (such as blood draw and

orthostatic maneuvers and blood pressure measurements). Prodromal symptoms often preceded the syncope. (See Section Special Warnings and Special Precautions for Use.)

Orthostatic hypotension has been reported in clinical trials. (See Section Special Warnings and Special Precautions for Use.)

The most common adverse drug reactions (≥ 5%) reported during clinical trials were headache, dizziness, nausea, diarrhoea, insomnia and fatigue. The most common events leading to discontinuation were nausea (2.2% of PRILIGY-treated subjects) and dizziness (1.2% of PRILIGY-treated subjects).

Adverse drug reactions reported by ≥ 1% of PRILIGY-treated subjects in these trials are shown in Table 3.

Table 3: Adverse Drug Reactions Reported by ≥ 1% of PRILIGY-treated Subjects in 5 Double Blind, Placebo-Controlled Clinical Trials of PRILIGY

System/organ class Adverse drug reaction	PLACEBO (n=1857) %	PRILIGY 30 mg as needed (n=1616[1]) %	PRILIGY 60 mg as needed (n=21061) %	PRILIGY 60 mg once daily[2] (n=502) %
Investigations				
Blood pressure increased[3]	0.2	0.4	1.1	2.2
Nervous system disorders				
Dizziness[4]	2.2	5.8	11.0	14.9
Headache	4.8	5.6	8.8	11.2
Somnolence[5]	0.6	3.1	4.8	4.0
Tremor	0.2	0.5	0.9	1.6
Disturbance in attention	0.5	0.4	0.8	2.6
Paraesthesia	0.3	0.4	0.8	1.2
Eye disorders				
Vision blurred[6]	0.4	0.2	0.6	2.0
Ear and labyrinth disorders				
Tinnitus	0.4	0.2	0.5	1.2
Respiratory, thoracic and mediastinal disorders				
Sinus congestion	0.3	0.7	1.0	1.6
Yawning	0	0.4	0.9	1.2
Gastrointestinal disorders				
Nausea	2.2	11.0	22.2	17.1
Diarrhoea[7]	1.7	3.5	6.9	9.4
Abdominal pain[8]	1.2	2.2	2.6	4.4
Dry mouth	0.7	1.2	2.6	3.4
Vomiting	0.4	1.0	2.3	1.8
Dyspepsia	0.4	0.9	1.4	0.8
Flatulence	0.1	0.4	0.9	1.4
Constipation	0.3	0.3	0.4	1.8
Abdominal	0.3	0.1	0.6	1.0

distention				
Skin and subcutaneous tissue disorders				
Hyperhidrosis	0.2	0.8	1.2	3.0
Vascular disorders				
Flushing[9]	0.3	0.9	1.3	1.4
General disorders and administration site conditions				
Fatigue	1.2	2.0	4.1	9.2
Irritability	0.8	0.1	1.1	3.6
Reproductive system and breast disorders				
Erectile dysfunction	1.6	2.3	2.6	1.2
Psychiatric disorders				
Insomnia[10]	1.6	2.3	4.3	9.0
Anxiety	0.5	1.1	2.0	2.2
Nervousness[11]	0.5	0.6	1.2	3.0
Libido decreased[12]	0.4	0.6	0.9	1.4
Depression[13]	0.6	0.4	0.9	1.2
Apathy[14]	0.1	0.4	0.2	1.0
Abnormal dreams[15]	0.3	0.2	0.4	2.0

[1] One randomized patient never received study medication
[2] Treatment duration up to approximately 70 days
[3] Also includes blood pressure diastolic increased and blood pressure orthostatic increased
[4] Also includes dizziness postural and dizziness exertional
[5] Also includes hypersomnia and sudden onset of sleep
[6] Also includes visual disturbance
[7] Also includes defaecation urgency
[8] Also includes abdominal pain upper, stomach discomfort, abdominal discomfort and epigastric discomfort
[9] Also includes hot flush
[10] Also includes middle insomnia and initial insomnia
[11] Also includes agitation and restlessness
[12] Also includes loss of libido
[13] Also includes depressed mood
[14] Also includes indifference
[15] Also includes nightmare

Additional adverse drug reactions that occurred in < 1% of PRILIGY-treated subjects are listed below in Table 4.

Table 4: Adverse Drug Reactions Reported by < 1% of PRILIGY-treated Subjects in 5 Double-Blind, Placebo-Controlled Clinical Trials of PRILIGY
System/organ class
Adverse drug reaction
Cardiac disorders
Tachycardia[16]
Sinus bradycardia

Sinus arrest
Nervous system disorders
Depressed level of consciousness[17]
Dysgeusia
Syncope[18]
Akathisia
Eye disorders
Mydriasis
Ear and labyrinth disorders
Vertigo
Skin and subcutaneous tissue disorders
Pruritus
Cold sweat
Vascular disorders
Hypotension
Systolic hypertension
General disorders and administration site conditions
Asthenia
Feeling abnormal
Feeling hot
Feeling jittery
Feeling drunk
Reproductive system and breast disorders
Ejaculation failure
Male orgasmic disorder[19]
Paraesthesia of genital male
Psychiatric disorders
Euphoric mood
Mood altered
Confusional state
Sleep disorder
Bruxism
Disorientation
Hypervigilance
Thinking abnormal

[16] Also includes heart rate increased
[17] Also includes sedation
[18] Also includes syncope vasovagal
[19] Also includes anorgasmia (also moved from Psychiatric disorders system organ class)

Adverse drug reactions reported in the long term open-label extension trial were consistent with those reported in the double-blind studies and no additional adverse drug reactions were reported.

If you experience any of these side effects or side effects that are not listed in this packaging leaflet, contact your doctor or pharmacist. You can also report complaints of side effects or uncomfortable conditions directly to the Pharmaceutical Industry via the following contact: Idn.ae@menariniapac.com.

By reporting side effects, you can help provide more information about the safety of this drug.

4.9 Overdose

There have been no reports of overdose during clinical trials.

There were no unexpected adverse events in a clinical pharmacology study of PRILIGY with daily doses up to 240 mg (two 120 mg doses given 3 hours apart). In general, symptoms of overdose with SSRIs include serotonin-mediated adverse reactions such as somnolence, gastrointestinal disturbances such as nausea and vomiting, tachycardia, tremor, agitation and dizziness.

In cases of overdose, standard supportive measures should be adopted as required. Due to high protein binding and large volume of distribution of dapoxetine hydrochloride, forced diuresis, dialysis, hemoperfusion and exchange transfusion are unlikely to be of benefit. No specific antidotes for PRILIGY are known.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other Urologicals. ATC code: G04BX14

Mechanism of action

The mechanism of action of dapoxetine in premature ejaculation is presumed to be linked to the inhibition of neuronal reuptake of serotonin and the subsequent potentiation of the neurotransmitter's action at pre- and postsynaptic receptors.

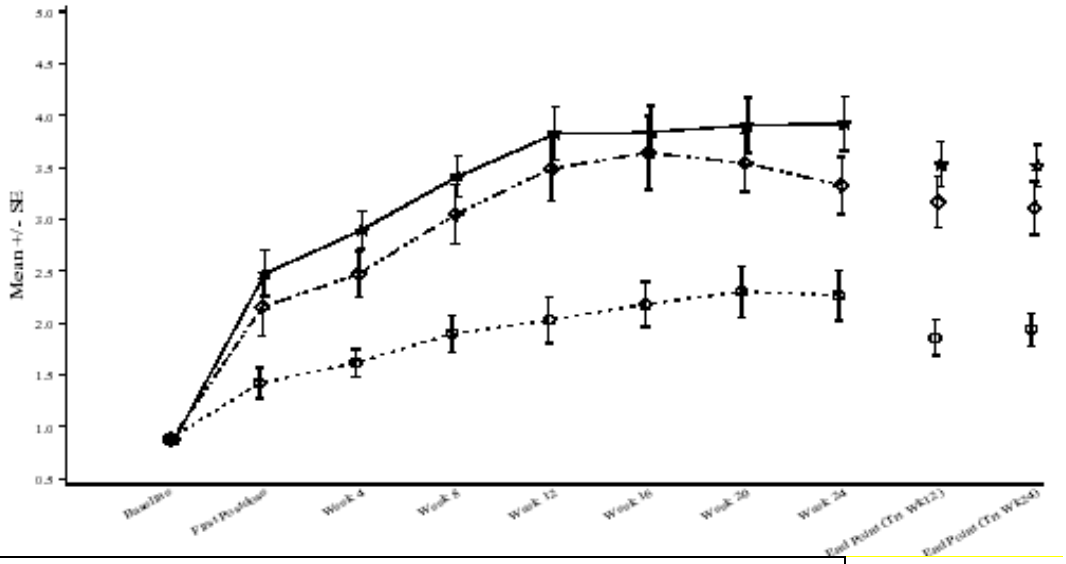
Human ejaculation is primarily mediated by the sympathetic nervous system. The ejaculatory pathway originates from a spinal reflex center, mediated by the brain stem, which is influenced initially by a number of nuclei in the brain (medial preoptic and paraventricular nuclei). In the rat, dapoxetine inhibits the ejaculatory expulsion reflex by acting at a supraspinal level with the lateral paragigantocellular nucleus (LPGi) as a necessary brain structure for the effect. Post ganglionic sympathetic fibers that innervate the seminal vesicles, vas deferens, prostate, bulbourethral muscles, and bladder neck cause them to contract in a coordinated fashion to achieve ejaculation. Dapoxetine modulates this ejaculatory reflex in rats, causing an increase in pudendal motoneuron reflex discharge (PMRD) latency and a reduction in PMRD duration.

Clinical trials

The effectiveness of PRILIGY in the treatment of premature ejaculation has been established in five double-blind, placebo-controlled clinical trials, in which a total of 6081 subjects were randomized. Subjects were 18 years of age or older and had a history of PE in the majority of intercourse experiences in the 6-month period prior to enrollment. In four of the studies, subjects had an intravaginal ejaculatory latency time (IELT; time from vaginal penetration to the moment of intravaginal ejaculation) of ≤ 2 minutes in a minimum of 75% of evaluable sexual intercourse events during the baseline period. In the fifth study, subjects had the same entry criteria; however, IELT was not measured using a stopwatch. Subjects with other forms of sexual dysfunction, including erectile dysfunction, or those using other forms of pharmacotherapy for the treatment of PE were excluded from all studies. In four studies, the primary endpoint of average IELT was measured using a stopwatch during each episode of sexual intercourse.

Results of all randomized studies were consistent. In a representative study (R096769–PRE-3001) with the longest treatment duration (24 weeks), 1162 subjects were randomized, 385 to placebo, 388 to PRILIGY 30 mg as needed, and 389 to PRILIGY 60 mg as needed. The mean average IELT at baseline and study endpoint for all treatment groups is shown in Figure 1. Increases in mean average IELT at the Week 24 endpoint (LPOCF) were statistically significant ($p<0.001$) in both PRILIGY groups versus placebo. The magnitude of IELT prolongation was related to baseline IELT and was variable between individual subjects. The clinical relevance of PRILIGY treatment effects are described below in terms of patient reported response rates.

Figure 1: Mean (+/- SE) in Average IELT (min) over Time
Study R096769-PRE-3001



	Sample size (N) for each visit in Figure 1									
	Baseline	First Postdose	Wk 4	Wk 8	Wk 12	Wk 16	Wk 20	Wk 24	Endpoint Wk 12	Endpoint Wk 24
Placebo	382	339	332	280	238	221	195	182	339	339
DPX 30 mg PRN	385	363	356	303	264	240	221	218	363	363
DPX 60 mg PRN	387	355	347	287	249	229	214	198	355	355

Treatment Group:---○ PLACEBO---◇ DPX 30 MG PRN
End Point (TRT WK12) = LPOCF to Week 12. End Point (TRT WK24) = LPOCF to Week 24

LPOCF is last post-baseline observation carried forward.

In addition to the primary endpoint of average IELT, meaningful treatment benefit to the patient in the above study was demonstrated using a definition of treatment response consisting of a composite of at least a 2-category increase in control over ejaculation plus at least a 1- category decrease in ejaculation-related distress. A statistically significantly greater percentage of subjects responded in each of the PRILIGY groups versus placebo beginning at Week 4 and up to and including Week 24 ($p=0.003$ for dapoxetine 30 mg versus placebo at Week 16, all other comparisons $p \leq 0.001$). Significant decrease in subject distress and significant improvement in subject satisfaction with sexual intercourse were also observed. Improvements at Weeks 12 and 24 (LPOCF) for the key secondary endpoints are presented in Table 1.

Table 1: Percentage of Subjects with Improvement in Key Secondary Endpoints; Study R096769–PRE-3001

Key Secondary Endpoint (at LPOCF20)	Placebo %	PRILIGY 30mg %	PRILIGY 60mg %
Treatment Response Composite (change ≥2 in control and ≤-1 in distress)	(n=346)	(n=359)	(n=353)
Week 12	12.1	27.3[20]	34.0[20]
Week 24	13.0	25.3[20]	37.1[20]
Change ≤-1 in Distress	(n=347)	(n=360)	(n=353)
Week 12	46.1	63.1[20]	65.4[20]

Week 24	47.8	60.0[20]	68.6[20]
Change ≥1 in Satisfaction	(n=347)	(n=359)	(n=353)
Week 12	31.7	51.3[20]	56.1[20]
Week 24	35.7	48.5[20]	55.8[20]

[20] p-value <0.001 for PRILIGY versus placebo; LPOCF is last post-baseline observation carried forward

Other secondary patient reported outcome (PRO) endpoints were assessed in the clinical trials including clinical global impression of change in condition, CGIC, a commonly used measure in which patients assess the status of their condition. Patients were asked to compare their premature ejaculation from the start of the study, with response options ranging from much better to much worse. Endpoints for CGIC showed statistically significant improvement compared to placebo when tested at the nominal significance level of 0.05 (2-sided). CGIC results by treatment group reported at the end of the above study are shown in Table 2.

Table 2: Results of Clinical Global Impression of Change in Condition at Study Endpoint (LPOCF[21]); Study R096769–PRE–3001

CGIC Response Outcome	Placebo n (%)	PRILIGY 30 mg n (%)	PRILIGY 60 mg n (%)
No Change or Worse[22]	236 (68.0%)	152 (42.3%)	97 (27.6%)
Slightly Better[23]	57 (16.4%)	97 (27.0%)	117 (33.2%)
Better	41 (11.8%)	74 (20.6%)	96 (27.3%)
Much Better	13 (3.7%)	36 (10.0%)	42 (11.9%)
Total	347 (100%)	359 (100%)	352 (100%)

[21] LPOCF is last post-baseline observation carried forward
[22] No Change or Worse includes No Change, Slightly Worse, Worse or Much Worse
[23] At least Slightly Better CGIC response rate includes Slightly Better, Better and Much Better: Placebo (32%), PRILIGY 30 mg (57.7%) and PRILIGY 60 mg (72.4%) with p-value <0.0001 for PRILIGY 30 mg versus placebo and PRILIGY 60 mg versus placebo

The withdrawal effects of chronic daily and as needed dosing with 60 mg PRILIGY in the treatment of premature ejaculation were evaluated in a placebo-controlled, double-blind, parallel-group study in which 1238 subjects were randomized. Subjects received placebo or 60 mg PRILIGY either once daily or as needed for 62 days followed by a withdrawal assessment period of 7 days of additional PRILIGY treatment or placebo. Withdrawal effects after abrupt cessation of therapy were measured using the Discontinuation Emergent Signs and Symptoms (DESS), a clinician-rated instrument that queries for symptoms and signs associated with the discontinuation of serotonin reuptake inhibitor treatment. For each subject, discontinuation syndrome was defined as an increase in the weekly DESS score by at least 4 points from Day 63 to Day 70. In this study, there was no clear evidence of discontinuation (withdrawal) syndrome upon abrupt discontinuation of PRILIGY therapy. Consistent with the lack of discontinuation syndrome based on DESS, adverse event data showed little evidence of withdrawal symptoms. Similar results were seen in a second double-blind clinical trial with a 24-week treatment phase of 30 and 60 mg doses as needed followed by a 1-week withdrawal assessment period.

In the two multidose Phase 3 studies, where the CYP2D6 metabolizer status was identified, a total of 120 poor metabolizers and 1598 extensive metabolizers were enrolled and treated with PRILIGY. No overall differences were seen in efficacy or safety between poor and extensive metabolizers.

5.2 Pharmacokinetic properties

Absorption

Dapoxetine is rapidly absorbed with maximum plasma concentrations (Cmax) occurring approximately 1–2 hours after tablet intake. The absolute bioavailability is 42% (range 15-76%). Following single oral doses of 30 mg and 60 mg in the fasted state, peak plasma concentrations of dapoxetine were 297 ng/ml after 1.01 hours, and 498 ng/ml after 1.27 hours, respectively.

Ingestion of a high fat meal modestly reduced the Cmax (by 10%) and modestly increased the AUC (by 12%) of dapoxetine and slightly delayed the time for dapoxetine to reach peak concentrations;

however, the extent of absorption was not affected by consumption of a high fat meal. These changes are not clinically significant. PRILIGY can be taken with or without food.

Distribution
More than 99% of dapoxetine is bound *in vitro* to human serum proteins. The active metabolite desmethyldapoxetine is 98.5% protein bound. Dapoxetine appears to have a rapid distribution with a mean steady state volume of distribution of 162 L. Following intravenous administration in humans, mean estimated initial, intermediate, and terminal half-life values for dapoxetine were 0.10, 2.19, and 19.3 hours respectively.

Biotransformation
In vitro studies suggest that dapoxetine is cleared by multiple enzyme systems in the liver and kidneys, primarily CYP2D6, CYP3A4, and flavin monooxygenase (FMO1). Following oral dosing in a clinical study designed to explore the metabolism of 14C-dapoxetine, dapoxetine was extensively metabolized to multiple metabolites primarily through the following biotransformational pathways: N-oxidation, N-demethylation, naphthyl hydroxylation, glucuronidation and sulfation. There was evidence of presystemic first-pass metabolism after oral administration.

Intact dapoxetine and dapoxetine-N-oxide were the major circulating species in the plasma. Additional metabolites include desmethyldapoxetine, which is equipotent to dapoxetine, and didesmethyldapoxetine, which has approximately 50% of the potency of dapoxetine. Taking into account potency and unbound plasma concentrations, only desmethyldapoxetine may contribute to the effects of dapoxetine *in vivo* (see PHARMACOKINETICS IN SPECIAL POPULATIONS; Hepatic impairment and CYP2D6 Polymorphism below). The half-life of desmethyldapoxetine is similar to that of dapoxetine.

Elimination
The metabolites of dapoxetine were primarily eliminated in the urine as conjugates. Unchanged active substance was not detected in the urine. Dapoxetine has a rapid elimination, as evidenced by a low concentration (less than 5% of peak) 24 hours after dosing. There was minimal accumulation of dapoxetine following daily dosing. The terminal half-life is approximately 19 hours following oral administration.

Pharmacokinetics in special populations

Race
Analyses of single dose clinical pharmacology studies using 60 mg dapoxetine indicated no statistically significant differences between Caucasians, Blacks, Hispanics, and Asians. A clinical study conducted to compare the pharmacokinetics of dapoxetine in Japanese and Caucasian subjects showed 10% to 20% higher plasma levels (AUC and peak concentration) of dapoxetine in Japanese subjects due to lower body weight. The slightly higher exposure is not expected to have a meaningful clinical effect.

Elderly (age 65 years and over)
Analyses of a single dose clinical pharmacology study using 60 mg dapoxetine showed no significant differences in pharmacokinetic parameters (Cmax, AUCinf, Tmax) between healthy elderly males and healthy young adult males.

Renal impairment
In a single dose clinical pharmacology study using 60 mg dapoxetine, no correlation was noted between creatinine clearance and dapoxetine Cmax or AUCinf in subjects with mild (creatinine clearance 50 to 80 mL/min), moderate (creatinine clearance 30 to < 50 mL/min), and severe (creatinine clearance < 30 mL/min) renal impairment. Dapoxetine pharmacokinetics have not been evaluated in patients requiring renal dialysis. There are limited data in patients with severe renal impairment (see Sections Posology and Method of Administration and Section Special Warnings and Special Precautions for Use).

Hepatic impairment
The pharmacokinetics of dapoxetine and desmethyldapoxetine are unchanged in patients with mild hepatic impairment. In patients with moderate hepatic impairment (Child-Pugh Class B), unbound Cmax of dapoxetine is increased by 55% and unbound AUC is increased by 120%. The unbound Cmax and AUC of the active fraction were unchanged and doubled, respectively.

In severe hepatic impairment, the unbound Cmax of dapoxetine was unchanged but the unbound AUC was increased more than 3-fold. The AUC of the active fraction was increased severalfold (see Sections Posology and Method of Administration and Section Contraindications).

CYP2D6 Polymorphism
In a single dose clinical pharmacology study using 60 mg PRILIGY, plasma concentrations in poor metabolizers of CYP2D6 were higher than in extensive metabolizers (approximately 31% higher for Cmax and 36% higher for AUCinf) of dapoxetine and 98% higher for Cmax and 161% higher for AUCinf of desmethyldapoxetine). Thus, the active fraction of PRILIGY may be increased by approximately 46% at Cmax and by approximately 90% for AUC. This increase may result in a higher incidence and severity of dose dependent adverse events. The safety of PRILIGY in poor metabolizers of CYP2D6 is of particular concern with concomitant administration of other medicinal products that may inhibit the metabolism of dapoxetine such as moderate and potent CYP3A4 inhibitors (see Sections Posology and Method of Administration, Section Contraindications and Section Special Warnings and Special Precautions for Use.).

Plasma concentrations of dapoxetine and desmethyldapoxetine in CYP2D6 ultrarapid metabolizers are expected to be decreased.

5.3 Preclinical safety data

In studies with oral administration, dapoxetine was not carcinogenic to rats when administered daily for approximately two years at doses up to 225 mg/kg/day, yielding approximately twice the exposures (AUC) seen in human males given the Maximum Recommended Human Dose (MRHD) of 60 mg. Dapoxetine also did not cause tumors in Tg.rasH2 mice when administered at the maximum possible doses of 100 mg/kg for 6 months and 200 mg/kg for 4 months. The steady state exposures of dapoxetine in mice following 6-months oral administration at 100 mg/kg/day were less than the single dose exposures observed clinically at 60 mg.

Daily topical administration for 6 months to Tg.AC transgenic mice at 375, 750, or 1500 mg/kg/day produced some tumor promoter activity (papillomas at the application site) at 750 mg/kg/day or higher. Systemic medicinal product exposure, as measured by AUC of dapoxetine and its major human metabolites, was approximately 1 to 2 fold the exposures in
males given the Maximum Recommended Human Dose (MRHD) of 60 mg. The topical exposure model is not relevant for orally administered medicinal products.

Dapoxetine and its major human metabolite were not mutagenic in the *in vitro* bacterial Ames assay or the forward mutation test in mouse lymphoma cells. Dapoxetine was not clastogenic in the *in vitro* chromosomal aberration test in Chinese hamster ovary cell or the *in vivo* mouse micronucleus assay.

Based on data from the 2–year rat carcinogenicity study, 6-month Tg.rasH2 carcinogenicity study, and genetic toxicology studies, dapoxetine is not expected to have carcinogenic risk.

There were no effects on fertility, reproductive performance or reproductive organ morphology in male or female rats and no adverse signs of embryotoxicity or fetotoxicity in the rat or rabbit.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core
Lactose monohydrate

Microcrystalline cellulose
Croscarmellose sodium
Colloidal anhydrous silica
Magnesium stearate

Tablet coating
Lactose monohydrate
Hypromellose
Titanium dioxide (E171)
Triacetin
Black iron oxide (E172)
Yellow iron oxide (E172)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months for all climatic zones.

6.4 Special precautions for storage

Store below 30°C

6.5 Nature and contents of container

Information to be supplied locally.

6.6 Special precautions for disposal

No special requirements.

7. PHARMACOVIGILANCE (PV) CONTACT

Idn.ae@menariniapac.com

HOW SUPPLIED
PRILIGY 30 mg film-coated tablet
Box @ 1 blister @ 3 film-coated tablets Reg.No.: DKI1924100217A1
Box @ 2 blisters @ 3 film-coated tablets Reg. No.: DKI1924100217A1

PRILIGY 60 mg film-coated tablet
Box @ 1 blister @ 3 film-coated tablets Reg. No.: DKI1924100217B1
Box @ 2 blisters @ 3 film-coated tablets Reg. No.: DKI1924100217B1

HARUS DENGAN RESEP DOKTER

Manufactured, packed and released by Menarini – Von Heyden GmbH, Dresden, Germany
Imported by PT. Menarini Indria Laboratories, Bekasi, Indonesia
Licensed by A. Menarini Asia-Pacific Holdings Pte. Ltd., 30 Pasir Panjang Road, Mapletree Business City, Singapore 117440

Leaflet kemasan: Informasi untuk pengguna

Priligy 30 mg tablet salut selaput
Priligy 60 mg tablet salut selaput
dapoxetine

Baca seluruh isi leaflet ini dengan seksama sebelum anda mulai penggunakan obat ini karena leaflet ini memuat informasi penting untuk anda.

- Simpan leaflet ini. Anda mungkin perlu membacanya kembali.
- Apabila anda memiliki pertanyaan lebih lanjut, tanyakan pada dokter, apoteker atau perawat anda.
- Obat ini telah diresepkan hanya untuk anda. Jangan berikan obat ini kepada orang lain. Hal ini dapat membahayakan mereka, meskipun mereka memiliki gejala yang sama seperti anda.
- Apabila anda mengalami efek sampingm bicarakan pada dokter, apoteker, atau perawat anda. Hal ini termasuk juga kemungkinan efek samping yang tidak tercantum dalam leaflet ini. Lihat bagian 4.

Yang terkandung dalam leaflet ini

1. Apa itu Priligy dan apa kegunaannya

Priligy mengandung bahan aktif bernama „dapoxetine“. Bahan ini tergolong dalam kelompok obat bernama ‘*selective serotonin reuptake inhibitors’ (SSRIs)*. Priligy juga dikenal sebagai obat ‘urologis’.

Priligy meningkatkan waktu yang diperlukan untuk ejakulasi dan memperbaiki kontrol terhadap ejakulasi. Hal ini dapat mengurangi rasa frustasi dan kekhawatiran terhadap ejakulasi dini.

Priligy digunakan untuk mengobati ejakulasi dini pada pria dewasa usia 18 sampai 64 tahun.

Ejakulasi dini terjadi saat pria mengalami ejakulasi dengan sedikit stimulasi seksual dan sebelum waktu yang diinginkan pria tersebut. Hal ini dapat menyebabkan masalah bagi pria tersebut dan dapat menyebabkan masalah pada hubungan seksual.

2. Apa yang perlu anda ketahui sebelum mengkonsumsi Priligy

Jangan gunakan Priligy:

- Jika anda memiliki alergi terhadap dapoxetine atau bahan-bahan lain yang terkandung dalam obat ini (tertera pada bagian 6)
- Jika anda memiliki masalah jantung seperti gagal jantung atau masalah dengan ritme jantung.
- Jika anda memiliki riwayat pingsan
- Jika anda pernah mengalami mania (gejala meliputi perasaan semangat berlebihan, mudah marah, atau tidak dapat berpikir jernih) atau depresi berat.
- Jika anda sedang mengkonsumsi:
  - Obat-obatan untuk depresi golongan ‘*monoamine oxidase inhibitors*’ (MAOIs)
  - *Thioridazine* yang digunakan untuk skizofrenia
  - Obat-obatan lain untuk depresi
  - Litium – obat untuk gangguan bipolar
  - Linezolid – antibiotik untuk mengobati infeksi
  - *Tryptophan* – obat untuk membantu anda tidur

- *St John's wort* – obat herbal
- Tramadol – digunakan untuk mengobati nyeri hebat
- Obat-obatan yang digunakan untuk mengobati migrain.

Jangan gunakan Priligy pada saat bersamaan dengan obat-obatan lain yang tertera diatas. Apabila anda telah mengkonsumsi obat-obatan tersebut diatas, anda harus menunggu 14 hari setelah berhenti minum obat sebelum dapat memulai penggunaan Priligy. Setelah anda berhenti menggunakan Priligy, anda harus menunggu selama 7 hari sebelum dapat menggunakan obat- obatan yang tersebut diatas. Apabila anda tidak yakin, komunikasikan pada dokter atau apoteker anda sebelum meggunakan obat ini. (lihat bagian "**Obat-obatan lain dan Priligy**").

- Obat-obatan tertentu untuk infeksi jamur, seperti ketokonazol dan itrakonazol (lihat bagian "**Obat-obatan lain dan Priligy**")
- Obat-obatan lain untuk HIV, seperti ritonarir, saquinavir, nelfinavir, dan atazanavir (lihat bagian "**Obat-obatan lain dan Priligy**")
- Antibiotik tertentu untuk mengobati infeksi, termasuk telitromisin (lihat bagian "O**bat-obatan lain dan Priligy**")
- Nefazodone - obat antidepresan (lihat bagian "**Obat-obatan lain dan Priligy**")

- Jika anda memiliki gangguan hati derajat sedang atau berat.

Jangan gunakan obat yang tertera diatas apabila anda memiliki satu dari kondisi diatas. Apabila anda tidak yakin, bicarakan dengan dokter atau apoteker anda sebelum anda menggunakan obat ini.

Peringatan dan dan pencegahan

Bicarakan dengan dokter, apoteker, atau perawat anda sebelum menggunakan Priligy apabila:

- Anda belum didiagnosis dengan ejakulasi dini
- Anda memiliki permasalahan seksual lain seperti disfungsi ereksi
- Anda memiliki riwayat pusing yang diakibatkan oleh tekanan darah rendah
- Anda menggunakan obat-obatan jenis narkoba seperti ekstasi, LSD, narkotika, atau benzodiazepine
- Anda meminum alkohol (lihat bagian "**Priligy dengan makanan, minuman, dan alkohol**")
- Anda pernah mengalami gangguan mental seperti depresi, mania (gejala termasuk perasaan semangat berlebih, mudah tersinggung, atau tidak dapat berpikir jernih), gangguan bipolar (gejala termasuk situasi perasaan yang beralih cepat dari mania dan depresi), atau skizofrenia (penyakit psikiatri)
- Anda memiliki epilepsy
- Anda memiliki riwayat perdarahan atau masalah pembekuan darah
- Anda memiliki gangguan ginjal
- Anda memiliki atau memiliki potensi tekanan bola mata yang tinggi (glaukoma).

Apabila anda memiliki salah satu dari kondisi diatas (atau apabila anda tidak yakin), komunikasikan pada dokter atau apoteker anda sebelum menggunakan obat ini.
Sebelum anda mulai menggunakan obat ini, dokter anda harus menjalankan sebuah tes untuk memastikan tekanan darah anda tidak turun terlalu banyak pada saat anda berdiri segera sesudah berbaring.

Anak-anak dan remaja

Obat ini sebaiknya tidak digunakan pada anak-anak dan remaja dibawah usia 18 tahun.

Obat-obatan lain dan Priligy

Beritahukan dokter atau apoteker anda apabila anda sedang, baru-baru ini, atau mungkin akan menggunakan obat-obatan lain. Obat-obatan lain ini termasuk obat yang anda peroleh tanpa resep, seperti obat-obatan herbal. Hal ini disebabkan karena Priligy dapat mempengaruhi cara kerja obat lain. Obat-obatan lain juga dapat mempengaruhi cara kerja Priligy. Karena itu, penggunakan obat-obatan lain dapat mempengaruhi dosis maksimum dari Priligy yang dapat anda konsumsi.

Jangan gunakan Priligy pada saat yang bersamaan dengan obat-obatan berikut ini:

- Obat-obatan untuk depresi golongan *'monoamine oxidase inhibitors' (MAOIs)*
- Thioridazine yang digunakan untuk skizofrenia

- Obat-obatan lain untuk depresi
- Litium - obat untuk gangguan bipolar
- Linezolid - antibiotik untuk mengobati infeksi
- Tryptophan - obat untuk membantu anda tidur
- St John‟s wort - obat herbal
- Tramadol - digunakan untuk mengobati nyeri hebat
- Obat-obatan yang digunakan untuk mengobati migrain.

Jangan gunakan Priligy pada saat bersamaan dengan obat-obatan lain yang tertera diatas Apabila anda telah mengkonsumsi obat-obatan tersebut diatas, anda harus menunggu 14 hari setelah berhenti minum obat sebelum dapat memulai penggunaan Priligy. Setelah anda berhenti menggunakan Priligy, anda harus menunggu selama 7 hari sebelum dapat menggunakan obat- obatan yang tersebut diatas. Apabila anda tidakyakin, komunikasikan pada dokter atau apoteker anda sebelum meggunakan obat ini.

- Obat-obatan tertentu untuk infeksi jamur, seperti ketokonazol dan itrakonazol
- Obat-obatan lain untuk HIV, seperti ritonavir, saquinavir, nelfinavir, dan atazanavir
- Antibiotik tertentu untuk mengobati infeksi, termasuk telitromisin
- Nefazodone - obat antidepresan.

Beritahukan dokter atau apoteker anda apabila anda sedang mengkonsumsi obat-obatan berikut ini:

- Obat-obatan untuk gangguan mental selain depresi
- Obat-obatan anti-inflamasi non-steroid seperti ibuprofen atau asam asetilsalisilat
- Obat-obatan untuk mengencerkan darah anda, seperti warfarin
- Obat-obatan tertentu untuk mengobati disfungsi ereksi seperti sildenafil, tadalafil, atau vardenafil, karena obat-obatan ini dapat menurunkan tekanan darah anda, terutama saat berdiri.
- Obat-obatan tertentu yang digunakan untuk mengobati tekanan darah tinggi dan nyeri dada (angina) (seperti verapamil dan diltiazem), atau pembesaran prostat, karena obat-obatan ini dapat menurunkan tekanan darah anda, terutama saat berdiri
- Obat-obatan tertentu untuk infeksi jamur seperti flukonazol
- Obat-obatan tertentu untuk HIV, seperti amprenavir dan fosamprenavir
- Obat-obatan antibiotik tertentu untuk mengobati infeksi, seperti eritromisin dan klaritromisin
- Aprepitant - dikonsumsi untuk mengobati mual.

Apabila anda tidak yakin apakah hal-hal diatas berlaku untuk anda, komunikasikan dengan dokter atau apoteker anda sebelum menggunakan obat ini.

Priligy dengan makanan, minuman dan alkohol.

- Jangan minum jus grapefruit dalam waktu 24 jam sebelum mengkonsumsi obat ini karena dapat meningkatkan jumlah obat dalam tubuh Anda. Obat ini dapat digunakan dengan atau tanpa makanan.
- Anda sebaiknya mengkonsumsi obat ini dengan setidaknya segelas air.
- Hindari alkohol saat menggunakan obat ini.
- Efek alkohol seperti pusing, mengantuk, reaksi lambat, dapat bertambah dengan penggunaan obat ini.
- Minum alkohol sambal mengkonsumsi obat ini dapat meningkatkan risiko luka akibat pingsan atau akibat efek samping lain.

Kehamilan, menyusui, dan fertilitas

Obat ini sebaiknya tidak dikonsumsi oleh wanita.

Mengemudi dan mengoperasikan alat berat

Anda dapat merasa mengantuk, pusing, lesu, kesulitan konsentrasi dan pandangan kabur dengan penggunaan obat ini. Apabila anda merasakan salah satu dari yang tersebut diatas atau efek samping yang mirip, anda sebaiknya menghindari mengemudi atau mengoperasikan alat berbahaya. Efek alkohol dapat meningkat apabila digunakan bersamaan dengan obat ini dan anda memiliki risiko yang lebih tinggi untuk menderita luka akibat pingsan atau akibat efek samping lain apabila anda menggunakan obat ini bersamaan dengan alkohol.

Priligy mengandung laktosa

Obat ini mengandung laktosa (sejenis gula). Apabila anda telah diberitahukan oleh dokter anda bahwa anda mengidap intoleransi terhadap beberapa jenis gula, hubungi dokter anda sebelum menggunakan obat ini.

3. Bagaimana cara mengkonsumsi Priligy

Selalu gunakan obat ini sesuai dengan petunjuk dokter atau apoteker anda. Periksa dengan dokter atau apoteker anda apabila anda tidak yakin.

- Dosis yang direkomendasikan adalah 30 mg. Dokter anda dapat meningkatkan dosis hingga 60 mg.
- Gunakan obat hanya dalam rentang 1 sampai 3 jam menjelang aktifitas seksual.
- **Jangan gunakan obat ini lebih dari sekali dalam 24 jam / setiap hari.**
- Telan tablet seutuhnya untuk menghindari rasa pahit dengan setidaknya segelas air. Hal ini dapat membantu menurunkan risiko pingsan (lihat “Pingsan dan tekanan darah rendah” pada bagian 4).
- Obat ini dapat digunakan dengan atau tanpa makanan.
- Obat ini tidak untuk digunakan pria di bawah usai 18 tahun atau diatas usia 65 tahun
- Diskusikan pengobatan Priligy anda dengan dokter setelah pengobatan selama 4 minggu atau setelah 6 dosis untuk melihat apakah anda perlu melanjutkan pengobatan. Apabila pengobatan dilanjutkan, anda harus berkonsultasi dengan dokter anda setidaknya setiap enam bulan.

Apabila anda mengkonsumsi Priligy lebih banyak dari yang seharusnya

Beritahukan dokter atau apoteker anda bila anda telah mengkonsumsi tablet Priligy lebih banyak dari yang seharusnya. Anda dapat merasa sakit atau akan sakit.

Apabila anda berhenti menggunakan Priligy

Beritahukan dokter sebelum anda menghentikan penggunakan obat ini. Anda mungkin mengalami masalah sulit tidur atau merasa pusing setelah menghentikan penggunakan obat ini, meskipun anda tidak menggunakan obat ini setiap hari.
Apabila anda memiliki pertanyaan lebih lanjut mengenai penggunaan obat ini, tanyakan pada dokter, apoteker atau perawat anda.

4. Efek samping yang mungkin terjadi

Seperti semua obat, Priligy dapat menyebabkan efek samping, meskipun tidak semua orang mengalaminya.

Hentikan penggunaan Priligy dan temui dokter anda segera apabila:

- Anda mengalami kejang

- Anda pingsan atau merasa berkunang-kunang saat berdiri
- Anda merasakan perubahan suasana hati
- Anda memiliki pikiran untuk bunuh diri atau melukai diri sendiri.

Jika anda mengalami hal-hal diatas, hentikan penggunaan obat ini dan temui dokter anda segera.

Pingsan dan tekanan darah rendah

Obat ini dapat membuat anda pingsan atau menurukan tekanan darah anda secara tiba-tiba saat anda berdiri.
Untuk membantu menurunkan risiko kejadian ini:

- Konsumsi obat ini dengan setidaknya segelas air.
- Jangan gunakan obat ini apabila anda dehidrasi (anda tidak memiliki air yang cukup dalam tubuh anda).

Hal ini dapat terjadi jika:

- Anda tidak minum dalam 4-6 jam terakhir
- Anda telah berkeringat dalam jangka waktu yang lama
- Anda memiliki penyakit dimana anda memiliki temperatur tubuh yang tinggi, diare, atau sedang sakit

- Apabila anda merasa akan pingsan (seperti rasa tidak enak badan, pusing, berkunang-kunang, bingung, berkeringat, denyut jantung tidak normal), atau merasa berkunang-kunang saat anda berdiri, segera berbaring sehingga kepala anda berada dalam posisi yang lebih rendah dari tubuh anda atau duduk dengan kepala anda diantara kedua lutut anda sampai anda merasa lebih baik. Hal ini dapat menghentikan anda jatuh atau terluka akibat pingsan.
- Jangan berdiri terlalu cepat setelah periode duduk atau berbaring yang cukup lama.
- Jangan mengemudi atau mengoperasikan mesin atau alat-alat lain apabila anda merasa seperti ingin pingsan saat penggunaan obat ini.
- **Beritahukan dokter anda apabila anda merasa seperti ingin pingsan saat menggunakan obat ini.**

Efek samping yang sangat sering (mempengaruhi lebih dari 1 dari 10 orang):

- Pusing
- Sakit kepala
- Rasa tidak enak badan.

Efek samping sering (mempengaruhi maksimal sampai 1 dari 10 orang):

- Rasa mudah teriritasi, gelisah, mudah marah, tidak tenang
- Rasa kebas atau kesemutan
- Kesulitan mengalami atau mempertahankan ereksi
- Berkeringat lebih banyak atau muka merah
- Diare, konstipasi, atau sering buang angin
- Nyeri perut, kembung, atau merasa tidak enak badan
- Masalah tidur atau mimpi yang aneh
- Rasa lelah atau mengantuk, sering menguap
- Hidung tersumbat
- Peningkatan tekanan darah
- Kesulitan konsentrasi
- Gemetar
- Gairah seks kurang
- Telinga berdenging
- Pandangan kabur
- Gangguan pencernaan
- Mulut kering.

Efek samping tidak sering (mempengaruhi maksimal sampai 1 dari 100 orang):

- Pingsan atau pusing saat berdiri (lihat nasihat diatas)
- Perubahan suasana hati, rasa semangat berlebih atau paranoia
- Rasa bingung, disorientasi, atau tidak dapat berpikir jernih
- Ritme jantung melambat, irregular, atau meningkat
- Hilangnya dorongan seksual, masalah mencapai orgasme
- Rasa lemas, mengantuk, letargi atau tidak bertenaga
- Rasa depresi, takut, atau acuh tak acuh
- Rasa panas, gelisah, abnormal atau mabuk
- Gangguan penglihatan, nyeri pada mata, atau dilatasi pupil
- Tekanan darah tinggi atau rendah
- Rasa gatal atau keringat dingin
- Rasa berputar
- Rasa abnormal di lidah
- Gigi gemerutuk.

Efek samping jarang (mempengaruhi maksimal sampai 1 dari 1,000 orang):

- Rasa pusing setelah ejakulasi
- Keingingan tidur yang timbul tiba-tiba
- Dorongan buang air besar tiba-tiba.

Pelaporan efek samping

Apabila anda mengalami efek samping, bicarakan dengan dokter, apoteker, atau perawat anda. Hal ini termasuk efek samping lain yang tidak tercantum dalam lembaran ini.
Anda juga dapat melaporkan efek samping secara langsung melalui sistem pelaporan nasional yang dapat dilihat pada Appendix V. Anda dapat juga melaporkan keluhan efek samping atau kondisi tidak nyaman tersebut secara langsung ke Industri Farmasi melalui kontak berikut:
Idn.ae@menariniapac.com
Dengan melaporkan efek samping, anda membantu memperbanyak informasi tentang keamanan obat ini.

5. Bagaimana cara penyimpanan Priligy

- Simpan obat di bawah suhu 30^{o}C.
- Simpan obat ini jauh dari jarak pandang dan jangkauan anak-anak.
- Jangan gunakan obat ini setelah melampaui tanggal kadaluarsa yang tertera pada karton setelah EXP. Tanggal kadaluarsa yang dimaksud adalah tanggal terakhir dari bulan yang tercantum
- Jangan buang obat apapun melalui saluran air atau pembuangan sampah rumah tangga. Tanyakan apoteker anda bagaimana cara pembuangan obat yang sudah tidak anda pakai lagi. Perilaku ini membantu perlindungan lingkungan hidup.

6. Isi paket dan informasi lainnya

Apa yang dikandung Priligy

Bahan aktif Priligy adalah dapoxetine. Setiap tablet mengandung 30 mg atau 60 mg dapoxetine sebagai garam hidroklorida.

Bahan lainnya:

- Inti tablet: *lactose monohydrate, microcrystalline cellulose, croscarmellose sodium, colloidal anhydrous silica, magnesium stearate.*

- Selaput tablet: *lactose monohydrate, hypromellose, titanium dioxide (E171), triacetin, Iron Oxide Black (E172), Iron Oxide Yellow (E172).*

Bagaimana penampilan Priligy dan isi dari kemasan

- Priligy 30 mg tablet salut selaput berwarna abu-abu muda, bundar, konveks, berdiameter 6.5 mm dengan tulisan emboss "30" dalam segitiga pada salah satu sisinya.
- Priligy 60 mg tablet salut selaput berwarna abu-abu, bundar, konveks, berdiameter 8 mm dengan tulisan emboss "60" dalam segitiga pada salah satu sisinya.

Tablet tersedia dalam kemasan blister berisi 3 dan 6 tablet salut selaput.

Diimpor oleh:

PT. Menarini Indria Laboratories, Bekasi, Indonesia

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