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Editorial

# Evolution of Phosphodiesterase-5 Inhibitors

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After the launch of sildenafil citrate (Viagra®), the last great invention of the 20th century, in 1998, oral phosphodiesterase (PDE)-5 inhibitors were established as first-line treatment for erectile dysfunction (ED), representing a paradigm shift in the diagnosis and treatment of ED [1]. The big success of sildenafil in pharmaceutical research and development led to the subsequent development of the so-called second-generation Viagras, *e.g.*, tadalafil (Cialis®) and vardenafil (Levitra®) in 2003 [2]. Currently, these three PDE5 inhibitors are the most well-known PDE5 inhibitors worldwide. Following the early competition, PDE5 inhibitors have evolved continuously in competition for survival.

In Korea, another three kinds of PDE5 inhibitors have been developed: udenafil (Zydena®) in 2005 [3], mirodenafil (Mvix®) in 2007 [4], and avanafil (Zepeed®) in 2011 [5]. In addition, following expiration of the patent on sildenafil in Korea in 2012, 49 companies have released 60 generic versions of sildenafil. Similarly, with expiration of the patent on tadalafil in Korea in 2015, 64 companies have released 160 generic versions of tadalafil. The availability of generic sildenafil and tadalafil has led to less expensive PDE5 inhibitors, which cost as little as 1/5 the cost of the original PDE5 inhibitors. The dosage concept has also evolved from on-demand to daily low-dose and alternative dosages [6]. Approval of daily use was based on the proven safety through long-term use of sildenafil. Hence, the indication for daily low-dose PDE5 inhibitors also broadened beyond ED to pulmonary hypertension for sildenafil and benign prostatic hyperplasia/lower urinary tract symptoms (BPH/LUTS) for tadalafil and penile rehabilitation after radical prostatectomy for both [6]. With the launch of generic PDE5 inhibitors, the preparation also evolved from a tablet to orodispersible film, granule, and chewable forms. The oro-disposable film and chewable are favorable from patients in Korea [7].

In Korea, the recent impact of generic tadalafil has differed completely from that of generic sildenafil in 2012. The long half-life of tadalafil enabled its approval for BPH/LUTS with daily low-dose use. In turn, various preparations of generic tadalafil will also be developed, including orodispersible films and combinations with an antihypertensive for ED and hypertension, a PDE5 inhibitor with alpha blockers for ED and LUTS, and a PDE5 inhibitor with antidepressant for ED and premature ejaculation.

Since sildenafil citrate was launched in 1998, PDE5 inhibitors have evolved in various ways, including generics, changes in the dosage concept, broader indications beyond ED, and various preparations. In the future, various combination drugs will emerge for treating cross-risk factors, reducing pill burden and price, and eventually preventing and curing ED.

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## CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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