PROSTATE SERIES / 06

BPH MEDICINES

Three classes.
Three different jobs.

Alpha blockers · 5-ARIs · tadalafil



Illustrative clinical scene

Same symptoms. Different priorities.



Illustrative clinical scene

01 **Relief soon**

02 **Future risk**

03 **Sexual function**

Start with the cause and the person's goal.

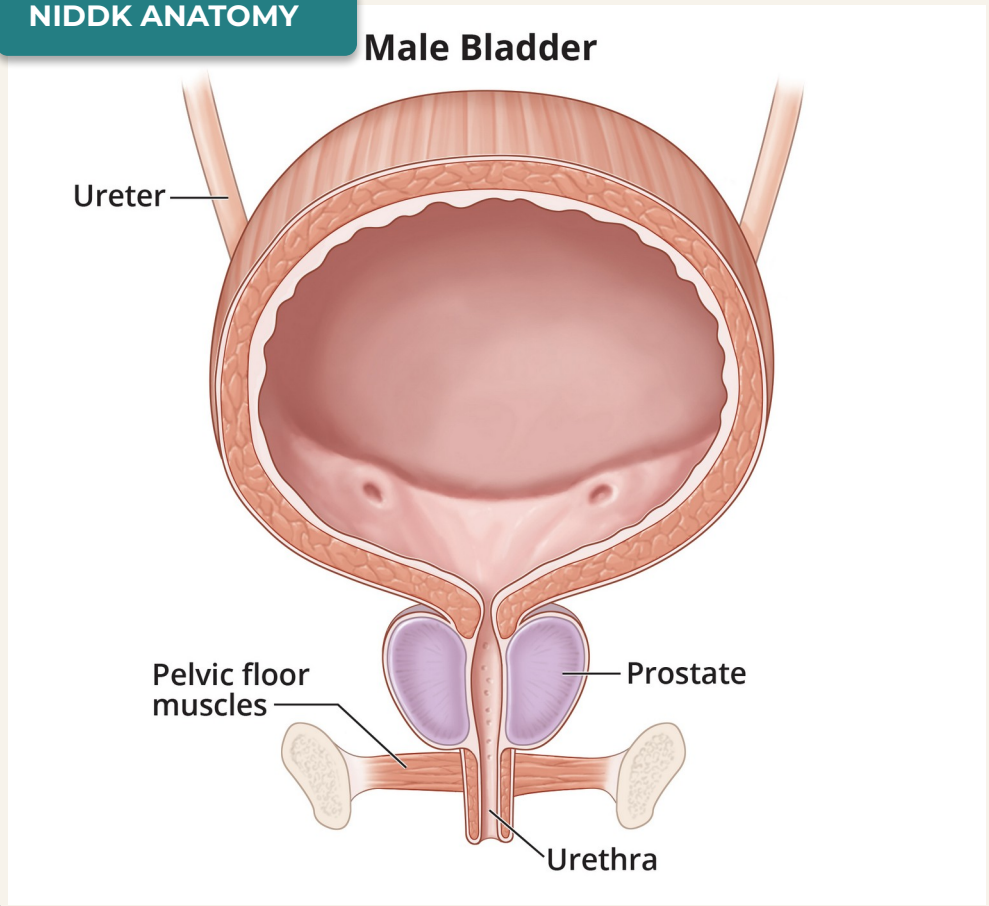
Three targets. Different clocks.

A mechanism is a starting point, not a promise of an individual result.

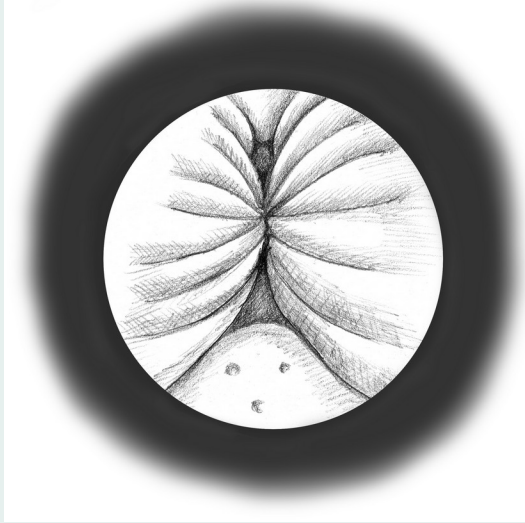


Where do these medicines act?

NIDDK ANATOMY



NIDDK ILLUSTRATION



Outlet muscle

Gland growth

Tissue signaling

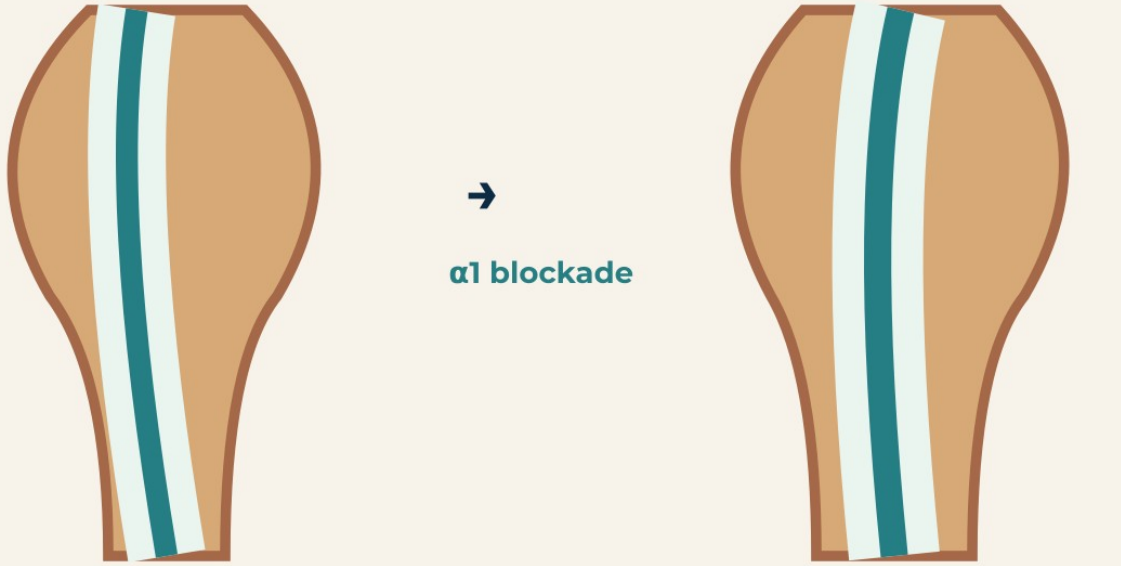
Structure alone does not diagnose the cause of symptoms.

1 / Alpha blockers: relax outlet muscle

Examples include tamsulosin, alfuzosin, silodosin, doxazosin and terazosin.

A change in muscle tone

Schematic, not to anatomical scale



How soon might symptoms change?

Benefit can begin within days. The full effect usually takes weeks.



What it does not do

Alpha blockers do not shrink the prostate or prevent acute urinary retention or surgery in long-term studies.

Alpha blockers / measured relief

EAU GUIDELINE · p. 21

5.2.1 α1-Adrenoceptor antagonists (α1-blockers)

Mechanism of action:

α1-blockers aim to inhibit the effect of endogenously released noradrenaline on smooth muscle cells in the prostate and thereby reduce prostate tone and BOO [160]. However, α1-blockers have a small effect on urodynamically determined bladder outlet resistance [161], and treatment-associated improvement of LUTS correlates poorly with obstruction [162]. Therefore, other mechanisms of action may also be relevant.

α1-adrenoceptors located outside the prostate (e.g. urinary bladder and/or spinal cord) and α1-adrenoceptor subtypes (α1B- or α1D-adrenoceptors) may play a role as mediators of effects. α 1-adrenoceptors in blood vessels, other non-prostatic smooth muscle cells and the central nervous system may mediate adverse events.

Currently available α1-blockers are: alfuzosin hydrochloride (alfuzosin); doxazosin mesylate (doxazosin); silodosin; tamsulosin hydrochloride (tamsulosin); terazosin hydrochloride (terazosin); and naftopidil. α1-blockers exist in various formulations. Although different formulations result in different pharmacokinetic and tolerability profiles, the overall difference in clinical efficacy between the difference formulations appears to be negligible.

Efficacy

All α1-blockers have a similar efficacy in appropriate doses [163] and the effects take a few weeks to develop fully, but significant efficacy over placebo can occur within hours to days [162].

Controlled studies show that α1-blockers typically reduce IPSS by approximately 30-40% and increase Q_{max} by approximately 20-25%. However, substantial improvements also occurred in the corresponding placebo arms [64, 164]. In open-label studies, an IPSS improvement of up to 50% and Q_{max} increase of up to 40% were documented [64, 164]. A SR and meta-analysis suggested that Q_{max} variation underestimates the real effect of

30–40%

Typical within-group IPSS reduction in controlled trials. Placebo groups improved too.

Alpha blocker tradeoffs

Discuss the adverse effect profile of the specific drug.

Dizziness / low pressure

Especially relevant with other pressure-lowering medicines or a fall risk.

Ejaculation changes

More common with selective agents such as tamsulosin or silodosin.

Cataract surgery

Tell the eye surgeon about current or past alpha blocker use.

Alpha blockers / safety

EAU GUIDELINE · p. 22

pharmacokinetic profiles of certain formulations may contribute to the tolerability profile of specific drugs. The most frequent adverse events of α1-blockers are asthenia, dizziness and (orthostatic) hypotension. Vasodilating effects are most pronounced with doxazosin and terazosin and are less common with alfuzosin and tamsulosin [173]. Patients with cardiovascular comorbidity and/or vasoactive comedication may be susceptible to α1-blocker-induced vasodilatation [174]. In contrast, the frequency of hypotension with the α1A-selective blocker silodosin is comparable with placebo [175]. In a large retrospective cohort analysis of men aged > 66 years treated with α1-blockers, the risks of falling (odds ratio [OR] 1.14) and of sustaining a fracture (OR: 1.16) was increased, most likely as a result of induced hypotension [176]. In terms of cardiovascular risk, a large population-based study reported an increased risk of cardiac failure with long-term α-blocker use (hazard radio [HR]: 1.22), which was higher for non-selective α-blockers [177]. Whilst there has been concern about a possible risk of dementia with long-term use of α1-blockers, a large nationwide Finnish case-control study of 24,602 cases and 98,397 controls did not find evidence of a significant association [178].

An adverse ocular event termed intraoperative floppy iris syndrome (IFIS) was reported in 2005, affecting cataract surgery [179]. A meta-analysis on IFIS after alfuzosin, doxazosin, tamsulosin or terazosin exposure showed an increased risk for all α1-blockers [180]. However, the OR for IFIS was much higher for tamsulosin. It appears prudent not to initiate α1-blocker treatment prior to scheduled cataract surgery, and the ophthalmologist should be informed about α1-blocker use.

An SR concluded that α1-blockers do not adversely affect libido or erectile function but can cause abnormal ejaculation (OR: 7.53) [181]. Originally, abnormal ejaculation was thought to be retrograde, but more recent data demonstrate that abnormal ejaculation is due to a decrease or absence of seminal fluid during ejaculation, with young age being an apparent risk factor. In a meta-analysis, ejaculatory dysfunction (EjD) was significantly more common with α1-blockers than with placebo (OR: 5.88). In particular, EjD was significantly more commonly related with tamsulosin or silodosin (OR: 8.57 and 32.5) than placebo, while both doxazosin and terazosin (OR: 0.80 and 1.78) were associated with a low risk of EjD [182]. In the meta-regression, the occurrence of EjD was independently associated with the improvement of urinary symptoms and flow rate, suggesting that the more effective the α1-blocker is the greater the incidence of EjD.

Practical considerations

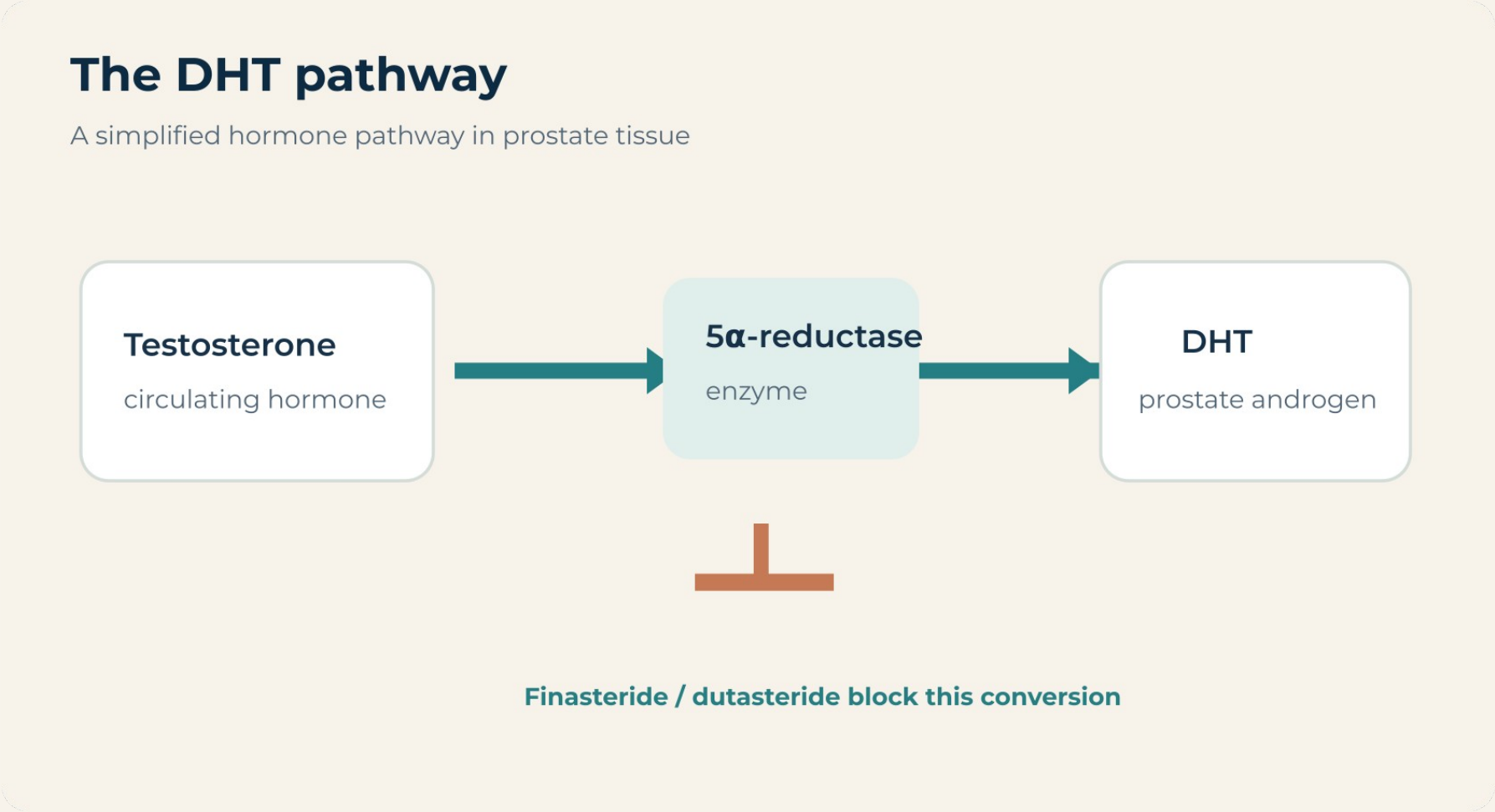
α1-blockers are usually considered the first-line drug treatment for MLUTS due to their rapid onset of action, good efficacy and low rate and severity of adverse events. However, α1-blockers do not prevent occurrence of urinary retention or need for surgery. Ophthalmologists should be informed about α1-blocker use prior to

NAME THE DRUG

Blood pressure, ejaculation and cataract surgery risks depend on the specific agent.

2 / 5-ARIs: lower DHT signaling

Finasteride and dutasteride act on the testosterone-to-DHT pathway.



Size changes the conversation.

>40 mL

EAU example of an enlarged prostate in its 5-ARI recommendation.

A clinician measures size and progression risk.

Summary of evidence	LE
After two to four years of treatment, 5-ARIs improve IPSS by approximately 15-30%, decrease prostate volume by 18-28% and increase Q_{max} by 1.5-2.0mL/s in patients with LUTS due to prostate enlargement.	1b
5α-reductase inhibitors can reduce risk of LUTS progression with regard to AUR and the need for surgery. Due to their slow onset of action, 5-ARIs are suitable only for long-term treatment (years).	1a
The most relevant urological adverse events of 5-ARIs are related to sexual function and include reduced libido, ED, and less frequently, EjD.	1b

Recommendations	Strength rating
Use 5α-reductase inhibitors (5-ARIs) in men who have moderate-to-severe LUTS and an increased risk of LUTS progression (e.g. prostate volume > 40mL).	Strong
Counsel patients about the slow onset of action and side effects of 5-ARIs.	Strong

Clinical effects take at least six months.

Long-horizon results have two parts

Symptom scores and prostate size are different outcomes.

15–30%

average IPSS improvement after 2–4 years

18–28%

average reduction in prostate volume after 2–4 years

Ranges summarize selected trial populations. They are not head-to-head estimates against other classes.

5-ARIs / the long view

EAU GUIDELINE · p. 23

concentration is reduced to a similar level (85-90%) by both 5-ARIs.

Clinical effects relative to placebo are seen after treatment of at least six months. After two to four years of treatment, 5-ARIs improve IPSS by approximately 15-30%, decrease prostate volume by 18-28% and increase Q_{max} by 1.5-2.0mL/s in patients with LUTS due to BPE [66, 168, 169, 186-192]. An indirect comparison and one direct comparative trial (12 months duration) indicated that dutasteride and finasteride are equally effective in the treatment of LUTS [185, 193]. Symptom reduction depends on initial prostate size.

Finasteride may not be more efficacious than placebo in patients with prostates < 40mL [194]. However, dutasteride seems to reduce IPSS, prostate volume and the risk of AUR, and to increase Q_{max} even in patients with prostate volumes of between 30 and 40mL [195, 196]. A long-term trial with dutasteride in symptomatic men with prostate volumes > 30mL and increased risk for disease progression showed that dutasteride reduced LUTS at least as much as the α1-blocker tamsulosin [168, 192, 197]. The greater the baseline prostate volume (or serum PSA level), the faster and more pronounced the symptomatic benefit of dutasteride as compared to tamsulosin.

5α-reductase inhibitors, but not α1-blockers, reduce the long-term (> one year) risk of AUR or need for surgery [66, 190, 198]. In the PLESS study, finasteride reduced the relative risk of AUR by 57% and need for surgery by 55% (absolute risk reduction 4% and 7%, respectively) at four years compared with placebo [190]. In the MTOPS study, finasteride reduced the relative risk of AUR by 68% and need for surgery by 64% (absolute risk reduction 2% and 3%, respectively), also at four years [66]. A pooled analysis of three RCTs with two-year follow-up data reported that treatment with finasteride decreased the relative risk of AUR by 57% and surgical intervention by 34% (absolute risk reduction 2% for both) in patients with moderately symptomatic LUTS [199]. Dutasteride has also demonstrated efficacy in reducing the risks for AUR and BPO-related surgery. Open-label trials have demonstrated relevant changes in urodynamic parameters [200, 201]. A large Danish registry study reported that treatment with 5-ARI versus α-blocker monotherapy was associated with a reduced risk of BPO-related surgery and AUR for up to 15 years of follow-up, and the absolute risk reduction was 4% [202].

Additionally, finasteride might reduce blood loss during transurethral prostate surgery, probably due to its effects on prostatic vascularisation, although evidence for a clinically significant effect is mixed [203-205].

Tolerability and safety

The most common adverse events are reduced libido, ED and, less frequently, EjD such as retrograde ejaculation, ejaculation failure or decreased semen volume [66, 169, 185, 206]. Gynaecomastia (with breast

MONTHS

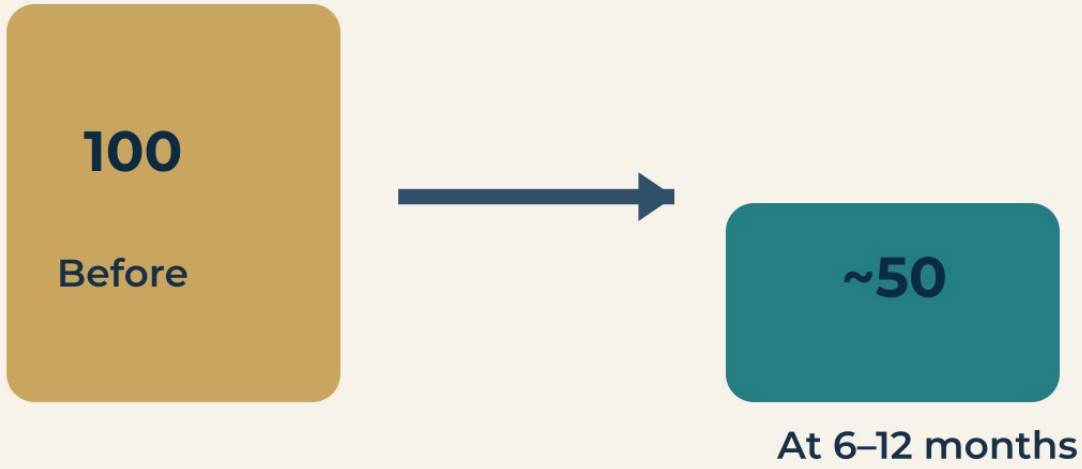
In selected men with enlargement, the class can reduce retention and surgery risk over time.

A PSA result needs context

5-ARIs can lower circulating PSA by about half after 6–12 months.

PSA results need a new baseline

Typical change during 5-ARI treatment, not a cancer test rule



Tell the clinician

which medicine you take

and for how long.

5-ARI tradeoffs to discuss

A long treatment horizon makes side effects and follow-up important.

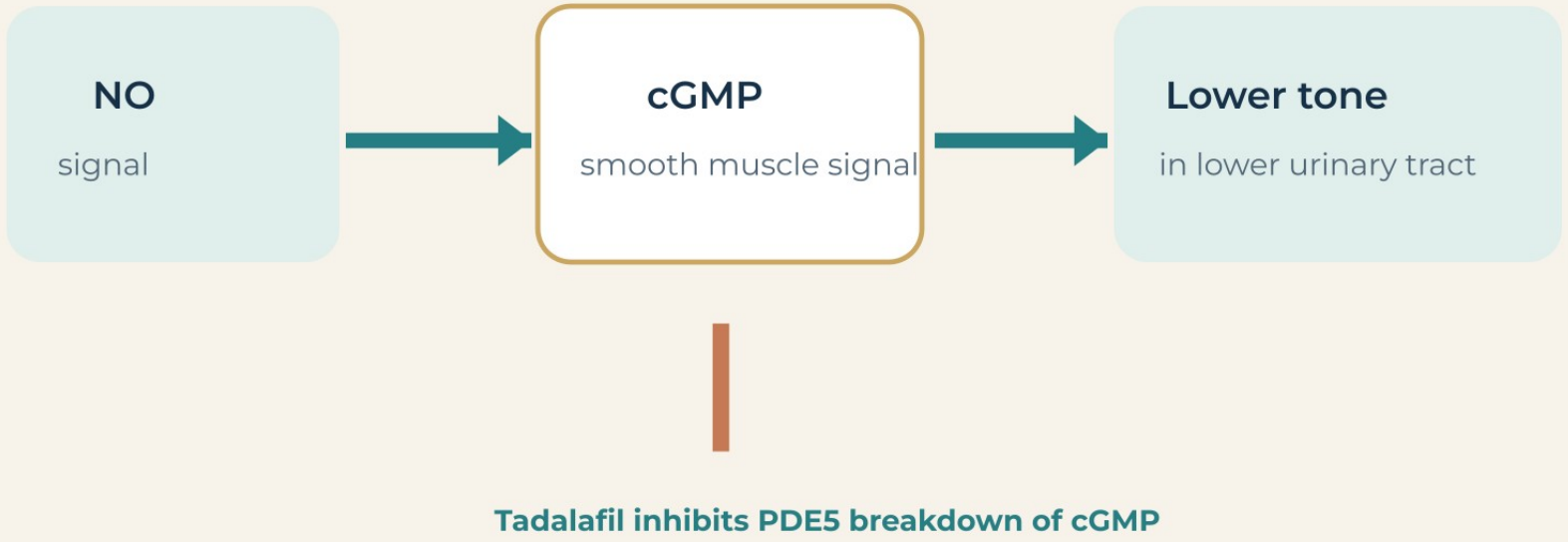
- Reduced libido, erectile or ejaculation problems can occur.
- Breast tenderness or enlargement is uncommon but possible.
- Report a change in mood promptly; finasteride carries an EMA warning.

3 / Tadalafil: PDE5 and cGMP

It can improve LUTS with or without erectile dysfunction.

A signaling pathway, with limits

The precise way this improves LUTS remains uncertain



Tadalafil / average symptom change

1.89

IPSS points lower than placebo in pooled trials

Mean group difference · short-term trials

EAU SOURCE EXCERPT

Mechanism of action

Phosphodiesterase type 5 inhibitors (PDE5Is) increase intracellular cyclic guanosine monophosphate, thus reducing smooth muscle tone of the detrusor, prostate and urethra. Nitric oxide and PDE5Is might also alter reflex pathways in the spinal cord and neurotransmission in the urethra, prostate or bladder [259]. Moreover, chronic treatment with PDE5Is appears to increase blood perfusion and oxygenation in the LUT [260]. Phosphodiesterase type 5 inhibitors could also reduce chronic inflammation in the prostate and bladder [261]. The exact mechanism of PDE5Is on LUTS remains unclear.

Although clinical trials of several selective oral PDE5Is have been conducted in men with LUTS, only tadalafil (5mg once daily) has been licensed for the treatment of MLUTS.

Efficacy

Randomised controlled trials have demonstrated that PDE5Is reduce IPSS, storage and voiding LUTS and improve QoL. However, Q_{max} did not significantly differ from placebo in most trials [262]. A Cochrane review included a total of 16 RCTs that examined the effects of PDE5Is compared to placebo and other standard of care drugs (α1-blockers and 5-ARIs) in men with LUTS [263]. In the updated meta-analysis, PDE5Is led to a small reduction (mean difference [MD] 1.89 lower; 95% confidence interval [CI]: 2.27 to 1.50 lower; n = 4293) in IPSS compared to placebo [263]. There was no difference between PDE5Is and α1-blockers in IPSS [264]. Most evidence was limited to short-term treatment up to 12 weeks. In other meta-analyses, PDE5Is were also found to improve IPSS and IIEF score, but not always Q_{max} [265, 266]. A meta-regression suggested that younger men with low body mass index and more severe LUTS benefit the most from treatment with PDE5Is [265].

In a *post hoc* analysis of data pooled from four blinded trials of tadalafil 5mg versus placebo once daily, a minimum improvement of 25% in IPSS score was found in 60% in the tadalafil and in 44% in the placebo group [267]. The maximum trial duration was 52 weeks [268]. A subgroup analysis of pooled data from four RCTs demonstrated a significant reduction in LUTS, regardless of baseline severity, age, previous use of α-blockers or PDE5Is, total testosterone level or predicted prostate volume [269]. In a *post hoc* analysis of pooled data from four RCTs, tadalafil was shown to also be effective in men with cardiovascular risk factors/comorbidities, except for patients receiving more than one antihypertensive medication. Among sexually active men > 45 years,

A second way to view the trial results

At least 25% IPSS improvement in a pooled post hoc analysis.



A responder definition, not a cure rate. Post hoc pooled analysis; individual results vary.

Before tadalafil: check the medicine list.

NITRATES

RIOCIGUAT

Contraindicated combinations

EAU GUIDELINE

Tadalafil is contraindicated in patients using nitrates or guanylate cyclase stimulators, such as Riociguat, and in men with cardiac disease for whom sexual activity is inadvisable [276]. Tadalafil is also contraindicated in patients with myocardial infarction within the last 90 days; patients with unstable angina or angina occurring during sexual intercourse; patients with New York Heart Association Class 2 or greater heart failure in the last six months; patients with uncontrolled arrhythmias, hypotension (< 90/50mm Hg), or uncontrolled hypertension; patients with a stroke within the last six months; or if anterior ischaemic optic neuropathy with sudden loss of vision is known or was reported after previous use of PDE5Is [276]. Detailed information regarding tolerability/safety of all available PDE5Is for the treatment of ED in men treated with α-blockers for LUTS are provided in the EAU Guidelines on Sexual and Reproductive Health [277].

Practical considerations

To date, only tadalafil 5mg once daily has been officially licensed for the treatment of MLUTS with or without ED. Long-term experience with tadalafil in men with LUTS is limited to one trial with a one-year follow-up [268], limiting conclusions about efficacy or tolerability greater than one year. There is limited information available on reduction of prostate size and no data on disease progression.

Summary of evidence	LE
Phosphodiesterase type 5 inhibitors significantly improve IPSS and IIEF score but not Q_{max}.	1a

Recommendation	Strength rating
Use phosphodiesterase type 5 inhibitors in men with moderate-to-severe LUTS with or without erectile dysfunction.	Strong

Compare the decision, not a “winner”

These dimensions matter more than ranking drugs by one score.

ALPHA BLOCKER

TARGET
Outlet tone

TIME
Days–weeks

LONGER TERM
No long-term shrinkage

DISCUSS
Dizziness / ejaculation

5-ARI

TARGET
DHT pathway

TIME
Months–years

LONGER TERM
Size and progression

DISCUSS
Sexual effects / PSA

TADALAFIL

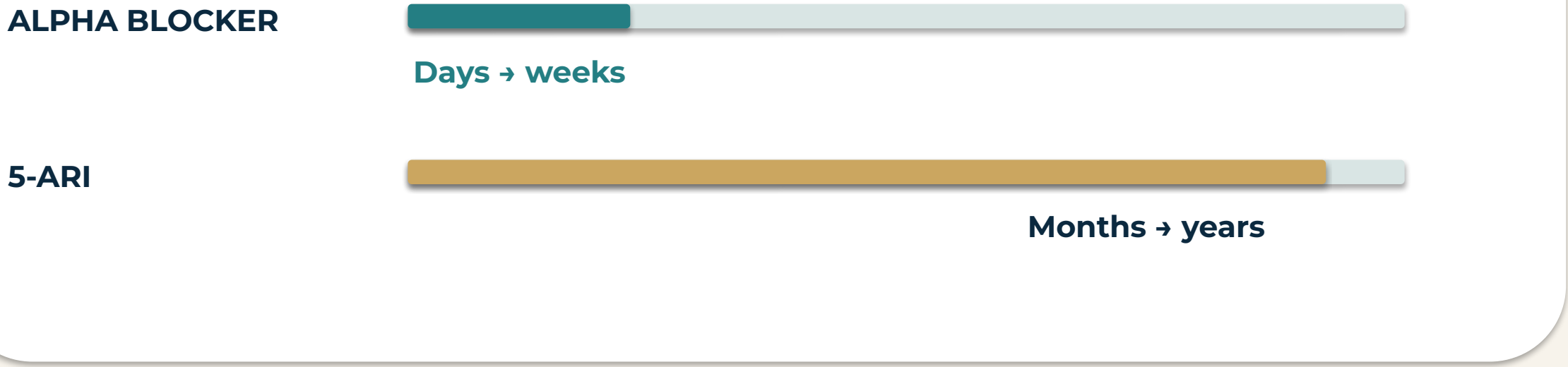
TARGET
PDE5 / cGMP

TIME
Weeks

LONGER TERM
No progression data

DISCUSS
Nitrates / pressure

Combination / two clocks, one plan



For selected men with enlargement and higher progression risk.

At the visit: choose the question

Two people can have the same symptom score and different priorities.

SCENARIO A

“I need relief soon.”

What is causing the symptoms? What is the risk from dizziness or an ejaculation change?

SCENARIO B

“Will it worsen later?”

Is the prostate enlarged? How would a long-term medicine affect PSA interpretation and sexual function?

Pause: match the mechanism

Which class blocks conversion of testosterone to DHT?

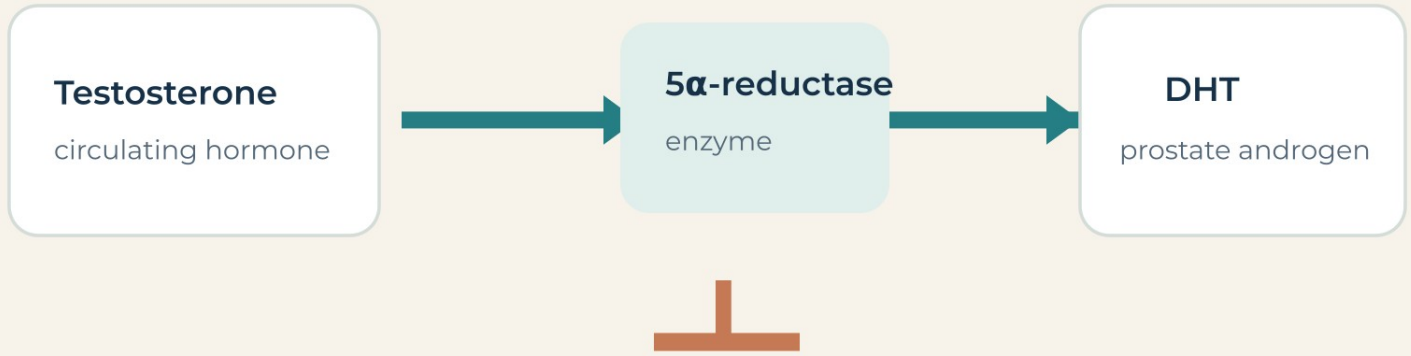
- **A** Alpha blockers
- **B** 5-ARIs
- **C** Tadalafil

Answer: B / 5-ARIs

Finasteride and dutasteride reduce conversion to DHT.

The DHT pathway

A simplified hormone pathway in prostate tissue



Finasteride / dutasteride block this conversion

Remember the clock

The hormonal effect is early. Symptom benefit is slow and best judged over months.

Five questions for the visit

01 Cause of symptoms?

02 Prostate size and risk?

03 Other medicines?

04 Side effect priorities?

05 When to review?

References & visual credits / 1

Source IDs printed on factual slides.

S04 European Association of Urology. Management of Non-neurogenic Male LUTS, 2026. Disease management §§5.2.1, 5.2.2, 5.2.5, 5.2.7.a.

https://uroweb.org/guidelines/management-of-non-neurogenic-male-luts/chapter/disease-management

S02 NIDDK. Enlarged Prostate (Benign Prostatic Hyperplasia) and anatomy media.

https://www.niddk.nih.gov/health-information/urologic-diseases/prostate-problems/enlarged-prostate-benign-prostatic-hyperplasia

NIDDK anatomy images credited to NIDDK, National Institutes of Health. EAU excerpt images credited to the EAU.

References & visual credits / 2

Clinical illustrations are original FBU diagrams; clinic scenes are illustrative AI-generated imagery.

S05 DailyMed. Tadalafil prescribing information, contraindications and interactions.

https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=82dfea4c-9fe5-438a-917f-8f7d395ee8ca

Image register

- EAU 2026 PDF excerpts: pages 21–23, 24, 27–28 and 30.
- NIDDK urinary tract and bladder anatomy images.
- Clinic scenes: illustrative AI-generated images, not actual patients.

NIDDK cystoscopic image: https://www.niddk.nih.gov/news/media-library/17957