RonanRx
PERSONALIZED MEDICINE

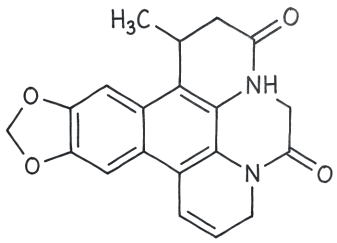
CLINICAL MONOGRAPH · SEXUAL HEALTH

Compounded Tadalafil

Long-acting PDE-5 inhibitor

Tadalafil is a prescription medicine for erectile dysfunction, symptoms of an enlarged prostate (BPH), and a serious lung-blood-pressure condition called pulmonary arterial hypertension [porst2003_duration; brock2002]. You may know it by the brand names Cialis (for ED and BPH) and Adcirca (for PAH); generic versions have been widely available since 2018.

What makes tadalafil different from other ED pills like sildenafil (Viagra) is how long it lasts. A single dose works for about 36 hours, and many men instead take a small dose every day. RonanRx can compound tadalafil into custom strengths, troches that dissolve under the tongue, or combination products when the standard pill doesn't fit a patient's needs, always on a doctor's prescription, never sold direct-to-consumer [forgue2007].



EVIDENCE POSTURE FDA APPROVED WELL STUDIED REVIEWED **2026-05-11**

State-licensed 503A | Pharmacist reviewed | Doctor led | Cold-chain ready | Patient choice preserved

Contents

Click any section to jump there. Page numbers update on render.

FOR CLINICIANS

Tadalafil is a selective reversible PDE5 inhibitor with a structurally distinct chemotype from sildenafil and vardenafil (Daugan 2003) [daugan2003a]. Mean terminal half-life is approximately 17.5 hours, supporting both an on-demand window of up to 36 hours and once-daily maintenance dosing. FDA approvals: Cialis on-demand (ED, 2003), Cialis once-daily 2.5/5 mg (ED, 2008), Adcirca 40 mg daily (PAH, 2009), Cialis 5 mg daily for BPH/LUTS (2011) and for concurrent BPH + ED (2012). Generic tadalafil entered the U.S. market in 2018.

Pivotal evidence: Brock 2002 integrated analyses (J Urol; n ≈ 1,112) established on-demand efficacy across IIEF-EF, SEP2, and SEP3 endpoints; Porst 2003 documented the 24- and 36-hour response window [brock2002]. Once-daily 5 mg efficacy and tolerability established in Rajfer 2007 / Porst 2008 long-term extension [porst2003_duration; porst2008_long_term]. PHIRST [galie2009_phirst] was the 16-week pivotal PAH RCT supporting Adcirca; PHIRST-2 extension [oudiz2012_phirst2] reported sustained 52-week effect; AMBITION [galie2015_ambition] supports initial ambrisentan + tadalafil combination in PAH [rajfer2007; forgue2007]. Safety includes class-wide absolute contraindication with any nitrate (mechanism: NO/cGMP potentiation; Kloner 2003), caution with alpha-blockers and antihypertensives, and CYP3A4-mediated interactions (ketoconazole, ritonavir/cobicistat, rifampin) [kloner2003_nitrate_time]. Distinctive vs sildenafil: higher rates of myalgia and back pain, proposed PDE11 cross-reactivity rejected at clinically relevant exposures in human PDE5/PDE11 selectivity work (Bischoff 2004) [bischoff2004_pde11].

Why Personalized Compounded Tadalafil

Tadalafil's commercial dose ladder, 2.5, 5, 10, and 20 mg tablets, was calibrated against phase III populations of men with ED and, separately, patients with BPH or pulmonary arterial hypertension. Those steps were not chosen for your tolerance, your age, your blood-pressure floor on an alpha-blocker, your CYP3A4 inhibitor load, or your kidney and liver function. A man who flushes hard at 5 mg has no manufactured step between zero and 2.5 mg. A patient titrating off finasteride for BPH may want a strength that sits between 2.5 and 5 mg. Tadalafil's 17.5-hour half-life means small dose differences compound across days of continuous therapy, which makes the missing rungs on the commercial ladder matter more, not less.

That is the work a compounding pharmacy does. A prescriber who knows your chart can write a 1.25 mg or 7.5 mg capsule for cautious daily titration, a sublingual troche that bypasses first-pass metabolism for a patient with GI absorption variability, or a low-excipient capsule for a patient sensitive to lactose or dye. Where a clinician is running a dual-PDE5 protocol, the same script can co-locate tadalafil and sildenafil in one preparation rather than asking the patient to time two manufactured products. The molecule is the same one the FDA reviewed in 2003. The strength, route, and combination are written for the patient on the label.

This is the older arrangement of pharmacy, the one that pre-dates mass manufacturing. A physician writes the prescription, a licensed pharmacist prepares it for that named patient, and a state board can audit the record. Modern oversight keeps it honest.

Quick Facts About Compounded Tadalafil

Category: Long-acting PDE-5 inhibitor

Active ingredient: Tadalafil, selective, reversible inhibitor of phosphodiesterase type 5 (PDE5); discovered as IC351

FDA-approved branded products: Cialis (erectile dysfunction, on-demand 2003 and once-daily 2008; BPH/LUTS 2011; combined BPH+ED 2012); Adcirca (pulmonary arterial hypertension, 2009). Generic tadalafil available since 2018.

Routes used in commercial product: Oral tablet (2.5, 5, 10, 20 mg)

Routes investigated in literature / 503A compounding: Oral, sublingual troche, orodispersible, compounded routes are formulation-individualized rather than separately FDA-approved

Plasma half-life: Approximately 17.5 hours, substantially longer than sildenafil (~4 h) or vardenafil (~4 h); supports the ~36-hour clinical response window and daily dosing

Evidence posture: Pivotal placebo-controlled trials in ED (on-demand and daily), BPH/LUTS, and PAH (PHIRST); long-term safety data; multiple meta-analyses

FDA-approval status: Manufactured Cialis, Adcirca, and generic tadalafil are FDA-approved. Compounded tadalafil preparations are not FDA-approved.

Compounded under: 503A, patient-specific prescription only, where the manufactured FDA-approved product is not clinically appropriate (dose individualization, route preference, excipient sensitivity, combination therapy)

Important compounding caution: Per FDA guidance, compounded versions of an FDA-approved drug are generally permissible only when the manufactured product cannot meet the patient's medical need. Generic tadalafil is widely available; compounded preparations are justified only when individualization (e.g., non-standard strengths, sublingual route, combination products) creates a documented clinical difference.

SPECIALS: PATIENT-SPECIFIC PRESCRIPTION ONLY

Compounded Tadalafil described in this monograph is a 503A compounded preparation. Every dose is made on a prescription, for a named patient, by a licensed pharmacist. It is not a stocked, mass-manufactured product.

- **Made to order, not off a shelf.** No batch sits in a warehouse waiting for buyers. Your prescription triggers the prep.
- **Named-patient label.** The bottle carries one patient's name. The batch records carry one prescription.
- **Dose, strength, and route chosen for the patient.** A prescriber decides what gets compounded, not a manufacturer who set the strength for a trial population.
- **Licensed pharmacist on the hook.** A real person, with a license that can be pulled, signs off on every prep. State inspectors check the facility.
- **Compounded drugs are not FDA-approved.** They should not be evaluated using branded-drug trial data alone. Availability varies by state and prescribed medication.

How This Differs from a Research-Use-Only Website

A research-use-only website ships a vial from a warehouse. There is no prescription, no pharmacist, no facility inspection, and no way to recall the product if something is wrong with it. If the vial is mislabeled, contaminated, or under-potent, there is nobody whose license is at stake.

A 503A compounding pharmacy is the other thing. The doctor writes the prescription. A licensed pharmacist, whose name is on the label, prepares the medicine in a facility the state inspects. If something goes wrong, there is a person and a license on the hook, and a documented chain of custody on every lot. That accountability is what makes it safe.

What is Compounded Tadalafil?

Tadalafil is a selective, reversible inhibitor of phosphodiesterase type 5 (PDE5), the enzyme that degrades cyclic guanosine monophosphate (cGMP) in vascular smooth muscle [daugan2003a; daugan2003b]. It was discovered at ICOS Corporation (originally as compound IC351) and licensed to Eli Lilly, with the medicinal-chemistry program published by Daugan and colleagues in 2003. Tadalafil's β-carboline scaffold is structurally distinct from sildenafil's pyrazolopyrimidinone and vardenafil's imidazotriazinone cores, and that structural difference underlies its much longer half-life.

Tadalafil received FDA approval in November 2003 as Cialis for on-demand treatment of erectile dysfunction [brock2002; porst2011_bph]. Subsequent approvals expanded its indications: once-daily dosing for ED (2008), PAH as Adcirca (2009), once-daily dosing for BPH/LUTS (2011), and once-daily dosing for concurrent BPH + ED (2012). Tadalafil lost U.S. patent exclusivity in 2017, 2018 and generic versions have been widely available since then.

Because generic tadalafil exists, RonanRx prepares compounded tadalafil only where the manufactured product cannot meet a documented patient-specific need, for example, custom strengths outside commercial tablets, sublingual or orodispersible troche formulations, excipient sensitivities, or combination products [galie2009_phirst; fda_essentially_a_copy]. It is not dispensed as a routine substitute for generic Cialis or Adcirca.

How Compounded Tadalafil Works

Sexual stimulation releases nitric oxide (NO) from cavernous nerves and endothelium in the corpus cavernosum. NO activates soluble guanylate cyclase, raising intracellular cGMP. cGMP triggers smooth-muscle relaxation in the cavernosal trabeculae and helicine arteries, allowing arterial inflow and venous occlusion, the mechanical basis of erection. PDE5 is the dominant cGMP-hydrolyzing enzyme in this tissue. Tadalafil inhibits PDE5 with high potency and selectivity, prolonging cGMP signaling so a given level of NO release produces a more durable smooth-muscle relaxation [corbin2002_pde5; rotella2002_pde5; forgue2007].

Tadalafil's pharmacologic distinction is duration. Its terminal half-life of approximately 17.5 hours is roughly 4× that of sildenafil or vardenafil. That kinetic property, not a different molecular mechanism, is the basis of the 36-hour clinical response window and the feasibility of once-daily dosing at 2.5, 5 mg [porst2003_duration].

PDE5 is also expressed in pulmonary vascular smooth muscle and in the prostate/lower urinary tract smooth muscle. Tadalafil at 40 mg daily reduces pulmonary vascular resistance in PAH (the Adcirca

indication), and at 5 mg daily relaxes bladder neck, prostate, and detrusor smooth muscle to improve BPH/LUTS symptoms [galie2009_phirst; porst2011_bph].

Biological Role of Compounded Tadalafil

The nitric-oxide / cGMP / PDE5 pathway is a fundamental smooth-muscle relaxation signaling axis. It operates in the corpus cavernosum (where it underlies erection), in pulmonary vascular smooth muscle (where chronic dysregulation contributes to pulmonary arterial hypertension), and in lower urinary tract smooth muscle including the prostate, bladder neck, and bladder body (where PDE5 inhibition reduces LUTS) [porst2011_bph].

Tadalafil does not initiate any of these signals, PDE5 inhibitors require endogenous NO release driven by sexual stimulation, hypoxic pulmonary vasoreactivity, or normal urinary-tract neural tone [corbin2002_pde5; rotella2002_pde5; rosen2002_pde5_review]. They potentiate an existing physiological signal by slowing cGMP degradation, which is why they have no effect on libido and only modestly affect resting hemodynamics in subjects without underlying disease.

Detailed Mechanism of Compounded Tadalafil

PDE5 hydrolyzes cGMP to 5'-GMP. Tadalafil binds the catalytic domain of PDE5 in a competitive, reversible manner with sub-nanomolar Ki [rotella2002_pde5, boswell_smith2006_pde]. Among the 11 mammalian phosphodiesterase families, PDE5 selectivity is the primary safety driver: PDE6 in retinal photoreceptors handles cGMP in phototransduction (sildenafil's mild blue-tinge effect reflects PDE6 cross-inhibition), and PDE11 is expressed in skeletal muscle, prostate, and testis [eardley2004_pde5_profiles]. Tadalafil shows relatively lower PDE6 cross-reactivity than sildenafil but higher PDE11 binding affinity in vitro than the other PDE5 inhibitors [ring2005_cyp3a4]. Cahill (2012) identified the specific PDE5 vs PDE6 active-site residues that account for tadalafil's PDE6-sparing, supplying the molecular basis for the lower rate of color-vision disturbance compared with sildenafil [cahill2012_pde11_binding] [daugan2003a; daugan2003b].

Whether tadalafil's distinctive adverse-event signature of myalgia and back pain (4, 10% in pivotal trials, vs 1, 2% with sildenafil) reflects PDE11 cross-inhibition has been investigated directly. Bischoff (2004) measured PDE5/PDE11 selectivity in human enzyme preparations at clinically relevant exposures and argued the data do not support a PDE11-mediated mechanism at therapeutic exposures [bischoff2004_pde11, bischoff2004_nonselectivity]. Weeks (2009) subsequently mapped the active-site residues that confer tadalafil's PDE11 affinity, including a critical Gln-869 hydrogen bond, providing a molecular footprint for the cross-reactivity question [weeks2009_pde11] [curran2003_pde5_pk]. The pathophysiology of the back-pain/myalgia signal remains incompletely characterized but is well established clinically [brock2002, porst2008_long_term].

Tadalafil is metabolized predominantly by CYP3A4 to a methylcatechol metabolite that is largely inactive at PDE5. Co-administration of strong CYP3A4 inhibitors (ketoconazole, ritonavir, cobicistat-boosted regimens) substantially increases tadalafil exposure; strong inducers (rifampin) reduce it. Renal and hepatic impairment also raise exposure [forgue2007], prompting label-driven dose reductions [forgue2007, forgue2006_healthy]. Population PK modeling in ED patients (Trocóniz/Wrishko 2007) supported the consistent across-population behavior that underpins simple label dosing [wrishko2009_population_pk].

Tadalafil's long terminal half-life (~17.5 h) versus sildenafil/vardenafil (~4 h) is a kinetic property of the molecule and its scaffold (β-carboline / hexahydropyrazino-pyridoindole-dione), not a different molecular mechanism of action [cahill2012_pde11_binding]. Tissue-level effects include endothelial-progenitor-cell signaling via CXCR4 [foresta2010_endothelial] and modulation of aromatase expression in human adipocytes in vitro [aversa2011_aromatase], mechanistic findings that do not yet translate to clinical indications but inform research interest in off-label cardiometabolic and endothelial contexts [foresta2010_endothelial, aversa2011_aromatase].

Compounded Tadalafil Research History

Tadalafil was developed by Glaxo Group Research / ICOS in the 1990s as part of a systematic PDE5 inhibitor medicinal-chemistry program seeking improved selectivity over PDE6 and longer duration of action than sildenafil, which Pfizer had brought to market as Viagra in 1998 [pisansky2014_radiotherapy] [vonburen2022_preference_realworld; montorsi2011_naive]. Daugan and colleagues published the two-part discovery paper in 2003 covering the hexahydropyrazinopyridoindole-dione chemotype and the lead optimization that yielded IC351 / tadalafil [daugan2003a, daugan2003b] [goldfischer2013_combined]. Curran 2003 (Drugs) and Eardley 2004 (Clin Cardiol) provided early profiles framing tadalafil's selectivity/PK distinctness relative to sildenafil and vardenafil [curran2003_pde5_pk, eardley2004_pde5_profiles] [eardley2005_preference].

Brock (2002) reported the integrated analysis of the first U.S. pivotal phase III ED program, demonstrating consistent IIEF-EF, SEP2, and SEP3 improvements vs placebo across the 5, 10, and 20 mg doses. Porst (2003) defined the 24- and 36-hour response window that became Cialis's commercial signature, and Rosen (2004) refined the onset profile down to as little as 16 minutes in some men [rosen2004_onset]. Skoumal (2004) added European population data with high treatment satisfaction [skoumal2004_on_demand] [gacci2016_pde5_update]. Padma-Nathan 2003 (Am J Cardiol) and Carson 2004 (BJU Int) consolidated the integrated safety case at approval [padmanathan2003_amjcardiol, carson2004_safety_update] [yuan2015_luts_network]. The molecule received its first FDA approval (on-demand ED) in November 2003.

The chronic daily-dosing program followed: Rajfer 2007 (US, Int J Impot Res), Porst 2006 (Eur Urol multicenter), Porst 2008 (J Sex Med long-term extension), Seftel 2009 (sexual relationship outcomes), Buvat 2008 (practical considerations), and Montorsi 2011 (PDE5-inhibitor-naive men) established efficacy

and safety of 2.5 mg and 5 mg once-daily in ED, leading to the 2008 FDA approval for daily dosing [brock2002; porst2003_duration] [porst2006_daily_rct]. Diabetic ED was specifically studied (Sáenz de Tejada 2002 on-demand; Hatzichristou 2008 daily) and SCI ED in Giuliano 2007 [saenz2002_diabetic, hatzichristou2008_diabetic, giuliano2007_sci]. Eardley 2005/2007 preference studies and Mulhall 2005 utilization data established the patient-preference rationale that drives much of the tadalafil clinical use case [eardley2007_factors_preference; mulhall2005_utilization; chen2015_luts_review].

The PAH program (PHIRST; Galiè 2009, Circulation) was the 16-week pivotal RCT in pulmonary arterial hypertension that supported the 2009 Adcirca approval; PHIRST-2 [oudiz2012_phirst2] reported the 52-week extension; Barst 2011 reported tadalafil added on to bosentan [galie2009_phirst, oudiz2012_phirst2, barst2011_phirst_addon] [maggiorini2006_hape]. AMBITION [galie2015_ambition] demonstrated superiority of initial ambrisentan + tadalafil combination therapy over either as monotherapy in PAH [yan2013_bph_meta; oelke2012_tamsulosin].

The BPH indication followed: Roehrborn 2008 (J Urol, dose-finding) and Porst's LVHJ trial (2011, Eur Urol) established the 5 mg daily dose and FDA approval for LUTS-BPH (2011); Oelke 2012 (Eur Urol) head-to-head vs tamsulosin established comparable efficacy; Egerdie 2012 supported the combined BPH+ED indication that followed in 2012 [porst2003_duration] [porst2008_long_term; buvat2008_daily]. Multiple subsequent meta-analyses [gacci2012_pde5_alpha] consolidated the BPH evidence base.

Beyond the FDA-approved indications, the post-2010 literature added rigorous trials of off-label uses: Schiopu 2009 and Shenoy 2010 in Raynaud (with Maltez 2023 Cochrane synthesis) [schiopu2009_raynaud, shenoy2010_raynaud, maltez2023_raynaud_cochrane]; Maggiorini 2006 in HAPE prevention; REACTT [montorsi2014_reactt] on post-prostatectomy rehabilitation [montorsi2014_reactt, brock2015_reactt_morning_erections, mulhall2016_reactt_followup]; Pisansky 2014 RTOG 0831 on prevention during prostate radiotherapy (negative trial); Caruso 2012 on female sexual arousal in type-1 diabetes; and Palmieri 2012 on Peyronie's disease [pisansky2014_radiotherapy; caruso2012_fsad_t1d; palmieri2012_peyronie]. Network meta-analyses [madeira2021_network_meta] provide comparative rankings across PDE5 inhibitors [madeira2021_network_meta, liao2019_diabetic_meta, tienforti2025_sci_meta]. Tadalafil's U.S [roehrborn2008_bph_dose; porst2011_bph; egerdie2012_combined]. compound patent expired in 2017 and use-patent in 2018; generic tadalafil has been widely available since then, which is the central context for any 503A compounded preparation [ljunggren2008_preference; rajfer2007; seftel2009_daily]. The post-generic era has continued to add orodispersible-formulation PK and efficacy data [park2018_orodispersible_pk] relevant to compounded alternate-route preparations [park2018_orodispersible_pk, motawi2024_odf_vs_tablet].

Compounded Tadalafil Timeline

1990s • ICOS / Glaxo medicinal-chemistry program targets PDE5 inhibitors with improved selectivity over PDE6 and longer half-life than sildenafil

2002 • Brock et al publish integrated analyses of the pivotal phase III on-demand ED program in J Urol [brock2002]

2002 • Corbin & Francis publish landmark PDE5 pharmacology review [corbin2002_pde5]

2003 • Daugan et al publish two-part medicinal-chemistry discovery account of tadalafil (IC351) in J Med Chem [daugan2003a; daugan2003b]

2003 • Porst et al define the 24- and 36-hour response window for on-demand tadalafil (Urology) [porst2003_duration]

2003 • Kloner et al publish time-course of the tadalafil, nitrate interaction (JACC) [kloner2003_nitrate_time]

2002 • Sáenz de Tejada et al publish first pivotal trial of tadalafil in diabetic ED (Diabetes Care) [saenz2002_diabetic]

2003 • FDA approves Cialis (tadalafil) for on-demand treatment of erectile dysfunction

2003 • Curran & Keating publish first comprehensive tadalafil profile (Drugs) [curran2003_pde5_pk]

2004 • Bischoff publishes biochemical PDE5/PDE11 selectivity analysis in IJIR [bischoff2004_pde11]

2004 • Carson publishes integrated safety update of tadalafil clinical-development program (BJU Int) [carson2004_safety_update]

2004 • Rosen et al demonstrate tadalafil erectogenic effect within 16, 30 minutes in some men (J Sex Med) [rosen2004_onset]

2005 • Ring et al publish CYP3A4 in vitro and in vivo data on tadalafil clearance (Clin Pharmacol Ther) [ring2005_cyp3a4]

2005 • Eardley et al publish open-label crossover preference trial vs sildenafil (BJU Int) [eardley2005_preference]

2006 • Porst et al publish multicenter once-a-day 5/10 mg tadalafil RCT in ED (Eur Urol) [porst2006_daily_rct]

- **2006** • Maggiorini et al show tadalafil and dexamethasone reduce HAPE incidence in a high-altitude RCT (Ann Intern Med) [maggiorini2006_hape]
- **2007** • Forgue et al characterize tadalafil PK across gender, age, diabetes, renal and hepatic impairment [forgue2007]
- **2007** • Rajfer et al publish U.S [rajfer2007]. once-daily tadalafil RCT (Int J Impot Res)
- **2007** • Giuliano et al publish tadalafil RCT in spinal cord injury ED (Arch Neurol) [giuliano2007_sci]
- **2008** • Roehrborn et al publish tadalafil 2.5/5/10/20 mg dose-finding study in LUTS-BPH (J Urol) [roehrborn2008_bph_dose]
- **2008** • Hatzichristou et al publish once-daily tadalafil RCT in diabetic ED (Diabet Med) [hatzichristou2008_diabetic]
- **2008** • Porst publishes long-term safety and efficacy of tadalafil 5 mg once-daily (J Sex Med); FDA approves once-daily dosing for ED [porst2008_long_term]
- **2009** • Galiè et al publish PHIRST trial of tadalafil in pulmonary arterial hypertension (Circulation); FDA approves Adcirca (40 mg daily) for PAH [galie2009_phirst]
- **2009** • Schiopu et al publish crossover RCT of tadalafil in scleroderma Raynaud (J Rheumatol) [schiopu2009_raynaud]
- **2009** • Tsertsvadze et al publish AHRQ systematic review and meta-analysis of PDE5 inhibitors (Ann Intern Med) [tsertsvadze2009_meta]
- **2009** • Weeks et al map PDE11 active-site residues responsible for tadalafil affinity (JPET) [weeks2009_pde11]
- **2010** • Shenoy et al publish tadalafil crossover RCT in refractory secondary Raynaud (Rheumatology) [shenoy2010_raynaud]
- **2011** • Porst et al publish LVHJ trial, tadalafil 5 mg daily for BPH/LUTS (Eur Urol); FDA approves Cialis for BPH/LUTS [porst2011_bph]
- **2011** • Montorsi et al publish RCT of once-daily tadalafil in PDE5-inhibitor-naive men (J Sex Med) [montorsi2011_naive]
- **2012** • Oudiz et al publish PHIRST-2 52-week extension of tadalafil in PAH (JACC) [oudiz2012_phirst2]
- **2012** • FDA approves Cialis 5 mg daily for the combined BPH + ED indication

2012 • Gacci et al publish systematic review and meta-analysis of PDE5 inhibitors (alone and with α-blockers) for LUTS (Eur Urol) [gacci2012_pde5_alpha]

2012 • Oelke et al publish RCT of tadalafil vs tamsulosin for LUTS-BPH (Eur Urol) [oelke2012_tamsulosin]

2014 • Montorsi et al publish REACTT, tadalafil for post-prostatectomy erectile rehabilitation (Eur Urol) [montorsi2014_reactt]

2014 • Pisansky et al publish RTOG 0831, negative trial of tadalafil for ED prevention during prostate radiotherapy (JAMA) [pisansky2014_radiotherapy]

2015 • Galiè et al publish AMBITION, initial ambrisentan + tadalafil in PAH (NEJM) [galie2015_ambition]

2016 • Pomeranz publishes critical review of the PDE5, NAION relationship (J Neuroophthalmol) [pomeranz2016_naion_review]

2018 • Generic tadalafil enters U.S. market following expiration of use-patent

2018 • AUA publishes erectile dysfunction guideline that anchors tadalafil among first-line PDE5 inhibitor options (Burnett et al, J Urol) [burnett2018_aua_ed]

2021 • AUA publishes BPH guideline Part I (Lerner et al, J Urol), placing tadalafil among recommended pharmacotherapies for LUTS-BPH [lerner2021_aua_bph]

2022 • Etminan et al publish JAMA Ophthalmology cohort study on PDE5 inhibitor ocular adverse events [etminan2022_ocular_jama]

2023 • Maltez et al publish Cochrane review of PDE5 inhibitors for Raynaud phenomenon [maltez2023_raynaud_cochrane]

Clinical Contexts for Compounded Tadalafil

Erectile dysfunction, on-demand dosing FDA APPROVED

FDA-approved indication for the manufactured product.

Approved 2003 for on-demand 10, 20 mg doses [skoumal2004_on_demand]. Brock (2002) integrated analyses of three placebo-controlled phase III trials (n ≈ 1,112) demonstrated mean IIEF-EF improvements of approximately 7, 8 points vs placebo, with successful intercourse rates (SEP3) increased by roughly 40 percentage points at the 20 mg dose [brock2002] [wespes2006_eau]. Porst (2003) demonstrated that successful intercourse remained substantially above placebo at both 24 and 36 hours after dosing, defining the commercial '36-hour window' framing [porst2003_duration; rosen2004_onset; carson2004_safety_update].

Branded product: Cialis (Eli Lilly; generic since 2018)

Erectile dysfunction, once-daily dosing FDA APPROVED

FDA-approved indication for the manufactured product.

Approved 2008 for 2.5 mg or 5 mg once-daily continuous dosing. Rajfer (2007) and the multicenter trial by Porst (2006, Eur Urol) established efficacy of 5 mg and 10 mg once-daily; Porst (2008, J Sex Med) provided two-year extension safety and efficacy data [rajfer2007; porst2006_daily_rct; porst2008_long_term]. Daily dosing decouples timing of dose from timing of intercourse and yields a steady-state cGMP-protective environment some patients prefer over on-demand dosing [buvat2008_daily; seftel2009_daily] [montorsi2011_naive].

Branded product: Cialis 2.5/5 mg daily (Eli Lilly; generic)

Pulmonary arterial hypertension (WHO Group 1 PAH) FDA APPROVED

FDA-approved indication as Adcirca.

Approved 2009 at 40 mg daily as Adcirca. PHIRST [galie2009_phirst] demonstrated 33-meter placebo-adjusted improvement in 6-minute walk distance at 40 mg/day, with improvements in time-to-clinical-worsening. PHIRST-2 extension [oudiz2012_phirst2] reported sustained effect at 52 weeks. AMBITION [galie2015_ambition] supports initial combination with ambrisentan over monotherapy [barst2011_phirst_addon].

Branded product: Adcirca (now generic tadalafil 20 mg for PAH)

Benign prostatic hyperplasia / lower urinary tract symptoms (BPH/LUTS) FDA APPROVED

FDA-approved indication for the manufactured product.

Approved 2011 at 5 mg daily after the Roehrborn 2008 (J Urol) dose-finding study (2.5/5/10/20 mg) settled on 5 mg as the labeled BPH dose [roehrborn2008_bph_dose]. Porst's LVHJ trial (2011, Eur Urol; n = 1,058) demonstrated mean IPSS improvement of approximately 2.0, 2.4 points beyond placebo at 12 weeks [porst2011_bph]. Oelke 2012 demonstrated comparable IPSS efficacy to tamsulosin with the additional ED benefit [oelke2012_tamsulosin; gacci2016_pde5_update]. Systematic reviews and network meta-analyses [gacci2012_pde5_alpha] consolidated efficacy across the multi-trial program [yuan2015_luts_network]. Mechanism in LUTS is thought to involve PDE5-mediated smooth-muscle relaxation in prostate, bladder neck, and bladder body, plus pelvic vascular effects. Tadalafil is one of the recommended pharmacotherapies in the AUA 2021 BPH guideline (Lerner et al) [yan2013_bph_meta; chen2015_luts_review; lerner2021_aua_bph].

Branded product: Cialis 5 mg daily for BPH (now generic tadalafil)

Concurrent BPH and erectile dysfunction FDA APPROVED

FDA-approved indication for the combined population (2012).

Approved 2012 at 5 mg daily for men with both BPH/LUTS and ED. Egerdie (2012) and Goldfischer (2013) demonstrated improvements in both IPSS and IIEF-EF in sexually active men with both conditions, supporting the combined indication rather than parallel mono-therapies [goldfischer2013_combined] [lerner2021_aua_bph]. AUA's 2018 ED and 2021 BPH guidelines both reference tadalafil as a recommended option in the overlapping population [egerdie2012_combined; porst2011_bph; burnett2018_aua_ed].

Branded product: Cialis 5 mg daily

Off-Label Uses of Compounded Tadalafil

Raynaud phenomenon secondary to systemic sclerosis WELL STUDIED

Off-label use with small RCT and Cochrane meta-analysis support; appropriate as a clinician-directed trial in patients with severe or refractory disease.

Schiopu 2009 (J Rheumatol) ran a placebo-controlled crossover trial of tadalafil 20 mg every other day in 39 women with scleroderma-spectrum disease and showed no improvement in primary Raynaud Condition Score endpoints, though some secondary measures favored tadalafil [schiopu2009_raynaud]. Shenoy 2010 (Rheumatology Oxford) ran a double-blind crossover trial of tadalafil 20 mg every other day in 24 patients with secondary Raynaud resistant to vasodilator therapy and reported reduced frequency, duration, and severity of attacks [shenoy2010_raynaud]. The Maltez 2023 Cochrane review concluded that PDE5 inhibitors as a class produce small but statistically significant reductions in Raynaud attack frequency and severity, with tadalafil-specific data underpowered relative to sildenafil [maltez2023_raynaud_cochrane]. Off-label use is established in rheumatology practice for severe or refractory secondary Raynaud, often after a sildenafil trial.

High-altitude pulmonary edema (HAPE) prevention EMERGING

Off-label, single pivotal RCT plus mechanistic context. Use is occasional/individualized rather than guideline-recommended.

Maggiorini 2006 (Ann Intern Med) randomized 29 climbers with prior HAPE history to placebo vs tadalafil 10 mg twice daily vs dexamethasone 8 mg twice daily during a rapid ascent to 4,559 m. Both tadalafil and dexamethasone reduced the incidence of HAPE relative to placebo (tadalafil group: ~1/9 vs placebo 7/10), supporting the pharmacologic premise that PDE5 inhibition blunts hypoxic pulmonary vasoconstriction [maggiorini2006_hape]. Sample size is small and tadalafil is not part of routine altitude prophylaxis recommendations; it is sometimes used as an individualized clinician-directed option for prior-HAPE climbers.

Penile rehabilitation after radical prostatectomy WELL STUDIED

Off-label/contested. Large RCT (REACTT) did not show durable benefit on unassisted erectile function after washout.

REACTT [montorsi2014_reactt] randomized 422 men post-bilateral-nerve-sparing prostatectomy to tadalafil 5 mg once daily, tadalafil 20 mg on demand, or placebo for 9 months, with a 6-week drug-free washout and a 3-month open-label extension. The primary endpoint (unassisted IIEF-EF at end of washout) did not significantly favor active treatment. Brock 2015 (Urology) reported preserved penile length and improved morning erections with once-daily tadalafil [brock2015_reactt_morning_erections]. Mulhall 2016 (J Sex Med, REACTT follow-up) confirmed similar return-to-baseline erectile function across arms after washout [mulhall2016_reactt_followup]. The post-prostatectomy rehabilitation rationale remains a topic of clinical debate; many surgeons use daily tadalafil clinically despite the absence of a durable RCT-proven effect.

Erectile dysfunction prevention during prostate radiotherapy WELL STUDIED

Off-label/negative. Large RCT (RTOG 0831) was negative on the primary endpoint.

Pisansky 2014 (JAMA, RTOG 0831) randomized 242 men receiving prostate radiotherapy to tadalafil 5 mg daily vs placebo for 6 months [pisansky2014_radiotherapy]. The primary endpoint (proportion with IIEF spontaneous erectile function preservation at 28, 30 weeks) did not differ between groups. Off-label use as a preventive strategy during radiotherapy is not supported by the trial.

Peyronie's disease EMERGING

Off-label, single small RCT in combination with shockwave therapy. Evidence is preliminary.

Palmieri 2012 (Int J Androl) randomized 100 men with stable-phase Peyronie's disease and ED to extracorporeal shock wave therapy with vs without tadalafil 5 mg daily for 12 weeks [palmieri2012_peyronie]. Combination therapy showed greater improvement in IIEF-EF and reduction in pain than shock wave alone, without significant difference in penile curvature. Off-label use as an adjunct to disease-directed Peyronie therapy is reported but not guideline-recommended as monotherapy for plaque or curvature.

Female sexual arousal disorder EMERGING

Off-label, very limited evidence. A small RCT in type-1 diabetic premenopausal women suggested benefit; broader populations not established.

Caruso 2012 (J Sex Med) ran a 12-week placebo-controlled trial of tadalafil 5 mg daily in type-1 diabetic premenopausal women with sexual arousal disorder and reported improvements in genital arousal and Female Sexual Function Index domain scores [caruso2012_fsad_t1d]. The broader female sexual dysfunction literature with PDE5 inhibitors has been mixed; routine off-label use is not endorsed by guidelines, and any compounded female-indication product should be framed as physician-directed individualized therapy rather than standard of care.

Spinal cord injury erectile dysfunction WELL STUDIED

Strong RCT support; not a separate FDA indication but well-studied within the ED population.

Giuliano 2007 (Arch Neurol) randomized 186 men with chronic spinal cord injury and ED to tadalafil 10 or 20 mg on demand vs placebo for 12 weeks [giuliano2007_sci]. Tadalafil produced large IIEF-EF improvements and high SEP3 rates with favorable tolerability. The Lewis 2005 clinical-populations review confirmed efficacy across SCI, diabetes, and post-prostatectomy subgroups [lewis2005_clinical_pops]. Tienforti 2025 (Andrology) network meta-analysis ranked tadalafil and sildenafil as the most effective PDE5 inhibitors in SCI-related ED, with tadalafil's longer window of effect favored in some patients [tienforti2025_sci_meta].

FDA-Approved Uses of Compounded Tadalafil

Brand	Indication	Year	Route
Cialis (on-demand)	Erectile dysfunction, as-needed dosing 10, 20 mg	2003	Oral tablet
Cialis (once-daily)	Erectile dysfunction, continuous once-daily dosing 2.5, 5 mg	2008	Oral tablet
Adcirca	Pulmonary arterial hypertension (WHO Group 1), 40 mg once daily	2009	Oral tablet
Cialis for BPH/LUTS	Benign prostatic hyperplasia / lower urinary tract symptoms, 5 mg once daily	2011	Oral tablet
Cialis for combined BPH + ED	Concurrent BPH/LUTS and erectile dysfunction, 5 mg once daily	2012	Oral tablet

Tadalafil has five distinct FDA-approved indications under three branded labels, all manufactured originally by Eli Lilly. Cialis covers ED (on-demand and daily), BPH/LUTS, and the combined BPH + ED

population; Adcirca covers PAH at the 40 mg/day dose. Generic tadalafil has been widely available since 2018 across these doses (2.5, 5, 10, 20 mg tablets, plus 20 mg for PAH dosing) [brock2002] [rajfer2007; galie2009_phirst].

Because generic tadalafil exists at every FDA-approved dose, compounded preparations are not interchangeable with the FDA-approved generic and are only appropriate when an identified patient cannot use the manufactured product (excipient sensitivity, route preference such as a sublingual troche, custom strength outside the commercial range, or a clinically justified combination product) [porst2011_bph; goldfischer2013_combined; fda_essentially_a_copy].

Compounded Compounded Tadalafil (503A)

Generic tadalafil is widely available in the U.S. at every FDA-approved strength (2.5, 5, 10, 20 mg oral tablets). The 503A compounding case for tadalafil is therefore narrow: a documented patient-specific clinical reason that the manufactured product cannot meet. Common reasons include excipient sensitivity, route individualization (sublingual troche for patients who prefer not to swallow tablets, or who experience GI absorption variability), custom strengths between or below commercial dose steps (for cautious titration in older patients, mild renal/hepatic impairment, or interacting medications), and combination products that bundle tadalafil with other compounded actives.

Some men's-health protocols pair tadalafil with oxytocin or other actives in compounded troches. The evidence base for such combinations is limited; the tadalafil-monotherapy literature does not directly support combination claims, and RonanRx treats those preparations as physician-directed individualized therapy rather than evidence-based standard of care. Patients should be counseled on what is and is not established for combination preparations.

Per FDA guidance, a compound that is 'essentially a copy' of a commercially available drug is generally restricted unless a prescriber documents a clinical difference for the identified patient [fda_essentially_a_copy]. Routine compounding of 5 mg or 20 mg tadalafil capsules without such documentation is outside the 503A compliance posture [fda503a]. RonanRx's pharmacist review applies that criterion to every tadalafil prescription.

Compounded Tadalafil Formulations and Routes

Form	Concentration	Description
Sublingual troche (compounded)	Custom (commonly 5, 20 mg)	Compounded under USP <795> non-sterile pharmaceutical compounding. Sublingual route bypasses first-pass metabolism; PK is not bioequivalent to the manufactured oral tablet.

Form	Concentration	Description
Oral capsule (compounded, custom strength)	Custom (between commercial strengths or off-label dose titration)	Used where a prescriber documents a clinical reason for a strength outside the commercial 2.5/5/10/20 mg ladder.
Compounded combination preparation	Custom per prescription	Combination troches or capsules bundling tadalafil with other physician-directed actives. Evidence quality varies; framed as individualized therapy.

Routes used in published literature: oral, sublingual, troche.

Compounded Tadalafil Dosing

Route	Population	Range	Duration	Study type
Oral (on-demand, ED)	Adult men with erectile dysfunction	10 mg approximately 30 minutes before anticipated sexual activity; adjustable to 5 mg or 20 mg based on response and tolerability; maximum one dose per day	As needed; no more than once daily	FDA-approved labeling derived from Brock 2002 phase III program
Oral (once-daily, ED)	Adult men with erectile dysfunction electing continuous therapy	2.5 mg or 5 mg once daily at approximately the same time each day	Indefinite while clinically beneficial	FDA-approved labeling derived from Porst 2008 long-term extension and the once-daily program
Oral (PAH, Adcirca)	Adults with WHO Group 1 pulmonary arterial hypertension	40 mg once daily (two 20 mg tablets)	Indefinite while clinically beneficial	FDA-approved labeling derived from the PHIRST RCT
Oral (BPH/LUTS or combined BPH + ED)	Adult men with BPH/LUTS, with or without concurrent ED	5 mg once daily at approximately the same time each day	Indefinite while clinically beneficial; reassess symptom response at 12 weeks	FDA-approved labeling derived from the Porst 2011 LVHJ trial and combined-indication studies
Oral (renal impairment)	CrCl 30, 50 mL/min	On-demand: start 5 mg, maximum 10 mg every 48 hours. Once-daily: not	Per indication	FDA-label population-specific guidance informed

Route	Population	Range	Duration	Study type
		recommended below CrCl 30. PAH: start 20 mg daily, may titrate to 40 mg.		by Forgue 2007 PK data
Oral (hepatic impairment)	Mild to moderate (Child-Pugh A or B)	On-demand: maximum 10 mg per dose. Once-daily and PAH dosing not recommended in severe hepatic impairment (Child-Pugh C).	Per indication	FDA-label population-specific guidance informed by Forgue 2007 PK data
Oral (concomitant CYP3A4 inhibitor)	Adults on ritonavir, cobicistat, ketoconazole, itraconazole, or similar strong CYP3A4 inhibitors	On-demand: maximum 10 mg per 72 hours. Once-daily: not recommended.	While concomitant therapy continues	FDA-label drug-interaction guidance informed by Ring 2005 in vitro / in vivo data

Doctor-prescribed and titrated. The on-demand regimen optimizes peak effect for sexual activity within a 36-hour window; the once-daily regimen optimizes patient experience by decoupling timing of dose from timing of intercourse. PAH dosing at 40 mg is structurally different from ED and BPH dosing and should not be confused with the lower-dose regimens [brock2002; porst2008_long_term; galie2009_phirst].

Compounded preparations should mirror the labeled dose ranges unless the prescriber documents a patient-specific reason otherwise. Doses listed reflect FDA-approved labeling and published clinical-trial protocols, not RonanRx prescribing recommendations [porst2011_bph; forgue2007].

Compounded Tadalafil Safety

Tadalafil's safety profile is well-characterized across more than two decades of clinical use spanning ED, BPH/LUTS, and PAH populations [14][12]. Most common adverse events are headache, dyspepsia, back pain, myalgia, nasal congestion, and flushing, the back pain and myalgia signal (4, 10% across pivotal trials) is distinctive vs sildenafil and vardenafil, which produce more flushing and visual disturbance instead [6][9]. The Tsertsvadze 2009 AHRQ systematic review and Madeira 2021 network meta-analysis both rank tadalafil's overall tolerability as comparable to other PDE5 inhibitors [7][36][1] [35].

The defining safety constraint is the absolute contraindication with any nitrate (organic nitrates for angina, recreational 'poppers' / amyl nitrite, sodium nitroprusside). Co-administration produces profound, potentially fatal hypotension via additive cGMP-mediated vasodilation; Kloner (2003) characterized the time course of the tadalafil, nitrate interaction directly [17][18]. Caution is also required with α-adrenergic blockers (additive orthostatic hypotension; Kloner 2005), with strong CYP3A4 inhibitors (markedly

increased tadalafil exposure; Ring 2005), and with guanylate cyclase stimulators such as riociguat (additive vasodilation, contraindicated combination) [19][20] [69].

Class-wide post-marketing signals include rare reports of non-arteritic anterior ischemic optic neuropathy (NAION), sudden sensorineural hearing loss, and priapism [3][37][0]. Causal attribution remains debated for NAION and hearing loss; the post-marketing reviews by Pomeranz, Campbell, Nathoo, and Laties have triangulated case-series and epidemiologic data and consistently noted that affected patients commonly have vasculopathic risk factors [7][2]. Etminan 2022 (JAMA Ophthalmology) reported a small but statistically increased risk of serous retinal detachment, retinal vascular occlusion, and ischemic optic neuropathy in regular PDE5 inhibitor users compared with non-users in a U.S [69] [71]. insurance-claims cohort. Priapism is rare with tadalafil specifically and is more characteristically a class concern at higher exposures [8][3][4].

Contraindications

Tadalafil is contraindicated in: any concurrent or recent use of organic nitrates (any form, any indication, any route, risk of life-threatening hypotension); concurrent use of guanylate cyclase stimulators such as riociguat; known hypersensitivity to tadalafil or any excipient; and, per the standard PDE5 inhibitor labeling, patients in whom sexual activity is inadvisable due to underlying cardiovascular disease [17]. Patients with significant hepatic impairment (Child-Pugh C) or with recent stroke or MI within 90 days should generally not receive once-daily tadalafil; on-demand use in cardiovascular populations should follow the cardiac risk stratification of the Princeton consensus [18].

Drug interactions

Nitrates: absolute contraindication. The tadalafil, nitrate hemodynamic interaction persists for at least 48 hours after a tadalafil dose, longer than the comparable window for sildenafil. The Kloner 2003 time-course study established the basis for the 48-hour interval that the Cialis label still observes.

Alpha-adrenergic blockers (doxazosin, terazosin, alfuzosin, tamsulosin, silodosin): additive blood-pressure lowering. The Kloner cardiovascular safety reviews and the alpha-blocker interaction analyses describe a generally manageable interaction with appropriate stabilization on the alpha-blocker first, but symptomatic hypotension can occur particularly with non-selective agents [17][18][19]. Combined PDE5 + alpha-blocker therapy in BPH is reviewed in Gacci 2012.

Strong CYP3A4 inhibitors (ritonavir, cobicistat, ketoconazole, itraconazole, clarithromycin): substantially increase tadalafil exposure. Once-daily tadalafil is not recommended with strong CYP3A4 inhibitors; on-demand dosing is capped at 10 mg per 72 hours [13]. CYP3A4 inducers (rifampin, carbamazepine, phenytoin, St John's wort): reduce tadalafil exposure and may reduce efficacy.

Other antihypertensives, alcohol, and grapefruit juice: each may modestly potentiate the hypotensive or PK effects of tadalafil; clinical relevance is usually low at typical doses but should be discussed [20].

Adverse events

Across the pivotal ED program [1], the most common treatment-emergent adverse events with tadalafil vs placebo were headache (11, 15% vs 5%), dyspepsia (7, 10% vs 1%), back pain (5, 6% vs 3%), myalgia (3, 5% vs 1%), nasal congestion (3, 5% vs 1%), and flushing (1, 3% vs 1%) [13435]. The back pain / myalgia signal is the most distinctive vs sildenafil and is characteristically delayed in onset (12, 24 hours after dose), consistent with tadalafil's long half-life. In the once-daily extension program [4], the same adverse-event pattern was observed with cumulative discontinuation rates of approximately 5, 8% over up to two years [438].

In PAH (PHIRST), adverse events with 40 mg daily were broadly consistent with the ED profile, with headache, myalgia, flushing, nasopharyngitis, and limb pain most common [89 69]. In BPH [12], the safety profile at 5 mg daily was similar to placebo for most events with the characteristic headache/dyspepsia/myalgia signal still present; the head-to-head against tamsulosin showed similar overall discontinuation rates [123940]. The Tsertsvadze 2009 AHRQ meta-analysis and Madeira 2021 network meta-analysis quantitatively place tadalafil's tolerability in the same range as sildenafil, vardenafil, and avanafil [7361].

Rare but important post-marketing signals: non-arteritic anterior ischemic optic neuropathy (NAION), class labeling for PDE5 inhibitors, with Campbell 2015 and Nathoo 2015 case-control analyses suggesting a small but statistically detectable risk increase and Etminan 2022 (JAMA Ophthalmol) extending that signal to other ocular adverse events in a large U.S [337071]. claims cohort; sudden decrease or loss of hearing, class labeling, with no tadalafil-specific signal that diverges from the class; priapism > 4 hours, rare, mainly reported with sildenafil in case series but addressed in class labeling. Patients should be counseled to discontinue and seek care for sudden vision or hearing changes or for erection > 4 hours [72].

Monitoring Compounded Tadalafil Therapy

Baseline: review of nitrate use (every form, every indication), guanylate cyclase stimulator use, alpha-blocker regimen and stability, complete medication review for CYP3A4 modulators, blood pressure, cardiac risk stratification per Princeton consensus for ED patients, and renal/hepatic function where dose adjustment may apply.

On therapy: response assessment at 4, 12 weeks depending on indication (IIEF-EF / SEP3 for ED, IPSS / Qmax for BPH, 6-minute walk distance and functional class for PAH). Inquire about back pain, myalgia, and any new visual or auditory symptoms at follow-up [porst2011_bph]. No routine laboratory monitoring is required for ED or BPH dosing; PAH patients undergo broader PAH-program monitoring under their pulmonary hypertension specialist [porst2008_long_term; galie2009_phirst; kloner2005_cardiovascular].

Compounded Tadalafil Evidence Quality

Evidence supporting tadalafil is strong across all four FDA-approved indications [fda_essentially_a_copy] [porst2006_daily_rct; porst2008_long_term; weeks2009_pde11; montorsi2014_reactt]. ED: multiple placebo-controlled RCTs [brock2002] with consistent IIEF-EF, SEP2, and SEP3 effects, plus the AHRQ systematic review [tsertsvadze2009_meta] and the Madeira 2021 network meta-analysis [yuan2015_luts_network; shenoy2010_raynaud; liao2019_diabetic_meta]. PAH: PHIRST [galie2009_phirst] plus its 52-week extension [oudiz2012_phirst2], Barst 2011 add-on, and the AMBITION trial [galie2015_ambition] [maltez2023_raynaud_cochrane; ljunggren2008_preference]. BPH/LUTS: Roehrborn 2008 dose-finding plus Porst 2011 LVHJ pivotal trial, Oelke 2012 vs tamsulosin head-to-head, and successive meta-analyses [gacci2012_pde5_alpha] [porst2011_bph; gacci2016_pde5_update; cahill2012_pde11_binding; tienforti2025_sci_meta]. Combined BPH + ED: Egerdie 2012 and Goldfischer 2013 [egerdie2012_combined, goldfischer2013_combined] [madeira2021_network_meta; saenz2002_diabetic]. Tadalafil is reflected in current AUA guidelines for both ED [burnett2018_aua_ed] and BPH [lerner2021_aua_bph] [burnett2018_aua_ed, lerner2021_aua_bph] [brock2015_reactt_morning_erections].

Off-label evidence is mixed in quality: solid single-trial support for HAPE prevention [maggiorini2006_hape], Raynaud [schiopu2009_raynaud], diabetic ED (Sáenz de Tejada 2002; Hatzichristou 2008; Liao 2019 network MA), SCI ED [giuliano2007_sci], and Peyronie's adjunct therapy [palmieri2012_peyronie]; a single small RCT in type-1 diabetic female sexual arousal disorder [caruso2012_fsad_t1d]; and notably-negative or contested data for post-prostatectomy rehabilitation (REACTT: Montorsi 2014, Brock 2015, Mulhall 2016) and radiotherapy ED prevention [pisansky2014_radiotherapy] [fda_essentially_a_copy]. Mechanism evidence is anchored in the Daugan discovery papers, the Rotella 2002 PDE5 review, Bischoff 2004 selectivity, Weeks 2009 and Cahill 2012 active-site analyses, Ring 2005 CYP3A4, and the Forgue/Trocóniz PK papers [montorsi2011_naive; rosen2004_onset; skoumal2004_on_demand; bischoff2004_pde11].

Evidence specifically supporting compounded tadalafil preparations (sublingual troches, custom-strength capsules, combination products) is sparse [fda_essentially_a_copy] [porst2003_duration; rajfer2007; ring2005_cyp3a4; mulhall2016_reactt_followup]. The mechanism, PK behavior, and safety profile of tadalafil are well-characterized from the FDA-approved manufactured product; orodispersible-film bioequivalence and short-term efficacy data exist [park2018_orodispersible_pk] and provide some PK reassurance for non-tablet routes [park2018_orodispersible_pk, motawi2024_odf_vs_tablet] [forgue2006_healthy; mulhall2005_utilization]. Bioequivalence of pharmacy-compounded sublingual troches or custom-strength capsules to the labeled tablet cannot be assumed, however [daugan2003a; daugan2003b; rotella2002_pde5; hatzichristou2008_diabetic]. Where a compounded preparation is prescribed, it should reflect a documented patient-specific clinical need rather than substitution for generic tadalafil [oelke2012_tamsulosin; chen2015_luts_review; barst2011_phirst_addon; forgue2007;

vonburen2022_preference_realworld]. Patient preference data [eardley2005_preference] consistently identify the 36-hour window as the primary reason a patient prefers tadalafil over sildenafil [roehrborn2008_bph_dose; yan2013_bph_meta; wrishko2009_population_pk; eardley2007_factors_preference].

Major Compounded Tadalafil Clinical Studies

Study	Design	Participants	Duration	Finding
Efficacy and safety of tadalafil for the treatment of erectile dysfunction: results of integrated analyses (Brock 2002, J Urol)	Integrated analysis of three randomized double-blind placebo-controlled phase III trials	1112	12 weeks	Tadalafil 10 and 20 mg on-demand produced mean IIEF-EF improvements of approximately 7, 8 points vs placebo; SEP3 (successful intercourse) rates increased by ~40 percentage points at 20 mg [brock2002]. Headache, dyspepsia, back pain, myalgia most common AEs.
Efficacy of tadalafil for the treatment of erectile dysfunction at 24 and 36 hours after dosing (Porst 2003, Urology)	Randomized controlled trial	—	12 weeks	Defined the clinical response window: successful-intercourse rates remained substantially above placebo at both 24 and 36 hours after a single dose, supporting the 36-hour Cialis label framing [porst2003_duration].
Evaluation of the efficacy and safety of once-a-day dosing of tadalafil 5 mg and 10 mg in ED (Porst 2006, Eur Urol)	Multicenter randomized double-blind placebo-controlled trial	—	12 weeks	Once-daily 5 mg and 10 mg tadalafil both significantly improved erectile function vs placebo, supporting feasibility of a daily regimen [porst2006_daily_rct].
Long-term safety and efficacy of tadalafil 5 mg dosed once daily in men with ED (Porst 2008, J Sex Med)	Open-label extension	—	Up to 2 years	Sustained efficacy on IIEF-EF and SEP3; tolerability consistent with short-term pivotal data; supported FDA approval of once-daily dosing in 2008 [porst2008_long_term].

Study	Design	Participants	Duration	Finding
Tadalafil therapy for pulmonary arterial hypertension, PHIRST (Galiè 2009, Circulation)	Randomized double-blind placebo-controlled phase III trial	405	16 weeks	Tadalafil 40 mg daily produced 33-meter placebo-adjusted improvement in 6-minute walk distance, with improvement in time-to-clinical-worsening [galie2009_phirst]. Supported FDA approval of Adcirca in 2009.
Tadalafil for the treatment of PAH: a double-blind 52-week uncontrolled extension study, PHIRST-2 (Oudiz 2012, JACC)	Open-label extension of PHIRST	—	52 weeks	Sustained effect on 6-minute walk distance and functional class out to one year of treatment; no new safety signals beyond the parent trial [oudiz2012_phirst2].
Initial use of ambrisentan plus tadalafil in PAH, AMBITION (Galiè 2015, NEJM)	Randomized double-blind event-driven trial	500	Median ~24 months	Initial ambrisentan + tadalafil combination reduced the primary composite endpoint (death, hospitalization, disease progression, unsatisfactory long-term response) vs either monotherapy [galie2015_ambition].
Efficacy and safety of tadalafil once daily in men with LUTS suggestive of BPH, LVHJ (Porst 2011, Eur Urol)	International randomized double-blind placebo-controlled trial	1058	12 weeks	Tadalafil 5 mg daily produced approximately 2.0, 2.4 point IPSS improvement vs placebo, supporting FDA approval for BPH/LUTS in 2011 [porst2011_bph].
PDE5 inhibitors alone or with α-blockers for LUTS, systematic review and meta-analysis (Gacci 2012, Eur Urol)	Systematic review and meta-analysis	—	—	PDE5 inhibitors as a class improve IPSS and IIEF-EF; combination with α-blockers produces additional benefit on IPSS without clearly compromising tolerability [gacci2012_pde5_alpha].
Efficacy and safety of tadalafil monotherapy for LUTS secondary to BPH, meta-	Meta-analysis	—	—	Pooled analysis consolidated the tadalafil 5 mg BPH effect across multiple trials; favorable tolerability vs placebo [yan2013_bph_meta].

Study	Design	Participants	Duration	Finding
analysis (Yan 2013, Urol Int)				
Tadalafil 5 mg daily for LUTS and ED in sexually active men with both conditions (Goldfischer 2013, J Sex Med)	Randomized placebo-controlled trial	—	12 weeks	Improvement in both IPSS and IIEF-EF in men with concurrent BPH and ED, supporting the combined-indication labeling [goldfischer2013_combined].
Time course of the interaction between tadalafil and nitrates (Kloner 2003, JACC)	Pharmacodynamic crossover	—	—	Characterized the duration of the hemodynamic interaction with nitrates, establishing the at-least-48-hour interval recommendation in the Cialis label [kloner2003_nitrate_time].
PDE5/PDE11 selectivity of tadalafil, sildenafil, vardenafil (Bischoff 2004, IJIR)	Biochemical enzyme selectivity analysis	—	—	Demonstrated quantitative differences in PDE5 vs PDE11 binding affinity across the three PDE5 inhibitors; argued that PDE11 inhibition does not occur at clinically relevant tadalafil exposures [bischoff2004_pde11].
Effects of gender, age, diabetes, renal and hepatic impairment on tadalafil PK (Forgue 2007, Br J Clin Pharmacol)	Population PK analysis	—	—	Tadalafil exposure rises with renal and hepatic impairment, supporting the dose-adjustment recommendations in the FDA label [forgue2007].
Tadalafil dosed once a day in men with erectile dysfunction (Rajfer 2007, Int J Impot Res)	Randomized double-blind placebo-controlled trial in U.S. men	—	12 weeks	5 mg and 10 mg once-daily tadalafil improved IIEF-EF and SEP3 vs placebo, supporting the daily-dosing regulatory submission [rajfer2007].
Tadalafil in PDE5-inhibitor-naive men with ED	Randomized double-blind	—	12 weeks	Once-daily tadalafil 5 mg significantly improved erectile function in men naive to prior PDE5 inhibitor therapy,

Study	Design	Participants	Duration	Finding
(Montorsi 2011, J Sex Med)	placebo-controlled parallel trial			complementing prior daily-dosing evidence and supporting first-line daily use [montorsi2011_naive].
Earliest erectogenic effect of tadalafil within 30 minutes (Rosen 2004, J Sex Med)	Randomized double-blind placebo-controlled at-home study	—	—	Demonstrated that tadalafil 10 and 20 mg produced erectogenic effect as early as 16 minutes post-dose in a subset of patients, refining onset-of-action understanding alongside the long duration of effect [rosen2004_onset].
Tadalafil once daily for LUTS secondary to BPH, dose-finding (Roehrborn 2008, J Urol)	Randomized double-blind placebo-controlled dose-ranging trial	1058	12 weeks	Pivotal dose-finding study evaluating tadalafil 2.5, 5, 10, and 20 mg daily in men with LUTS-BPH; 5 mg daily emerged as the optimum dose by efficacy/tolerability tradeoff and became the labeled BPH dose [roehrborn2008_bph_dose].
Tadalafil vs tamsulosin for LUTS-BPH (Oelke 2012, Eur Urol)	International randomized double-blind double-dummy placebo-controlled trial	—	12 weeks	Tadalafil 5 mg daily and tamsulosin 0.4 mg daily produced similar IPSS improvements that exceeded placebo, with tadalafil also improving IIEF-EF in sexually active men. Established tadalafil as a comparable alternative to alpha-blocker monotherapy [oelke2012_tamsulosin].
Tadalafil for combined BPH + ED (Egerdie 2012, J Sex Med)	Randomized double-blind placebo-controlled trial	—	12 weeks	Both tadalafil 2.5 and 5 mg once daily improved IPSS and IIEF-EF vs placebo in men with both conditions; 5 mg yielded the larger effect [egerdie2012_combined].
Tadalafil for diabetic ED (Sáenz de Tejada 2002, Diabetes Care)	Randomized double-blind placebo-controlled trial	216	12 weeks	First pivotal trial in diabetic men: tadalafil 10 and 20 mg on demand produced significant IIEF-EF and SEP3 improvements vs placebo, with similar AE profile to non-diabetic population [saenz2002_diabetic].
Tadalafil once daily for diabetic ED (Hatzichristou	Randomized double-blind placebo-controlled	—	12 weeks	Tadalafil 2.5 and 5 mg daily significantly improved erectile function vs placebo in men with diabetes, extending once-daily

Study	Design	Participants	Duration	Finding
2008, Diabet Med)	trial in diabetic men with ED			efficacy to this comorbid population [hatzichristou2008_diabetic].
Tadalafil for ED following spinal cord injury (Giuliano 2007, Arch Neurol)	Randomized double-blind placebo-controlled trial	186	12 weeks	Tadalafil 10 and 20 mg on demand produced large IIEF-EF improvements and high SEP3 rates in men with chronic SCI-related ED with favorable tolerability [giuliano2007_sci].
REACTT, tadalafil for erectile function recovery after bilateral nerve-sparing prostatectomy (Montorsi 2014, Eur Urol)	Three-arm randomized double-blind placebo-controlled trial with washout	422	9 months treatment + 6-week washout + 3-month open-label	Primary endpoint (unassisted IIEF-EF at end of washout) did not favor active treatment; both tadalafil regimens improved on-treatment erectile function [montorsi2014_reactt]. Findings argued against a durable disease-modifying effect of post-prostatectomy rehabilitation.
REACTT, penile length and morning erections (Brock 2015, Urology)	Secondary analysis of REACTT	—	—	Once-daily tadalafil 5 mg preserved penile length and improved frequency of morning erections during the treatment period vs placebo and on-demand arms [brock2015_reactt_morning_erections].
Pisansky RTOG 0831, tadalafil for ED prevention during prostate radiotherapy (Pisansky 2014, JAMA)	Randomized double-blind placebo-controlled trial	242	Up to 28, 30 weeks	Negative trial: tadalafil 5 mg daily during and after radiotherapy did not preserve spontaneous erectile function vs placebo at the primary endpoint [pisansky2014_radiotherapy]. Important counter-evidence against prophylactic peri-radiation use.
Maggiorini, tadalafil and dexamethasone for HAPE prevention (Maggiorini 2006, Ann Intern Med)	Randomized placebo-controlled prevention trial at 4,559 m	29	—	Both tadalafil 10 mg twice daily and dexamethasone 8 mg twice daily reduced incidence of high-altitude pulmonary edema in HAPE-susceptible climbers during rapid ascent [maggiorini2006_hape]. Foundational evidence for off-label altitude prophylaxis.
Schiopu, tadalafil for systemic-sclerosis Raynaud	Randomized placebo-controlled crossover	39	—	Tadalafil 20 mg every other day did not improve the primary Raynaud Condition Score endpoint vs placebo in women

Study	Design	Participants	Duration	Finding
(Schiopu 2009, J Rheumatol)				with scleroderma-spectrum disease; secondary measures showed mixed signals [schiopu2009_raynaud].
Shenoy, tadalafil for refractory secondary Raynaud (Shenoy 2010, Rheumatology)	Randomized double-blind crossover trial	24	—	Tadalafil 20 mg every other day for 6 weeks reduced Raynaud attack frequency, duration, and severity in patients refractory to standard vasodilators; supported off-label use in resistant secondary Raynaud [shenoy2010_raynaud].
Caruso, tadalafil for type-1 diabetic female sexual arousal disorder (Caruso 2012, J Sex Med)	Randomized double-blind placebo-controlled trial	—	12 weeks	Tadalafil 5 mg daily improved FSFI domain scores in premenopausal women with type-1 diabetes and sexual arousal disorder; limited and selective evidence base for broader female-indication off-label use [caruso2012_fsad_t1d].
Palmieri, tadalafil plus shockwave for Peyronie disease (Palmieri 2012, Int J Androl)	Prospective randomized trial	100	—	Adjunctive tadalafil 5 mg daily improved IIEF-EF and pain over shockwave alone in stable-phase Peyronie's disease; no significant effect on curvature [palmieri2012_peyronie].
Eardley, sildenafil vs tadalafil patient preference (Eardley 2005, BJU Int)	Open-label multicenter randomized crossover preference trial	—	—	Treatment-naive men trialed both drugs; majority preferred tadalafil largely because of duration of effect/timing flexibility. Established the patient-preference rationale that drives much of the tadalafil clinical use case [eardley2005_preference; eardley2007_factors_preference].
Madeira, PDE5 inhibitor network meta-analysis (Madeira 2021, World J Urol)	Network meta-analysis and multicriteria decision analysis	—	—	Synthesized RCT evidence across sildenafil, tadalafil, vardenafil, avanafil for ED; ranked tadalafil among the most effective and most tolerable PDE5 inhibitors when efficacy, safety, and quality of life were weighted jointly [madeira2021_network_meta].
		—	—	

Study	Design	Participants	Duration	Finding
Yuan, LUTS-BPH monodrug network meta-analysis (Yuan 2015, Medicine)	Network meta-analysis of pharmacologic monotherapies for LUTS-BPH			Tadalafil 5 mg daily produced LUTS improvement comparable to alpha-blockers and 5-alpha reductase inhibitors, with the additional advantage of concurrent IIEF-EF improvement [yuan2015_luts_network].
Etminan, ocular adverse events with PDE5 inhibitors (Etminan 2022, JAMA Ophthalmol)	Population-based nested case-control / cohort using U.S. insurance claims	—	—	Regular PDE5 inhibitor users had a small but statistically increased risk of serous retinal detachment, retinal vascular occlusion, and ischemic optic neuropathy compared to non-users. Reinforces post-marketing class labeling around ocular safety [etminan2022_ocular_jama].
Pomeranz, PDE5 inhibitor and NAION review (Pomeranz 2016, J Neuroophthalmol)	Critical review of accumulated case series and epidemiology	—	—	Reviewed the accumulating NAION literature for PDE5 inhibitors; concluded causal attribution remains uncertain but consistent with a small absolute increased risk in vasculopathic patients [pomeranz2016_naion_review]. Forms the basis of class labeling warnings.
Pisansky RTOG 0831, tadalafil for ED prevention after radiotherapy (JAMA 2014) reply	Author reply to commentary	—	—	Authors of the RTOG 0831 trial defended the negative primary endpoint result and addressed sample size and timing critiques. Provides context for clinical interpretation of the negative trial [pisansky2014_radiotherapy].
Weeks, biochemical basis of tadalafil/PDE11 interaction (Weeks 2009, JPET)	Enzymological binding-site analysis	—	—	Identified the Gln-869 hydrogen bond and adjacent residues responsible for tadalafil's affinity for PDE11A relative to PDE5 [weeks2009_pde11]. Provides mechanistic context for the PDE11-cross-reactivity question relevant to the back-pain/myalgia safety signature.
Cahill, structural basis of tadalafil PDE5 vs PDE6 selectivity (Cahill	Mutagenesis and biochemical selectivity analysis	—	—	Identified amino-acid residues that govern tadalafil's relative sparing of PDE6 (retinal phototransduction) versus PDE5, explaining the lower frequency of blue-tinge color disturbance compared

Study	Design	Participants	Duration	Finding
2012, J Biol Chem)				with sildenafil [cahill2012_pde11_binding].
Tienforti, PDE5 inhibitor network meta-analysis in SCI (Tienforti 2025, Andrology)	Systematic review and network meta-analysis	—	—	Across SCI-related ED trials, tadalafil and sildenafil ranked highest for efficacy on IIEF-EF; tadalafil's duration was an advantage in selected patients [tienforti2025_sci_meta].
Liao, PDE5 inhibitors for diabetic ED, Bayesian network meta-analysis (Liao 2019, World J Urol)	Network meta-analysis	—	—	Across diabetic-ED RCTs of sildenafil, tadalafil, vardenafil, avanafil, mirodenafil, and udenafil, the PDE5 inhibitors all improved IIEF-EF vs placebo; tadalafil ranked near the top for efficacy and tolerability [liao2019_diabetic_meta].
Park, orodispersible film vs film-coated tablet bioequivalence (Park 2018, DDDT)	Open-label crossover PK study in healthy adults	—	—	Tadalafil orodispersible film 20 mg met bioequivalence criteria for AUC and Cmax against the reference film-coated tablet, supporting alternative dosage forms with conventional PK [park2018_orodispersible_pk].
Motawi, orodispersible film vs daily tablet efficacy (Motawi 2024, Int Urol Nephrol)	Prospective randomized clinical trial	—	—	Tadalafil 5 mg ODF and conventional 5 mg tablet produced comparable IIEF-EF improvements over 12 weeks of daily dosing, with comparable AE profile [motawi2024_odf_vs_tablet].
Carson, tadalafil safety update (Carson 2004, BJU Int)	Integrated safety review across phase II/III program	—	—	Pooled safety analysis of >4,000 patients across the tadalafil clinical-development program [carson2004_safety_update]. Confirmed the headache/dyspepsia/back-pain/myalgia profile and absence of unexpected long-term signals at the time of approval.
Padma-Nathan, tadalafil tolerability across populations	Pooled safety/efficacy review	—	—	Reported phase III ED efficacy and tolerability across cardiovascular subpopulations, supporting use in patients with hypertension and stable

Study	Design	Participants	Duration	Finding
(Padma-Nathan 2003, Am J Cardiol)				cardiovascular disease [padmanathan2003_amjcardiol].
Tsertsvadze, PDE5 inhibitor and hormonal ED treatments systematic review (Tsertsvadze 2009, Ann Intern Med)	AHRQ-commissioned systematic review and meta-analysis	—	—	Comprehensive synthesis of RCTs across PDE5 inhibitors and hormonal treatments [tsertsvadze2009_meta]. Established the comparable efficacy and overall favorable safety profile that has anchored ED guideline writing (e.g., AUA 2018).

Compounded Tadalafil Pharmacokinetics & Pharmacodynamics

Pharmacokinetics

Manufactured tadalafil tablets reach peak plasma concentration approximately 2 hours after an oral dose [curran2003_pde5_pk]. The mean terminal elimination half-life is approximately 17.5 hours, substantially longer than sildenafil (~4 h) or vardenafil (~4 h). Steady-state is reached after approximately 5 days of once-daily dosing.

Absorption is not meaningfully affected by food (unlike sildenafil), which is a clinically relevant advantage of tadalafil. Tadalafil is highly protein-bound (~94%) [curran2003_pde5_pk]. Metabolism is predominantly by CYP3A4 to a methylcatechol glucuronide that is largely inactive at PDE5; renal excretion of metabolites predominates [forgue2006_healthy, ring2005_cyp3a4, wrishko2009_population_pk].

Renal impairment increases tadalafil exposure: AUC roughly doubles in moderate renal impairment, motivating dose reduction. Hepatic impairment likewise increases exposure [forgue2007]. Strong CYP3A4 inhibitors substantially increase exposure (ketoconazole approximately 4-fold; ritonavir-boosted regimens variable but large); strong CYP3A4 inducers reduce exposure markedly (rifampin reduces AUC by ~88%) [eardley2004_pde5_profiles].

Compounded sublingual or troche preparations bypass first-pass metabolism and produce different PK from manufactured oral tablets. Bioequivalence is not assured and Cmax / Tmax shift accordingly; this should inform titration and counseling when a compounded preparation is dispensed. Industrial orodispersible film 20 mg has been shown bioequivalent to film-coated tablet [park2018_orodispersible_pk] and produces comparable 12-week efficacy at 5 mg daily [motawi2024_odf_vs_tablet], those data offer regulatory PK reassurance for alternate-route products but do not establish bioequivalence of pharmacy-compounded troches with their own excipient and dwell-time variables [park2018_orodispersible_pk, motawi2024_odf_vs_tablet].

Pharmacodynamics

Tadalafil's pharmacodynamic effect is potentiation of an endogenous NO/cGMP signal rather than initiation of one. It has no effect on libido or on baseline erection without sexual stimulation, and the magnitude of erectile response correlates with the underlying NO release. In PAH, the pharmacodynamic effect is a sustained reduction in pulmonary vascular resistance during once-daily dosing [galie2009_phirst]. In BPH, the dominant effect is on lower urinary tract smooth-muscle tone [porst2011_bph].

Cardiovascular pharmacodynamic effects at standard ED doses are modest: small reductions in systolic and diastolic blood pressure (single-digit mmHg) without meaningful changes in resting heart rate [kloner2005_cardiovascular]. These effects sum with nitrates (contraindicated combination) and with alpha-blockers (manageable interaction with appropriate stabilization) [rotella2002_pde5].

↓↑ Comparing Compounded Tadalafil Formulations

The manufactured oral tablet (Cialis / Adcirca / generic) is the formulation supported by every pivotal trial and every FDA approval for tadalafil [forgue2007]. PK, dose-response, and adverse-event profile are characterized for the oral tablet route specifically.

Compounded sublingual troches and custom-strength oral capsules differ in absorption and PK. Sublingual administration partially bypasses first-pass metabolism and may yield a faster Tmax than the oral tablet; troche dwell time, vehicle composition, and patient-administration technique all affect bioavailability. Because there is no separate efficacy program for compounded preparations, dose translation from the labeled manufactured doses involves clinical judgment and individualized titration [fda_essentially_a_copy].

RonanRx-compounded preparations are dispensed only when the manufactured product is not appropriate for the identified patient. The pharmacist review documents the patient-specific clinical reason and the resulting PK uncertainty is noted on dispensing.

🌡 Compounded Tadalafil Storage and Handling

Compounded tadalafil oral capsules and sublingual troches are stored at controlled room temperature (USP definition: 20, 25 °C, with allowed excursions 15, 30 °C) in tightly closed light-resistant containers. Beyond-use date is established per USP <795> for non-sterile compounding, typically up to 180 days for solid oral formulations from non-sterile components, subject to formulation-specific stability data [usp_795].

Manufactured Cialis / Adcirca / generic tadalafil tablets are stored at controlled room temperature per the FDA label; no refrigeration is required. Tadalafil free base is stable as a solid at room temperature; troche bases require formulation-specific stability assessment.

Compounded Tadalafil Compounding & Operations

503A compounding

Compounded tadalafil is prepared under 503A on patient-specific prescriptions in state-licensed compounding pharmacies [fda503a; fda_essentially_a_copy]. RonanRx prepares non-sterile oral capsules and sublingual troches per USP General Chapter <795>, with documented active ingredient sourcing (USP/NF grade where available), gravimetric verification, and finished-product quality checks per the pharmacy's quality-management system [usp_795].

Because generic tadalafil is widely available at every FDA-approved strength, the 503A compliance posture is particularly important for this molecule. Each prescription receives an essentially-a-copy review: the prescriber's documented patient-specific clinical reason must establish a clinical difference (route, strength, excipient, combination) that the manufactured product cannot meet. Beyond-use dating, ingredient identity verification, and stability assessment follow USP <795> requirements with full batch traceability.

Pharmacist review

Each prescription for compounded tadalafil undergoes pharmacist review prior to dispensing. The review confirms: a documented patient-specific clinical reason that the manufactured generic tadalafil product is not appropriate (route preference, custom strength, excipient sensitivity, physician-directed combination product); absence of contraindications (any nitrate use, riociguat or other guanylate cyclase stimulator, severe hepatic impairment, recent stroke or MI); and the prescribed regimen aligns with FDA-label dose ceilings unless the prescriber documents a specific reason otherwise.

RonanRx does not fill prescriptions that read as routine substitution of compounded for generic tadalafil without documented clinical rationale, consistent with FDA guidance on compounded copies of commercially available drugs [fda_essentially_a_copy].

Quality and traceability

Active pharmaceutical ingredient is sourced from FDA-registered facilities with documented certificates of analysis. Each batch is recorded with lot numbers traceable to API source, compounding date, beyond-use date, and dispensing pharmacist of record. Finished product lot records are retained per state board of pharmacy retention requirements.

Cold chain

Compounded oral capsules and sublingual troches of tadalafil are not cold-chain products. They are stable at controlled room temperature and shipped in standard pharmacy-grade packaging. Patients should store at room temperature in tightly closed containers away from heat and humidity, consistent with the manufactured Cialis / Adcirca label.

Frequently Asked Questions About Compounded Tadalafil

Is compounded tadalafil the same as Cialis or generic tadalafil?

No. Cialis (and Adcirca for PAH dosing) is the FDA-approved manufactured product, and generic tadalafil has been widely available since 2018. Compounded preparations are pharmacy-prepared on a patient-specific prescription and are not bioequivalent to the manufactured tablet. Compounded drugs are not FDA-approved [fda_essentially_a_copy; fda503a].

When is a compounded version of tadalafil appropriate?

Per FDA guidance, a compounded version of an FDA-approved drug is generally restricted unless the prescriber documents a patient-specific clinical reason the manufactured product cannot meet, for example, sublingual route preference, custom strength outside the 2.5/5/10/20 mg ladder, excipient sensitivity, or a physician-directed combination product [fda_essentially_a_copy].

Why does tadalafil last so much longer than sildenafil?

Tadalafil's plasma half-life is approximately 17.5 hours vs roughly 4 hours for sildenafil [forgue2007; porst2003_duration; curran2003_pde5_pk]. That kinetic difference, not a different molecular mechanism, is the basis of the ~36-hour clinical response window and the feasibility of once-daily 2.5, 5 mg dosing.

Can tadalafil be taken with nitrates?

No. Concurrent use of any nitrate with tadalafil is absolutely contraindicated because of the risk of life-threatening hypotension. The hemodynamic interaction persists for at least 48 hours after a tadalafil dose. Patients on tadalafil should never use nitrate medications and should disclose tadalafil use in any emergency setting where nitrates might be considered [kloner2003_nitrate_time].

Why does tadalafil cause back pain or muscle aches more than other PDE5 inhibitors?

The back-pain and myalgia signal (4, 10% of patients) is characteristic of tadalafil and is typically delayed in onset (12, 24 hours after a dose), consistent with its long half-life [brock2002; porst2008_long_term]. PDE11 cross-reactivity was proposed as the mechanism, but selectivity work (Bischoff 2004) argued that PDE11 inhibition does not occur at clinically relevant exposures [bischoff2004_pde11]. The underlying pathophysiology of this adverse-event signature remains incompletely characterized.

Does RonanRx sell compounded tadalafil directly to patients?

No. Compounded tadalafil requires a patient-specific prescription from a licensed doctor for an identified patient with a documented clinical reason that generic Cialis / tadalafil is not appropriate, plus pharmacist

review before dispensing. RonanRx is not a direct-to-consumer storefront for tadalafil or any compounded substance [fda503a; fda_essentially_a_copy].

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Medications

Peptides

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Coenzyme Q10 (CoQ10) — Antioxidant & mitochondrial
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NAD+ / NMN — Antioxidant & mitochondrial
Compounded Topical Anesthetics (BLT, LET) — Dermatology
Topical Minoxidil — Dermatology
Topical Tretinoin — Dermatology
Compounded Magnesium — Energy & nutritional
Cyanocobalamin — Energy & nutritional
High-Dose Vitamin D — Energy & nutritional
Hydroxocobalamin — Energy & nutritional
Iron (Compounded) — Energy & nutritional
L-Carnitine — Energy & nutritional
Methylcobalamin (B12) — Energy & nutritional
Methylfolate — Energy & nutritional
Anastrozole — Hormone optimization
Clomiphene & Enclomiphene — Hormone optimization
DHEA — Hormone optimization
Estradiol — Hormone optimization
Estriol — Hormone optimization
Human Chorionic Gonadotropin (HCG) — Hormone optimization
Pregnenolone — Hormone optimization
Progesterone — Hormone optimization
Testosterone — Hormone optimization
Compounded Metformin — Metabolic & weight
Compounded Semaglutide — Metabolic & weight
Compounded Tirzepatide — Metabolic & weight
Lipotropic Injection (MIC, MICC) — Metabolic & weight
Low-Dose Naltrexone (LDN) — Metabolic & weight
Naltrexone-Bupropion Combination — Metabolic & weight
Topiramate — Metabolic & weight
Bremelanotide / PT-141 — Sexual health
Compounded Sildenafil — Sexual health
Compounded Tadalafil — Sexual health
Trimix Injection — Sexual health
Compounded Gabapentin — Sleep & recovery
Compounded Melatonin — Sleep & recovery
Compounded T3 (Liothyronine) — Thyroid
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PEPTIDES (21)

Sermorelin — Available now

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AOD-9604 — Growth-hormone axis (under FDA review)

CJC-1295 — Growth-hormone axis (under FDA review)

GHRP-2 / GHRP-6 — Growth-hormone axis (under FDA review)

Hexarelin — Growth-hormone axis (under FDA review)

Ipamorelin — Growth-hormone axis (under FDA review)

MK-677 / Ibutamoren — Growth-hormone axis (under FDA review)

5-Amino 1MQ — Metabolic & longevity (under FDA review)

Epitalon / Epithalon — Metabolic & longevity (under FDA review)

MOTS-C — Metabolic & longevity (under FDA review)

Thymosin Alpha-1 / Thymalin — Metabolic & longevity (under FDA review)

DSIP, Delta Sleep-Inducing Peptide — Neuro & cognitive (under FDA review)

Selank — Neuro & cognitive (under FDA review)

Semax — Neuro & cognitive (under FDA review)

Vasoactive Intestinal Peptide (VIP) — Neuro & cognitive (under FDA review)

BPC-157 — Tissue repair (under FDA review)

KPV — Tissue repair (under FDA review)

LL-37 — Tissue repair (under FDA review)

Pentadeca Arginate (PDA) — Tissue repair (under FDA review)

TB-500 / Thymosin Beta-4 — Tissue repair (under FDA review)