

EAU GUIDELINES ON MALE SEXUAL DYSFUNCTION: Erectile Dysfunction and Premature Ejaculation

(Partial text update March 2015)

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Eur Urol 2006 May;49(5):806-15

Eur Urol 2010 May;57(5):804-14

Eur Urol 2012 Sep;62(3):543-52

ERECTILE DYSFUNCTION

Erectile dysfunction (ED) is defined as the persistent inability to attain and maintain an erection sufficient to permit satisfactory sexual performance. Erectile dysfunction may affect physical and psychosocial health and may have a significant impact on the quality of life (QoL) of sufferers and their partners. There is increasing evidence that ED can be an early manifestation of coronary artery and peripheral vascular disease; therefore, ED should not be regarded only as a QoL issue, but also as a potential warning sign of cardiovascular disease (CVD).

Table 1: Pathophysiology of ED

Vasculogenic	
•	Cardiovascular disease (hypertension, coronary artery disease, peripheral vasculopathy, etc)
•	Diabetes mellitus
•	Hyperlipidaemia
•	Smoking

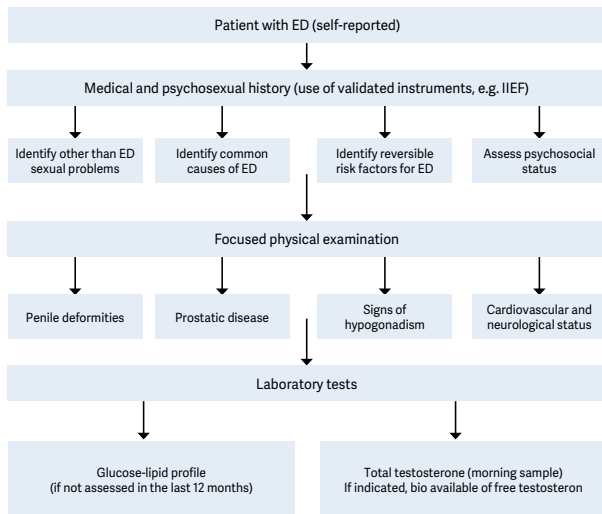
•	Major pelvic surgery (RP) or radiotherapy (pelvis or retroperitoneum)
Neurogenic	
<i>Central causes</i>	
•	Degenerative disorders (multiple sclerosis, Parkinson's disease, multiple atrophy, etc)
•	Spinal cord trauma or diseases
•	Stroke
•	Central nervous system tumours
<i>Peripheral causes</i>	
•	Type 1 and 2 diabetes mellitus
•	Chronic renal failure
•	Polyneuropathy
•	Surgery (major surgery of pelvis/retroperitoneum, RP, colorectal surgery, etc)
•	Surgery of the urethra (urethral stricture urethroplasty etc.)
Anatomical or structural	
•	Hypospadias, epispadias
•	Micropenis
•	Peyronie's disease
Hormonal	
•	Hypogonadism
•	Hyperprolactinaemia
•	Hyper- and hypothyroidism
•	Hyper- and hypocortisolism (Cushing's disease, etc)
•	Panhypopituitarism and multiple endocrine disorders
Drug-induced	
•	Antihypertensives (thiazide diuretics, etc)
•	Antidepressants (selective serotonin reuptake inhibitors, tricyclics)

•	Antipsychotics (neuroleptics, etc)
•	Antiandrogens (GnRH analogues and antagonists)
•	Recreational drugs (alcohol, heroin, cocaine, marijuana, methadone, synthetic drugs, anabolic steroids, etc.)
Psychogenic	
•	Generalised type (e.g., lack of arousability and disorders of sexual intimacy)
•	Situational type (e.g., partner-related, performance-related issues or due to distress)
Trauma	
•	Penile fracture
•	Pelvic fractures

RP = radical prostatectomy.

Diagnostic evaluation

Figure 1: Minimal diagnostic evaluation (basic work-up) in patients with ED



ED = erectile dysfunction; IIEF = International Index of Erectile Function.

Table 2: Cardiac risk stratification (based on 2nd Princeton Consensus)

Low-risk category	Intermediate-risk category	High-risk category
Asymptomatic, < 3 risk factors for CAD (excluding sex)	≥ 3 risk factors for CAD (excluding sex)	High-risk arrhythmias
Mild, stable angina (evaluated and/or being treated)	Moderate, stable angina	Unstable or refractory angina
Uncomplicated previous MI	Recent MI (> 2, < 6 weeks)	Recent MI (< 2 weeks)
LVD/CHF (NYHA class I)	LVD/CHF (NYHA class II)	LVD/CHF (NYHA class III/IV)
Post-successful coronary Revascularisation	Non-cardiac sequelae of Atherosclerotic disease (e.g., stroke, peripheral vascular disease)	Hypertrophic obstructive and other cardiomyopathies
Controlled hypertension		Uncontrolled hypertension
Mild valvular disease		Moderate-to-severe valvular disease

CAD = coronary artery disease; CHF = congestive heart failure; LVD = left ventricular dysfunction; MI = myocardial infarction; NYHA = New York Heart Association.

Table 3: Indications for specific diagnostic tests

Primary ED (not caused by organic disease or psychogenic disorder).
Young patients with a history of pelvic or perineal trauma, who could benefit from potentially curative vascular surgery.
Patients with penile deformities which might require surgical correction (e.g., Peyronie's disease, congenital curvature).
Patients with complex psychiatric or psychosexual disorders.
Patients with complex endocrine disorders.
Specific tests may be indicated at the request of the patient or his partner.
Medico-legal reasons (e.g., implantation of penile prosthesis, sexual abuse).

Table 4: Specific diagnostic tests

NTPR using Rigiscan
Vascular studies
- Intracavernous vasoactive drug injection
- Penile Dynamic Duplex Doppler study
- Penile Dynamic Infusion Caverosometry and Caverosography
- Internal pudendal arteriography
Neurological studies (e.g., bulbocavernosus reflex latency, nerve conduction studies)
Endocrinological studies
Specialised psychodiagnostic evaluation

Recommendations for the diagnostic evaluation of ED	LE	GR
Take a comprehensive medical and sexual history in every patient.	3	B
Use a validated questionnaire related to ED to assess all sexual function domains and the effect of a specific treatment modality.	3	B
Include a physical examination in the initial assessment of men with ED to identify underlying medical conditions that may be associated with ED.	4	B
Assess routine laboratory tests, including glucose-lipid profile and total testosterone, to identify and treat any reversible risk factors and lifestyle factors that can be modified.	4	B
Include specific diagnostic tests in the initial evaluation only in the presence of the conditions presented in table 3.	4	B

ED = erectile dysfunction.

Disease management

Figure 2: Treatment algorithm for ED

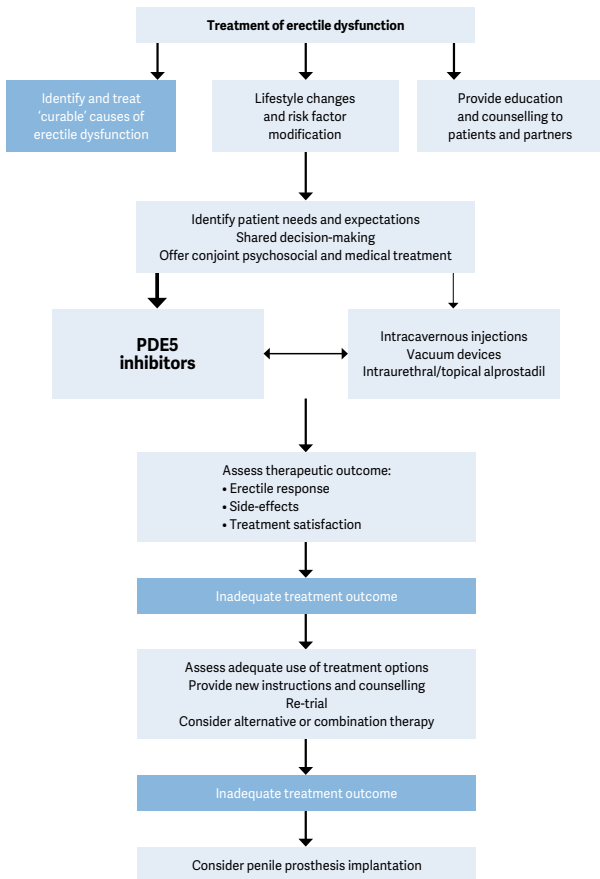


Table 5: Summary of the key pharmacokinetic data for the four PDE5 inhibitors currently EMA-approved to treat ED*

Parameter	Sildenafil, 100 mg	Tadalafil, 20 mg	Vardenafil, 20 mg	Avanafil 200mg
C_{max}	560 µg/L	378 µg/L	18.7 µg/L	5.2 µg/L
T_{max} (median)	0.8-1 h	2 h	0.9 h	0.5-0.75 h
T1/2	2.6-3.7 h	17.5 h	3.9 h	6 – 17 h
AUC	1685 µg.h/L	8066 µg.h/L	56.8 µg.h/L	11.6 µg.h/L
Protein binding	96%	94%	94%	99%
Bioavailability	41%	NA	15%	8-10%

* Fasted state, higher recommended dose. Data adapted from EMA statements on product characteristics.

C_{max} : maximal concentration, T_{max} : time-to-maximum plasma concentration; T1/2: plasma elimination halftime;

AUC: area under curve or serum concentration time curve.

Table 6: Common adverse events of the four PDE5 inhibitors currently EMA-approved to treat ED*

Adverse event	Sildenafil	Tadalafil	Vardenafil	Avanafil 200mg
Headache	12.8%	14.5%	16%	9.3%
Flushing	10.4%	4.1%	12%	3.7%
Dyspepsia	4.6%	12.3%	4%	uncommon
Nasal congestion	1.1%	4.3%	10%	1.9%
Dizziness	1.2%	2.3%	2%	0.6%
Abnormal vision	1.9%		< 2%	none
Back pain		6.5%		< 2%
Myalgia		5.7%		< 2%

* Adapted from EMA statements on product characteristics.

Recommendations for the treatment of ED	LE	GR
Enact lifestyle changes and risk factor modification prior to or accompanying ED treatment.	1a	A
Start pro-erectile treatments at the earliest opportunity after RP.	1b	A
Treat a curable cause of ED first, when found.	1b	B
Use PDE5Is as first-line therapy.	1a	A
Assess all patients for inadequate/incorrect prescriptions and poor patient education, since they are the main causes of a lack of response to PDE5Is.	3	B
Use VED as a first-line therapy in well-informed older patients with infrequent sexual intercourse and comorbidity requiring non-invasive, drug-free management of ED.	4	C

Use intracavernous injections as second-line therapy.	1b	B
Use implantation of a penile prosthesis as third-line therapy.	4	C

ED = erectile dysfunction; RP = radical prostatectomy; VED = vacuum erection devices; PDE5I = phosphodiesterase type 5 [inhibitors].

PREMATURE EJACULATION

Although PE is a common male sexual dysfunction, it is poorly understood. Patients are often unwilling to discuss their symptoms and many physicians do not know about effective treatments. As a result, patients may be misdiagnosed or mis-treated.

PE (lifelong and acquired) is a male sexual dysfunction characterized by the following:

1. Ejaculation that always or nearly always occurs prior to or within about 1 minute of vaginal penetration (lifelong PE) or a clinically significant and bothersome reduction in latency time, often to about 3 minutes or less (acquired PE).
2. The inability to delay ejaculation on all or nearly all vaginal penetrations.
3. Negative personal consequences, such as distress, bother, frustration, and/or the avoidance of sexual intimacy.

Diagnostic evaluation

Recommendations for the diagnostic evaluation of PE	LE	GR
Perform the diagnosis and classification of PE based on medical and sexual history, which should include assessment of IELT (self-estimated), perceived control, distress and interpersonal difficulty due to the ejaculatory dysfunction.	1a	A
Do not use stopwatch-measured IELT in clinical practice.	2a	B
Do not use patient-reported outcomes (PROs) in clinical practice.	3	C
Include physical examination in the initial assessment of PE to identify anatomical abnormalities that may be associated with PE or other sexual dysfunctions, particularly ED.	3	C
Do not perform routine laboratory or neurophysiological tests. They should only be directed by specific findings from history or physical examination.	3	C

PE = premature ejaculation; IELT = intravaginal ejaculatory latency time; ED = erectile dysfunction.

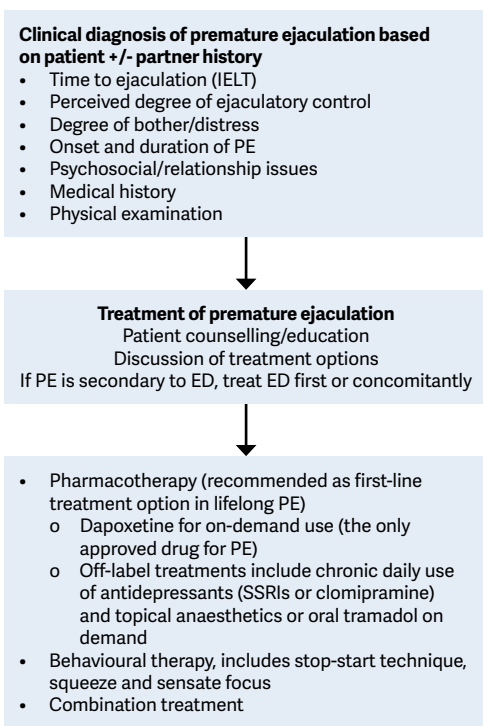
Disease management

Recommendations for the treatment of PE	LE	GR
Treat erectile dysfunction, other sexual dysfunction or genitourinary infection (e.g. prostatitis first).	2a	B
Use pharmacotherapy as first-line treatment of lifelong premature ejaculation.	1a	A

Use off-label topical anaesthetic agents as a viable alternative to oral treatment with SSRIs.	1b	A
Use tramadol on demand as a weak alternative to SSRI's.	2a	B
Do not use PDE5Is in patients with PE without ED.	3	C
Use psychological/behavioural therapies in combination with pharmacological treatment in the management of acquired premature ejaculation.	3	C

ED = erectile dysfunction; PE = premature ejaculation; PDE5Is = phosphodiesterase type 5 inhibitors; SSRI = selective serotonin reuptake inhibitor.

Figure 4: Management of PE*




* Adapted from Lue et al. 2004.

ED = erectile dysfunction; PE = premature ejaculation;

IELT = intravaginal ejaculatory latency time;

SSRI = selective serotonin receptor inhibitor.



This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-90-79754-98-4), available to all members of the European Association of Urology at their website, <http://www.uroweb.org>.