Erectile Dysfunction (ED) - Prescribing guidelines in primary care for adults aged 18 years and above

Key messages

- Lifestyle changes should be discussed, and psychosexual causes explored before pharmacological treatments are considered for ED. Management of comorbidities should be optimised (e.g. diabetes, cardiovascular disease).
- Consider whether the patient may be suffering from medication-induced ED.
- Phosphodiesterase-5 (PDE-5) inhibitors have no effect in the treatment of ED in the absence of sexual stimulation.
- Prescribe **generic sildenafil** (when required frequency - PRN) or if treatment with sildenafil is not tolerated/ ineffective/contraindicated and the patient fulfils Selected List Scheme (SLS) criteria, prescribe **generic tadalafil** (when required frequency - PRN) as the first choice oral PDE-5 inhibitors for ED.
- In general, PDE-5 inhibitors are prescribed as one treatment dose per week on the NHS. However, for men who prefer spontaneous (rather than planned) sexual activity, or who anticipate frequent sexual activity (at least twice a week), daily tadalafil 5mg can be considered.
- If a patient cannot tolerate tadalafil 5 mg once daily, they should be switched back to a PRN regimen (sildenafil or tadalafil). Splitting tablets is unlicensed use and is not advised. 2.5mg tadalafil tablets are **non-formulary** across SWL.
- Advise patients on the availability of Over the Counter (OTC) sildenafil and tadalafil products to purchase from pharmacies.
    - ED medications are amongst the most counterfeited medicines in Europe.
    - Buying online should only be through legitimate sources e.g., pharmacies registered with the General Pharmaceutical Council (GPhC).
- Review the prescribing of PDE-5 inhibitors for the treatment of ED:
    - Arrange follow-up 6–8 weeks after initiation of treatment to assess the efficacy and safety of the treatment as well as patient satisfaction.
    - Patients prescribed other PDE-5 inhibitors should be reviewed to replace treatment with generic sildenafil or tadalafil where appropriate.
- Change existing patients prescribed Cialis® to generic tadalafil 5mg once daily, 10mg or 20mg PRN (Cialis® is on average 33 times more expensive than generic tadalafil).
- All other oral PDE-5 inhibitors (avanafil and vardenafil) are **non-formulary** across NHS SWL.

- For information on contraindications, cautions, dosing information and side effects please refer to the SPCs/BNF.
- A patient with ED should receive 4-8 doses of a PDE-5 inhibitor with sexual stimulation at a maximum dose before being classified as a non-responder/oral treatment deemed ineffective.
- If failed response to 2 oral PDE-5 inhibitors, refer to alternative treatment options (specialist recommendation only).

ED treatment pathway

Confirm diagnosis of Erectile Dysfunction in adults aged 18 years and above

- Assess for causative factors, offer lifestyle advice and assess cardiac risk.
- Management of comorbidities should be optimised.

Prescribe generic sildenafil or tadalafil on FP10

- Usual starting dose of sildenafil is 50mg PRN, increasing to 100mg if ineffective or decreasing to 25mg where clinically appropriate.
- If treatment with sildenafil is not tolerated/ ineffective/contraindicated and the patient fulfils Selected List Scheme (SLS) criteria, prescribe generic tadalafil (when required frequency - PRN).
- Usual starting dose of tadalafil is 10mg PRN, increasing to 20mg if ineffective. For men who prefer spontaneous (rather than planned) sexual activity, or who anticipate frequent sexual activity (at least twice a week), daily tadalafil 5mg can be considered.
- Refer to SPC for full dosing information, contraindications, and drug interactions.
- Advice on recommended quantity to supply can be found here.

Follow up treatment 6-8 weeks after initiation

- If treatment is tolerated and effective (a patient should receive 4-8 doses of a PDE-5 inhibitor at a maximum tolerated dose with sexual stimulation before treatment is classified as non-effective), continue with treatment on an FP10.
- Note, all treatments for ED (except generic sildenafil) require an SLS endorsement to be prescribed on the NHS.
- If SLS criteria is not met, offer a private prescription for an alternative ED treatment.
- A patient should trial at least two different PDE-5 inhibitors taken sequentially before being classed as a 'non-responder' (trialling each PDE-5 inhibitor for 4-8 doses at a maximum tolerated dose with sexual stimulation before switching to an alternative drug).

If treatment failure on 2 oral PDE-5 inhibitors, consider alternate therapy options (specialist recommendation only)

Topical preparations:

These have an Amber 1 prescribing status i.e., primary care initiation, on the recommendation of a specialist.

- **Alprostadil transurethral application:**
  - **MUSE®** urethral sticks
  - **Vitaros®** cream

Vacuum erectile dysfunction pump:

These have an Amber 1 prescribing status i.e., primary care initiation, on the recommendation of a specialist.

- Initial pump training to be provided to the patient by the Acute Trust recommending the device. Training is provided by the supplier.
- Specialist recommending the initiation of the device must communicate clearly in writing to the patients GP what product is to be prescribed.
- Only devices included in the Drug Tariff are to be recommended for patients fulfilling SLS criteria.
- Patients who do not fulfil the SLS criteria will have to purchase the device privately.

Injectable preparations

These are Amber 2 prescribing status i.e., secondary care initiation with continuation in primary care* (or via specialist primary care services where available):

- **Alprostadil intracavernosal injection:**
  - **Caverject® Dual Chamber:** 10 & 20 microgram injections
  - **Viridal Duo®:** 10, 20 & 40 microgram injections

- **Aviptadil with phentolamine mesylate** is reserved for patients who cannot use intracavernosal alprostadil due to pain, OR supply issues OR no response from 40mcg alprostadil:
  - **Invicorp®:** 25micrograms/2mg/0.35ml solution for injection ampoules

* Injectable devices are to be initiated and supplied in secondary care. GPs can continue prescribing in primary care if treatment is deemed effective after 1 month. Initial sharps bin to be provided by secondary care, ongoing sharps bins can be provided in the community.

Visual summary flow chart of ED treatment pathway

Confirm diagnosis of Erectile Dysfunction in adults over 18 years old
Assess for causative factors, offer lifestyle advice & assess cardiac risk. Management of comorbidities should be optimised.

***Note**: All treatments for ED (except generic sildenafil) require an **SLS** endorsement to be prescribed on the NHS.

Does patient fulfil SLS* criteria?

NO

Offer generic sildenafil or offer private prescription for alternate ED treatments.

YES

Prescribe generic Sildenafil OR Tadalafil on FP10

Sildenafil:

- Usual starting dose is 50mg when required (PRN), increasing to 100mg if ineffective or decreasing to 25mg where clinically appropriate.
  Refer to SPC for full dosing information, contraindications, and drug interactions
- Advice on recommended quantity to supply can be found here.
- **Generic sildenafil does not require SLS** endorsement to be prescribed on NHS

Tadalafil:

- Usual starting dose is 10mg PRN; increase to 20mg if ineffective.
- For men who prefer spontaneous (rather than planned) sexual activity, or who anticipate frequent sexual activity (at least twice a week), daily tadalafil 5mg can be considered.
- Refer to SPC for full dosing information contraindications, and drug interactions.
- Advice on recommended quantity to supply can be found here.

Follow up after 6-8 weeks
Is treatment effective* and tolerated?
*(*A patient should receive 4-8 doses of a PDE-5 inhibitor at a maximum tolerated dose with sexual stimulation before treatment is classified as non-effective)*

Is treatment effective?

NO

YES

Maintain generic sildenafil/tadalafil* treatment on FP10
(*A private prescription is required for tadalafil if SLS criteria not met.)

Trial alternate PDE-5 inhibitor
A patient should trial at least two different PDE-5 inhibitors taken sequentially before being classed as a 'non-responder' (trialling each PDE-5 inhibitor for 4-8 doses at a maximum tolerated dose with sexual stimulation before switching to an alternative drug).

If treatment failure on 2 oral PDE-5 inhibitors, seek specialist advice for alternate therapy options

Specialist recommendation only

PRIMARY CARE INITIATION (following specialist recommendation)
Alprostadil transurethral application-Amber 1⁺;

- **MUSE®** urethral sticks
- **Vitaros®** cream

Vacuum erectile dysfunction pump-Amber 1⁺:
Initial pump training to be provided for the patient at the Acute Trust recommending the device. Training is provided by the supplier. Specialist recommending the initiation of the device must communicate clearly in writing to the patients GP what product is to be prescribed. Only devices included in the Drug Tariff are to be recommended for patients fulfilling SLS criteria. Patients who do not fulfil the SLS criteria will have to purchase the device privately.

SECONDARY CARE INITIATION (or via specialist primary care services where available)
Injectable devices are to be initiated and supplied in secondary care. GPs can continue prescribing in primary care if treatment is deemed effective after 1 month. Initial sharps bin to be provided by secondary care, ongoing sharps bins can be provided in community.
Alprostadil intracavernosal injection-Amber 2⁺:

- **Caverject® Dual Chamber:** 10 & 20 microgram injections
- **Viridal Duo®:** 10, 20 & 40 microgram injections

Aviptadil with phentolamine mesylate-Amber 2⁺:

- **Invicorp®**:** 25micrograms/2mg/0.35ml solution for injection ampoules

**Treatment with Invicorp® is reserved for patients who cannot use intracavernosal alprostadil due to pain, OR supply issues OR no response from 40mcg alprostadil.

⁺Key:

AMBER
1. Recommendation by a specialist but is considered non urgent and therefore could be started in primary care.

AMBER 2: Initiation by a specialist, stabilisation for a specified time, then continuation in primary care under an individual management plan.

Prescribing information

NHS SWL supports the prescribing of the following oral PDE-5 inhibitors for ED only:

- Generic sildenafil 50mg PRN (based on efficacy and tolerability, the dose may be increased to 100mg or decreased to 25mg).
- Generic tadalafil 10mg PRN (based on efficacy and tolerability, this can be increased to the maximum dose of 20mg).
- Generic tadalafil 5mg daily for men who prefer spontaneous (rather than planned) sexual activity, or who anticipate frequent sexual activity (at least twice a week).
- Change existing patients prescribed Cialis® to generic tadalafil 5mg once daily, 10mg or 20mg PRN (Cialis® is on average 33 times more expensive than generic tadalafil).
- If a patient cannot tolerate tadalafil 5 mg once daily, they should be switched back to a PRN regimen (sildenafil or tadalafil). Splitting tablets is unlicensed use and is not advised. 2.5mg tadalafil tablets are non-formulary across SWL.
- All other oral PDE-5 inhibitors (avanafil and vardenafil) are **non-formulary** in SWL.

Refer to a specialist if treatment failure on 2 different oral PDE-5 inhibitors for consideration of alternative treatment options (a patient should trial at least two different PDE-5 inhibitors taken sequentially before being classed as a 'non-responder'. Each PDE-5 inhibitor should be trialled for 4-8 doses at a maximum tolerated dose with sexual stimulation before switching to an alternative drug).

Selected List Scheme (SLS)

Prescribing of drugs for ED is restricted nationally under the SLS on the grounds of cost to the NHS. If a patient has any of the following conditions, they fulfil SLS criteria and can be treated for ED on an NHS prescription:

- Diabetes, multiple sclerosis, Parkinson's disease, poliomyelitis, prostate cancer, severe pelvic injury, single gene neurological disorder, spina bifida, spinal cord injury, receiving treatment for renal failure by dialysis, a man who has had the following surgery - prostatectomy, radical pelvic surgery or renal failure treated by transplant.

All treatments for ED (except generic sildenafil) require an SLS endorsement to be prescribed on the NHS.

Offer a private prescription if the patient does not fulfil SLS criteria for branded sildenafil (Viagra®) or generic/branded tadalafil (Cialis®).

For further information on SLS, refer to Part XVIIIB of the Drug Tariff.

Private prescriptions

- Generic sildenafil cannot be prescribed privately for any NHS patients using it for ED.

- Other ED medication cannot be prescribed privately for NHS patients with ED that fulfil SLS criteria.
- PDE-5 inhibitors can be prescribed privately for patients that **do not** fulfil the SLS criteria.

Quantity

Generally, for most patients it is recommended that the quantity prescribed is 4 tablets per month for ED (Department of Health [DoH] recommendation).

- All patients should be offered a trial of 4 doses of a PDE-5 inhibitor unless contraindicated.
- 4 tablets a month is deemed to provide an equitable quantity with respect to the population needs.
- This advice is based on research by the DoH on impotence about the frequency of sexual intercourse which showed that for the average 40-60 age range this is once a week.
- Prescribers should be aware of the risks of excessive prescribing which can lead to unlicensed, unauthorised, diversion of supply (PDE-5 inhibitors have "street value") and/or possible dangerous use.
- However, if the prescriber in exercising their clinical judgement considers that more than one treatment a week is appropriate, then the prescriber can prescribe that amount on the NHS.
- If a patient prefers spontaneous (rather than planned) sexual activity, or who anticipate frequent sexual activity (at least twice a week), daily tadalafil 5mg can be considered.

Daily Tadalafil

In line with the updated guidance NHS England Items which should not routinely be prescribed in primary care, the prescribing of daily tadalafil 5mg is permitted across NHS SWL. Daily tadalafil tablets 2.5mg are non-formulary and should not be prescribed.

- Once daily tadalafil was included in the 2017 and 2019 versions of the guidance. At that time, it was much more expensive than the equally clinically effective "as required" formulation.
- Once daily tadalafil is a safe, effective medicine and its price is now comparable with the "as required" formulation.
- Daily tadalafil 5mg can be considered for men who prefer spontaneous (rather than planned) sexual activity, or who anticipate frequent sexual activity (at least twice a week).
- If a patient cannot tolerate tadalafil 5 mg once daily, they should be switched back to a PRN regimen (sildenafil or tadalafil). Splitting tablets is unlicensed use and is not advised. 2.5mg tadalafil tablets are non-formulary across SWL.

Contraindications and Cautions

Contraindications

Do **not** prescribe a PDE-5 inhibitor to patients with any of the following co-morbidities:

- Hypotension (systolic BP<90/50 mmHg)
- Loss of vision in 1 eye due to non-arteritic anterior ischaemic optic neuropathy (NAION)
- Recent MI (within past 90 days)
- Recent stroke (within past 6 months)
- Severe/unstable heart disease (vasodilation/sexual activity not recommended)
- Taking nitrate medications
- Unstable angina/angina during sexual intercourse
- Hereditary degenerative retinal disorders*
- Severe hepatic impairment*
- New York Heart Association (NYHA) class II or greater heart failure (within the last 6 months)**
- Uncontrolled arrhythmias**
- Uncontrolled hypertension**
- *Sildenafil only
- **Tadalafil only

Cautions

For a full list of cautions and contraindications please refer to individual SPCs.

Prescribe a PDE-5 inhibitor **with caution** to a patient with any of the following co-morbidities:

- Cardiovascular disease. Consider the potential cardiac risk of sexual activity in men with pre-existing cardiovascular disease before prescribing a PDE-5 inhibitor. Refer to NICE CKS Cardiac risk stratification section for further information.
- Left ventricular outflow obstruction (for example aortic stenosis and idiopathic hypertrophic subaortic stenosis).
- Anatomical deformation of the penis (for example angulation, cavernosal fibrosis, or Peyronie's disease).
- A predisposition to priapism (for example in sickle-cell disease, multiple myeloma, or leukaemia).
- Prescribe sildenafil with caution to men with active peptic ulceration or bleeding disorders.

Drug interactions

Most common drug interactions

For a full list of interactions and contraindications please refer to individual SPCs.

- **Nitrates** — GTN, isosorbide mononitrate, or isosorbide dinitrate, nicorandil, or

amyl nitrate ('poppers' used for recreation) are absolutely contraindicated.

- **Alpha-blockers** — can increase the risk of postural hypotension as both are vasodilators.
- **Cytochrome P450 (CYP) 3A4 and 2C9 inhibitors** (e.g. ritonavir, ketoconazole, itraconazole, erythromycin, cimetidine, and grapefruit juice) - co-administration should be avoided if possible.
- **CYP3A4 inducers** (e.g. rifampicin, phenobarbital, phenytoin, and carbamazepine) - co-administration should be avoided if possible.

Common adverse effects

For a full list of adverse effects please refer to individual SPCs.

- Back pain, dizziness, dyspepsia, flushing, migraine, myalgia, nasal congestion, nausea, and vomiting.

Drugs which can cause ED

- **Diuretics**: Thiazides (for example bendroflumethiazide), spironolactone
- **Antihypertensives**: Methyldopa, clonidine, beta-blockers (for example propranolol), verapamil
- **Fibrates**: Clofibrate, gemfibrozil
- **Antipsychotics**: Phenothiazines (for example chlorpromazine), butyrophenones (for example haloperidol)
- **Antidepressants**: TCAs (e.g. amitriptyline), MAOIs (e.g. phenelzine), SSRIs(e.g. fluoxetine), lithium
- **Hormones**: Oestrogens, progesterone, corticosteroids, cyproterone acetate, 5-alpha reductase inhibitors (e.g. finasteride)
- **Cytotoxics:** Cyclophosphamide, methotrexate
- **Recreational drugs**: Alcohol, tobacco, cannabis
- **Histamine antagonists**: Cimetidine, ranitidine
- **Anti-arrhythmics & anticonvulsants**: Disopyramide, carbamazepine

Patient advice

Around 30 - 35% of men fail to respond to initial treatment with PDE-5 inhibitors largely due to inadequate counselling and unrealistic expectations. Therefore, advise patients of the following:

- ED usually responds well to a combination of lifestyle changes and drug treatment.
- Lifestyle changes include (where applicable) losing weight, reducing stress, stopping smoking, reducing alcohol consumption, stopping illicit drug use and increasing exercise.
- Counsel patients on possible side effects including headache, flushing (common), visual disturbance, and priapism (very rare).
- Advise patients to not stop taking prescribed medication unless instructed to by a healthcare professional.
- Advise patients not to take unlicensed herbal remedies for ED. They could

contain prescription-only medicines which may be contraindicated or interact with prescribed medication.
- Advise patients that there is a delay in onset of action with PDE-5 inhibitors and sexual stimulation is required.

Sildenafil

- To be taken 1 hour before sexual activity.
- Takes 30-120 minutes (median 60 minutes) to reach maximum plasma concentration.
- Takes 25 minutes (range 12-37 minutes) to cause an erection.
- Patients should be able to still produce an erection 4-5 hours post dose.
- Rate of absorption is reduced by an average of 60 minutes when consumed with food.

Tadalafil

- To be taken at least 30 minutes before sexual activity.
- Takes 2 hours (median) to reach maximum plasma concentration.
- Takes 16 minutes-36 hours to cause an erection.
- Patients should be able to still produce an erection 36 hours post dose.
- Rate of absorption is not affected by food intake.

Cycling

- If cycling >3hours/week, advise patients to try a period of time without cycling.
- If it is not possible for them to stop cycling, preventative measures, such as the use of a properly fitted, well-padded bicycle seat and riding with the seat in a suitable position, may help prevent impairment of erectile function.

Alternative treatment options if failed response to 2 oral PDE-5 inhibitors (specialist recommendation only)

Topical preparations, injectable devices and Vacuum pumps are alternatives to oral PDE-5 inhibitors for the treatment of ED. Patients should be assessed for suitability for these products by a specialist. Patients and their partners must be counselled appropriately to ensure they can use the treatment effectively to maximise concordance, efficacy of treatment and patient satisfaction with treatment.

Alprostadil

- The combination of alprostadil with other ED agents is not approved nor recommended.
- Alprostadil can **ONLY** be provided on the NHS for patients who fulfil NHS SLS criteria.
- All products listed below require SLS endorsement on an NHS prescription.

Topical formulary preparations (Amber 1):

This is a better option for patients on medications that may increase bleeding risk. They can be initiated in primary care under the advice of a specialist.

- MUSE®
  - Intraurethral application
  - 30-60% efficacy (refer to individual SPC for more information).
- Vitaros®
  - Topical cream.
  - 31-40% efficacy (refer to individual SPC for more information).

Intracavernous injection formulary preparations (Amber 2):

- Caution should be advised in patients receiving concomitant medications, which could increase the risk of bleeding, such as anticoagulants or platelet aggregation inhibitors.
- Not to be initiated in primary care, for continuation only after recommendation and initiation by a specialist.
- Intracavernous alprostadil has 70-80% efficacy (refer to individual SPCs for more information).
- Viridal Duo®
  - Preferred product over Caverject® Dual Chamber (DC) for patients requiring a 40mcg dose as it is more user friendly.
  - Patient can inject 1x40mcg Viridal® Duo injection compared to having to inject 2x20mcg Caverject® DC (Caverject® DC is not available in a 40mcg strength).
  - Prescribing 1x40 mcg Viridal® Duo is more cost effective than 2x20mcg Caverject® DC.
- Caverject® Dual chamber

  N.B Caverject® powder for solution for injection vials is **non formulary.** It should not be initiated for new patients. It is only to be used for existing patients across SWL.

Aviptadil with phentolamine mesylate

- 2nd line injectable option for ED.
- Reserved for patients who cannot use intracavernosal alprostadil due to pain, OR supply issues OR no response from 40mcg alprostadil**.**
- Not to be initiated in primary care, for continuation only after recommendation and initiation by a specialist.
- Invicorp®
  - 25micrograms/2mg/0.35ml solution for injection ampoules.

Vacuum erectile dysfunction (VED) pump:

- VED pumps are only to be prescribed by a GP based on a specialist recommendation following patient assessment and training.
- VEDs are contraindicated in men with bleeding disorders or those taking anti-

coagulant therapy.
- These should only be prescribed for patients fulfilling SLS criteria. Patients who do not fulfil the criteria will have to purchase privately.

References/resources

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- EMC. (2021). *Viridal Duo 10 micrograms/ml Powder and Solvent for Solution for Injection*.
- Adapted from: South East London urology adult primary care guidelines, November 2023
- Adapted from: Treatment of erectile dysfunction in primary care, West Essex Clinical Commissioning Group, October 2017
- Adapted from: Guideline for the management of Erectile Dysfunction in adults >18 years, Sunderland Clinical Commissioning Group April 2019
- The British Association of Urological Surgeons (BAUS) Erectile Dysfunction Patient information guide
- European Association of Urology (EAU) Guidelines on Male Sexual Dysfunction, 2023
- National Institute for Health and Care Excellence (NICE) CKS: Erectile Dysfunction
- NHS England (October 2023) Items which should not routinely be prescribed in primary care: policy guidance

Document History

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Updates:

- Document made accessible (removal of tables, colour)
- Addition of avaptadil with phentolamine mesylate as a treatment option.
- Removal of Viridal® continuation packs from guidance (product discontinued.)
- Addition of tadalafil as an OTC option.
- Reference links updated.

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Updates:

- RAG rating of vacuum erectile pumps changed from AMB2 to AMB1.
- Removal of restrictions on daily tadalafil prescribing and information updated.
- Treatment pathway updated to reflect inclusion of daily tadalafil 5mg in guidance.
- Number of doses required to warrant treatment failure changed to 4-8 to reflect NICE guidance.
- Reference links updated.

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