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## DRUG POINTS

# Epileptic seizures can follow high doses of oral vardenafil

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## Case report

An otherwise healthy 60 year old man was prescribed 10 mg of vardenafil (Levitra, Bayer) for sexual dysfunction. Because this was ineffective, he increased the dose to 40 mg. Three hours later, he had a tonic-clonic seizure, seen by his relatives. On admission to hospital, neurological examination, brain magnetic resonance imaging, and electroencephalography after sleep deprivation were normal. Stress electrocardiography, echocardiography, and cardiac scan with dipyridamole test as well as carotid doppler ultrasonography did not show concomitant cardiac diseases. The man was told to stop using vardenafil.

Two months later he had a new tonic-clonic seizure, four hours after taking 30 mg of vardenafil. At eight months' follow-up he is seizure-free without treatment.

## Discussion

In this man, the seizures were unlikely to be the manifestation of other diseases: a complete screening ruled this out. And in both occasions seizure occurred within a few hours after he took vardenafil.

Vardenafil is a selective oral phosphodiesterase type 5 (PDE5) inhibitor effective in erectile dysfunction.<sup>1</sup> Adverse events include headache, flushing, nasal congestion, and dyspepsia.<sup>1-2</sup> Convulsions were not reported to Bayer during clinical trials of vardenafil.<sup>1-2</sup> However, people taking sildenafil (Viagra, Pfizer), another inhibitor of this type, have had seizures.<sup>3</sup>

PDE5 inhibitors increase nitric oxide leading to increased cyclic guanosine monophosphate (cGMP), with relaxation of the smooth muscle in the corpus

cavernosum and increased blood flow to the penis.<sup>1-2</sup> Recent evidence indicates that these inhibitors may increase effects mediated by nitric oxide. Although the role of nitric oxide in the pathophysiology of epilepsy remains debated, the effects of nitric oxide and cGMP signalling pathway on seizure threshold<sup>4</sup> raise the possibility that nitric oxide may mediate mechanisms that alter susceptibility to seizure. Furthermore, sildenafil has shown a pro-convulsant effect on seizure threshold, interacting with exogenously and endogenously released nitric oxide.<sup>5</sup> However, the exact role of PDE5 in altering susceptibility to seizure via this pathway remains unclear.

After we submitted this drug point, a 78 year old patient presented with partial epileptic seizure after oral intake, for the second time, of 10 mg of vardenafil.<sup>6</sup> This confirms that epileptic seizures may occur during treatment with phosphodiesterase inhibitors.

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