GUIDELINES ON MALE SEXUAL DYSFUNCTION: Erectile Dysfunction and Premature Ejaculation

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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

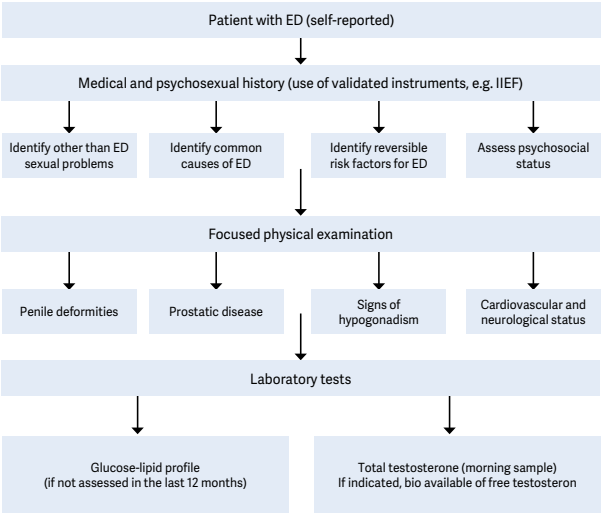
Vasculogenic	
-	Cardiovascular disease (hypertension, coronary artery disease, peripheral vasculopathy, etc)
-	Diabetes mellitus
-	Hyperlipidaemia
-	Smoking

-	Major pelvic surgery (RP) or radiotherapy (pelvis or retroperitoneum)
Neurogenic	
Central causes	
-	Degenerative disorders (multiple sclerosis, Parkinson's disease, multiple atrophy, etc)
-	Spinal cord trauma or diseases
-	Stroke
-	Central nervous system tumours
Peripheral causes	
-	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
-	Hyperprolactinemia
-	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

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 Cavernosometry and Cavernosography
- 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
A comprehensive medical and sexual history is needed.	3	B
Clinical use of validated questionnaire related to ED may help to assess all sexual function domains and the effect of a specific treatment modality.	3	B
Physical examination is needed in the initial assessment of men with ED to identify underlying medical conditions that may be associated with ED.	4	B
Routine laboratory tests, including glucose-lipid profile and total testosterone, are required to identify and treat any reversible risk factors and lifestyle factors that can be modified.	4	B
Specific diagnostic tests are indicated by only a few conditions.	4	B

ED = erectile dysfunction.

Disease management

Figure 3: Treatment algorithm for ED

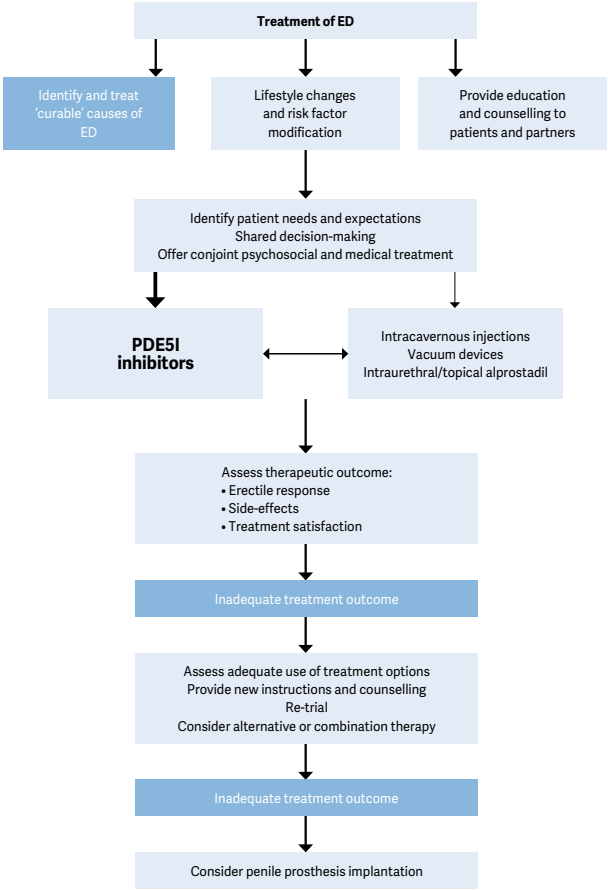


Table 5: Summary of the key pharmacokinetic data for the four PDE5 inhibitors currently EMA-approved to treat ED*

Parameter	Sildenafil, 100 mg	Tadalafil, 20 mg	Vardenafil, 20 mg	Avanafil 200mg
Cmax	560 µg/L	378 µg/L	18.7 µg/L	5.2 µg/L
Tmax (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%

Cmax: maximal concentration, Tmax: time-to-maximum plasma concentration; T1/2: plasma elimination halftime; AUC: area under curve or serum concentration time curve.

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

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
Lifestyle changes and risk factor modification must precede or accompany ED treatment.	1a	A
Pro-erectile treatments have to be given at the earliest opportunity after RP.	1b	A
When a curable cause of ED is found, it must be treated first.	1b	B
PDE5Is are first-line therapy.	1a	A
Inadequate/incorrect prescription and poor patient education are the main causes of a lack of response to PDE5Is.	3	B
A VED can be used in patients with a stable relationship.	4	C
Intracavernous injection is second-line therapy.	1b	B
Penile implant is 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 mistreated.

PE (lifelong and acquired) is a male sexual dysfunction characterised 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
Diagnosis and classification of PE is based on medical and sexual history. It should be multidimensional and assess IELT, perceived control, distress and interpersonal difficulty due to the ejaculatory dysfunction.	1a	A
Clinical use of self-estimated IELT is adequate. Stopwatch-measured IELT is necessary in clinical trials.	2a	B
Patient-reported outcomes (PROs) have the potential to identify men with PE. Further research is needed before PROs can be recommended for clinical use.	3	C
Physical examination may be necessary in initial assessment of PE to identify anatomical abnormalities that may be associated with PE or other sexual dysfunctions, particularly ED.	3	C
Routine laboratory or neurophysiological tests are not recommended. 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.

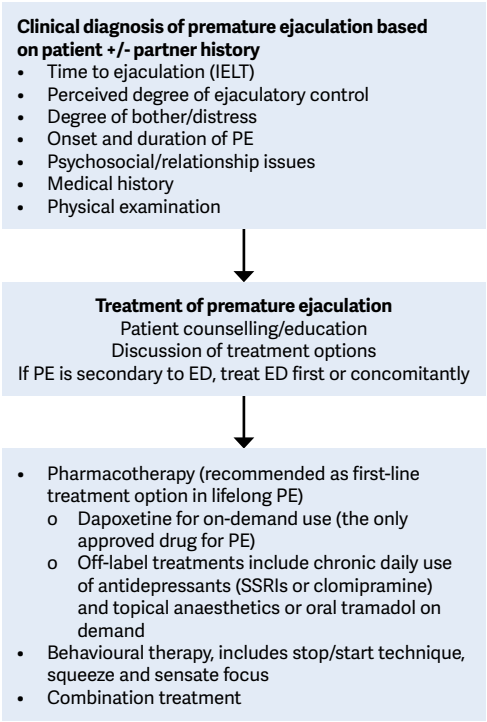
Disease management

Recommendations for the treatment of PE	LE	GR
Erectile dysfunction, other sexual dysfunction or genitourinary infection (e.g. prostatitis) should be treated first.	2a	B
Pharmacotherapy should be given as first-line treatment of lifelong PE.	1a	A
Pharmacotherapy includes either dapoxetine on demand (a short-acting SSRI that is the only approved pharmacological treatment for PE) or other off-label antidepressants, i.e. daily SSRIs and clomipramine, that are not amenable to on-demand dosing. With all antidepressant treatment for PE , recurrence is likely after treatment cessation.	1a	A
Off-label topical anaesthetic agents can be offered as a viable alternative to oral treatment with SSRIs.	1b	A
Behavioural and sexological therapies have a role in the management of acquired PE. They are most likely to be best used in combination with pharmacological treatment.	3	C
Psychological/behavioural therapies.	3	C
On-demand treatment of PE		
PDE5 inhibitor.	3	C
Dapoxetine on demand.	1a	A
Tramadol on demand.	2a	B
Chronic treatment of PE		
Off-label chronic treatment i.e. daily with selective serotonin receptor inhibitors (SSRIs) and clomipramine antidepressants.	1a	A

On-demand topical therapy for PE		
Lidocaine-prilocaine cream.	1b	A

ED = erectile dysfunction; PE = premature ejaculation; 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 978-90-79754-80-9), available to all members of the European Association of Urology at their website, http://www.uroweb.org.