

Platinum Opinion

Combination of Tadalafil and Finasteride for the Treatment of Urinary Tract Symptoms Related to Benign Prostatic Hyperplasia: Commercialization of the Prescribing Cascade

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In December 2021, the US Food and Drug Administration (FDA) approved Entadfi™, a daily fixed-dose oral capsule combining finasteride (a 5 α -reductase inhibitor) and tadalafil (a phosphodiesterase type 5 inhibitor) as initial treatment for signs and symptoms of benign prostatic hyperplasia (BPH) in men with an enlarged prostate for up to 26 wk. While the safety and efficacy of tadalafil 5 mg combined with finasteride 5 mg have been demonstrated in a 26-wk placebo-controlled randomized trial published in 2014 [1], this combination is not currently supported by American and European urological guidelines as data on this combination are considered as emerging [2,3]. Tadalafil monotherapy, while listed in guidelines, is supported by moderate evidence; there are no reports detailing disease progression beyond 1 yr. We believe that this new formulation has a limited role in the management of lower urinary tract symptoms secondary to an enlarged prostate. Combination therapy with finasteride and tadalafil represents an avoidable prescribing cascade that may spur additional significant side effects, ultimately resulting in low-value care.

Co-administration of finasteride and tadalafil has been suggested specifically for 5 α -reductase inhibitor responders with erectile dysfunction [4]. Tadalafil, in addition to improving the short-term efficacy of finasteride therapy, also mitigates erectile dysfunction, which is one of the sexual side effects commonly reported with finasteride use [5]. In other words, combination therapy with finasteride and tadalafil embraces the prescribing cascade rather than avoiding it in this population [6]. In traditional prescribing cascades, an adverse drug effect is misdiagnosed as a new medical condition and treated with a potentially unneces-

sary drug that may further cause additional, avoidable adverse drug effects. Considering the breadth of medical and abundant newer surgical options available to patients suffering from lower urinary tract symptoms secondary to an enlarged prostate due to BPH, men with baseline erectile dysfunction or those who develop it after finasteride use should discontinue finasteride use. This would avoid a prescribing cascade with tadalafil. Patients and providers should consider alternative treatment options for BPH and erectile dysfunction. Possible alternatives for patients who wish to preserve their sexual function include tadalafil monotherapy and surgical treatment with new minimally invasive surgical techniques that have better sexual outcomes [7]. In addition, sexually active patients suffering from erectile dysfunction in any context should undergo a full work-up for their condition to ensure that sexual function is optimized.

There is growing evidence that finasteride use is associated with important side effects. In addition to erectile dysfunction, finasteride is associated with libido and ejaculation disorders [5]. A recent study by our group revealed evidence of an increase in suicidality and depression among finasteride users, especially younger users [8]. Considering that the combination of finasteride and tadalafil is particularly attractive for younger, sexually active men with lower urinary tract symptoms and enlarged prostates due to BPH with concomitant or subsequent erectile dysfunction following initiation of finasteride therapy, caution is advised when prescribing to this population.

Lastly, inappropriate prescribing of tadalafil in combination therapy with finasteride to mitigate finasteride-induced or finasteride-exacerbated sexual dysfunction may

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be expensive. Thus, when the cost of this new combination therapy is factored in with the lack of long-term evidence of the efficacy of tadalafil alone or in combination with finasteride, this option ultimately represents potentially low value care. Considering the rising health care spending in the USA and other high-income countries, with pharmaceuticals being one of the main drivers, there is a need to eliminate low-value, wasteful health care services rather than approving their inclusion in the present offering [9].

Despite these major drawbacks, the management of BPH relies strongly on shared decision-making and should be tailored to the goals and preferences of the patient [10]. The combination option may be useful for the small group of sexually active patients with concomitant or secondary erectile dysfunction who refuse or are deemed ineligible for surgery and for whom alternative medical therapies have failed. For these patients, a single fixed-dose oral capsule combining the two medications rather than two capsules may enhance the safety and tolerability of their medical therapy. However, the population of sexually active patients ineligible for surgery is increasingly diminishing with the advent of true minimally invasive, office-based surgical procedures for the treatment of BPH.

In conclusion, while a combination capsule of finasteride and tadalafil for short-term treatment of BPH in men with an enlarged prostate may be effective and safe according to a single randomized controlled trial, there is an armamentarium of medical and surgical alternatives that should be considered for the initial and subsequent management of lower urinary tract symptoms secondary to BPH. If used for the treatment of erectile dysfunction secondary to finasteride use, the combination medication is an example of a prescribing cascade that should be avoided. In the context of increasing polypharmacy, there is a need for consideration of alternative monotherapies and drug de-escalation.

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