Amber with Guidance (Amber-G) = To be recommended or initiated by a specialist with follow up prescribing and monitoring by primary care clinicians.*
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NHS Barnsley Hospital NHS Foundation Trust | NHS South West Yorkshire Partnership NHS Foundation Trust | NHS South Yorkshire Integrated Care Board

Dapoxetine Amber G Guidance

The details of side-effects, cautions, contraindications and interactions are not a complete list and the current BNF (https://www.medicinescomplete.com/#/) and the SPC (https://www.medicines.org.uk/emc/) remain authoritative.

Background Information	Dapoxetine should be initiated or recommended by a specialist in premature ejaculation in males aged 18 to 64 years
BNF therapeutic class	7.4.2: Erectile and ejaculatory conditions; premature ejaculation
Indication	**Indication** Dapoxetine (Priligy®) is licensed for the treatment of premature ejaculation (PE) in adult men aged 18 to 64 years. Dapoxetine should only be prescribed to patients who meet all the following criteria: • An intravaginal ejaculatory latency time (IELT) of less than two minutes; and • 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; and • A history of premature ejaculation in the majority of intercourse attempts over the prior 6 months. Dapoxetine should be administered only as **on-demand treatment** before anticipated sexual activity. Dapoxetine should not be prescribed to delay ejaculation in men who have not been diagnosed with PE. **Mechanism of action** Dapoxetine is a short-acting selective serotonin-reuptake inhibitor (SSRI). 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.
Dosage and administration	**Adult men (aged 18 to 64 years)** The recommended starting dose for all patients is 30 mg, taken as needed approximately 1 to 3 hours prior to sexual activity. ***Treatment with Dapoxetine should not be initiated with the 60 mg dose.*** Dapoxetine is not intended for continuous daily use. Dapoxetine should be taken only when sexual activity is anticipated. Dapoxetine must not be taken more frequently than once every 24 hours. If the individual response to 30 mg is insufficient and the patient has not experienced moderate or severe adverse reactions or prodromal symptoms suggestive of syncope, the dose may be increased to a maximum recommended dose of 60 mg taken as needed approximately 1 to 3 hours prior to sexual activity. The incidence and severity of adverse events is higher with the 60 mg dose. If the patient experiences orthostatic reactions on the starting dose, no dose escalation to 60 mg should be performed. **Method of administration** Dapoxetine is available as 30mg and 60mg tablets for oral use. Tablets should be swallowed whole to avoid the bitter taste (do not chew or crush). It is recommended that tablets be taken with at least one full glass of water. Dapoxetine may be taken with or without food ***Refer to monitoring requirements below for information on duration of use.***

Quantity to prescribe	***Up to 6 doses every 1 -2 months is recommended for the majority of patients. (It is more cost-effective to supply one box of 6 tablets rather than 2 boxes of 3 tablets).***
Contra-indications	Hypersensitivity to the active substance or to any of the excipients *(refer to SPC)* Significant pathological cardiac conditions such as: • Heart failure (NYHA class II-IV) • Conduction abnormalities such as AV block or sick sinus syndrome • Significant ischemic heart disease • Significant valvular disease • A history of syncope or postural hypotension A history of mania, bipolar disorder or severe depression. Uncontrolled epilepsy. 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 dapoxetine has been discontinued. Concomitant treatment with **thioridazine**, or within 14 days of discontinuing treatment with thioridazine. Similarly, thioridazine should not be administered within 7 days after dapoxetine has been discontinued. 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 dapoxetine has been discontinued. Concomitant treatment of **potent CYP3A4 inhibitors** such as ketoconazole, itraconazole, ritonavir, saquinavir, telithromycin, nefazadone, nelfinavir, atazanavir, etc. Moderate and severe hepatic impairment.
Cautions	**Other forms of sexual dysfunction** Before treatment, subjects with other forms of sexual dysfunction, including erectile dysfunction, should be carefully investigated by physicians. **Orthostatic hypotension (postural hypotension)** Before treatment initiation, a careful medical examination including history of orthostatic events should be performed by the physician. An orthostatic test should be performed before initiating therapy (blood pressure and pulse rate, supine and standing). In case of a history of documented or suspected orthostatic reaction, treatment with dapoxetine should be avoided. **Syncope** *(refer to adverse drug reactions and patient counselling below)* **Patients with cardiovascular risk factors** Syncope has been reported with dapoxetine *(refer to adverse drug reactions and patient counselling below)*. 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 cardiovascular disease. **Mania** Dapoxetine 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, dapoxetine should be discontinued in any patient who develops seizures and avoided in patients with unstable epilepsy. Patients with controlled epilepsy should be carefully monitored. **Depression and/or psychiatric disorders** Men with underlying signs and symptoms of depression should be evaluated prior to treatment with dapoxetine to rule out undiagnosed depressive disorders. Concomitant treatment of dapoxetine with antidepressants, including SSRIs and SNRIs, is contraindicated. Discontinuation of treatment for ongoing depression or anxiety in order to initiate dapoxetine for the treatment of PE is not recommended. Dapoxetine 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, dapoxetine should be discontinued. **Haemorrhage** There have been reports of bleeding abnormalities with SSRIs. Caution is advised in patients with a history of bleeding or coagulation disorders. *(Refer to interactions section; medicinal products affecting platelet function and anticoagulants)* **Renal impairment** Dapoxetine is not recommended for use in patients with severe renal impairment (CrCL < 30 mL/min). and caution is advised in patients with mild or moderate renal impairment (CrCL 30–80 mL/min). **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. Dapoxetine has shown mild withdrawal symptoms with a slightly higher incidence of insomnia and dizziness in subjects switched to placebo after daily dosing. **Eye disorders** The use of dapoxetine has been associated with ocular effects such as mydriasis and eye pain. Dapoxetine should be used with caution in patients with raised intraocular pressure or those at risk of angle closure glaucoma. **Lactose intolerance** Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine. Dapoxetine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium free'
Pregnancy and breast feeding	Dapoxetine is not indicated for use by women. Animal studies do not indicate direct or indirect harmful effects with respect to fertility, pregnancy or embryonal/foetal development. It is not known if either dapoxetine or its metabolites are excreted in human milk.
Adverse Drug Reactions	**Very common (>1/10)** Dizziness, Headache, Nausea **Common (≥ 1/100 to < 1/10)** Anxiety, Agitation, Restlessness, Insomnia, Abnormal dreams, Libido decreased, Tremor, Paraesthesia, Somnolence, Disturbance in attention, Blurred vision, Tinnitus,

	Flushing, Sinus congestion, Yawning, Diarrhoea, Vomiting, Constipation. Abdominal pain, Dyspepsia, Flatulence, Stomach discomfort, Abdominal distention, Dry mouth, Hyperhidrosis, Erectile Dysfunction, Fatigue, Irritability or Increased blood pressure. **Uncommon (≥ 1/1000 to < 1/100)** Include syncope*, postural dizziness, hypotension Orthostatic hypotension as been reported in clinical trials. **In the clinical trials, cases of syncope characterized as loss of consciousness, with bradycardia or sinus arrest observed in patients wearing Holter monitors, 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.* Serious adverse reactions should be reported to the MHRA via the Yellow Card scheme: https://yellowcard.mhra.gov.uk/
Monitoring	**Specialist monitoring** Test for orthostatic (postural) hypotension before starting treatment *(see cautions above).* **Monitoring in primary care** • Patient should have a follow up appointment in primary care 4 weeks after commencing dapoxetine (or at least after 6 doses of treatment) to determine whether continuing treatment is appropriate (careful appraisal of individual benefit risk). • Patient should be reviewed in primary care every 6 months to ensure the treatment is still appropriate. Data regarding the efficacy and safety of Dapoxetine beyond 24 weeks are limited. The clinical need of continuing and the benefit risk balance of treatment with dapoxetine should be re-evaluated.
Interactions	***Refer to contraindications above.*** **Use with recreational drugs** Patients should be advised not to use dapoxetine 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 dapoxetine. Use of dapoxetine with recreational drugs with sedative properties such as narcotics and benzodiazepines may further increase somnolence and dizziness. **Ethanol** Combining alcohol with dapoxetine 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 dapoxetine. **Medicinal products with vasodilatation properties** Dapoxetine should be prescribed with caution in patients taking medicinal products with vasodilatation properties (such as alpha adrenergic receptor antagonists and nitrates) due to possible reduced orthostatic tolerance. **Moderate CYP3A4 inhibitors** Caution is advised in patients taking moderate CYP3A4 inhibitors and the dose is restricted to 30 mg. Concomitant treatment with moderate CYP3A4 inhibitors (e.g., erythromycin, clarithromycin, fluconazole, amprenavir, fosamprenavir, aprepitant, verapamil, diltiazem) may give rise to significantly increased exposure of dapoxetine and

	desmethyldapoxetine, especially in CYP2D6 poor metabolizers. The maximum dose of dapoxetine should be 30 mg if dapoxetine is combined with any of these drugs. **Potent CYP2D6 inhibitors** Caution is advised if increasing the dose to 60 mg in patients taking potent CYP2D6 inhibitors or if increasing the dose to 60 mg in patients known to be of CYP2D6 poor metabolizer genotype, as this may increase exposure levels, which may result in a higher incidence and severity of dose dependent adverse events. **Medicinal products affecting platelet function and anticoagulants** There have been reports of bleeding abnormalities with SSRIs. Caution is advised in patients taking dapoxetine, 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). **PDE5 inhibitors** Dapoxetine should not be used in men with erectile dysfunction (ED) who are using PDE5 inhibitors (possible reduced orthostatic tolerance).
Additional information	**Patient Counselling** • Due to the possibility of orthostatic (postural) hypotension, 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. • Patients need to be made aware that they could experience syncope at any time with or without prodromal symptoms during their treatment with dapoxetine. Prescribers should counsel patients about the importance of maintaining adequate hydration and about how to recognise 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 (dizziness, lightheadedness), 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 its prodromal symptoms occur. • Patients should be advised not to use dapoxetine in combination with alcohol. • Grapefruit juice (potent CYP3A4 inhibitor) should be avoided within 24 hours prior to taking dapoxetine. **Treatment cessation** The dose should preferably be reduced gradually over about 4 weeks, or longer if withdrawal symptoms emerge (6 months in patients who have been on long-term maintenance treatment).

Contact names and details

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References

1. Priligy® 30mg film-coated tablets SPC. Available at: https://www.medicines.org.uk/emc/product/1269/smpc Accessed <12.07.22>
2. BNF Dapoxetine. Available at: https://www.medicinescomplete.com/#/content/bnf/_598547509?hspl=dapoxetine Accessed <12.07.22>

https://www.england.nhs.uk/wp-content/uploads/2018/03/responsibility-prescribing-between-primary-secondary-care-v2.pdf

Development Process

This guidance has been produced following an AMBER-G classification status of Dapoxetine by the Barnsley Area Prescribing Committee. This guideline was ratified by the Area Prescribing Committee on 12th October 2022.