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► **To cite this version:**

John Dean, Richard Klep, Joseph Aquilina. Counterfeit Dapoxetine Sold on the Internet Contains Undisclosed Sildenafil. *International Journal of Clinical Practice*, 2010, 64 (9), pp.1319. 10.1111/j.1742-1241.2010.02436.x . hal-00552663

**HAL Id: hal-00552663**

**<https://hal.science/hal-00552663>**

Submitted on 6 Jan 2011

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Journal:	<i>International Journal of Clinical Practice</i>
Manuscript ID:	IJCP-03-10-0180.FT10
Manuscript Type:	Short Report
Date Submitted by the Author:	18-Mar-2010
Complete List of Authors:	Dean, John; The London Clinic Klep, Richard; Johnson & Johnson Pharmaceutical Research & Development Aquilina, Joseph; Johnson & Johnson Pharmaceutical Research & Development
Specialty area:	



**Title**

Counterfeit Dapoxetine Sold on the Internet Contains Undisclosed Sildenafil

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**Disclosures**

John Dean is a clinical trial investigator for Johnson & Johnson and for Plethora, and current President of ISSM which received an unrestricted educational grant from Johnson & Johnson.

Joseph W. Aquilina and Richard Klep are employees of Johnson & Johnson, and they are stockholders of the company.

## Summary

There is growing problem with medications and herbal products sold via the Internet containing inappropriate quantities or the absence of active ingredients or whose ingredients are inaccurately represented, which may or may not be harmful to the user. We report on a counterfeit medication whose active ingredient is dapoxetine, a short-acting selective serotonin reuptake inhibitor, for the treatment of premature ejaculation. The counterfeit dapoxetine was sold on the Internet and contained an undisclosed phosphodiesterase type 5 inhibitor ingredient. Moreover, the Internet site only sold a 60 mg dose and did not indicate that the recommended starting dose of the medication for all patients is 30 mg.

## What's already known about this topic?

There is growing number of reports identifying medications and herbal products sold via the Internet containing inappropriate quantities or the absence of active ingredients or whose ingredients are inaccurately represented, which may or may not be harmful to the user. Most frequently reported are counterfeit phosphodiesterase type 5 inhibitor (PDE5i) medications for erectile dysfunction (ED).

## What does this article add?

This article reports on a counterfeit medication whose active ingredient is dapoxetine, a short-acting selective serotonin reuptake inhibitor, for the treatment of premature ejaculation (PE). The counterfeit dapoxetine was sold on the Internet and contained undisclosed PDE5i. The Internet site only sold a 60 mg dose and does not indicate that the recommended starting dose of the medication for all patients is 30 mg. This report will help to increase knowledge and awareness within the medical community of potential issues related Internet to purchase of medications from unreliable sources.

## Introduction

There is growing number of reports identifying medications and herbal products sold via the Internet containing inappropriate quantities or the absence of active ingredients or whose ingredients are inaccurately represented, which may or may not be harmful to the user. From a public health perspective, it is important to identify specific products and unlicensed pharmacies that could place unsuspecting patients at risk. In addition, raising public awareness of the problem and increasing knowledge within the medical community regarding the availability and prevalence of these products will help protect patients and consumers.[1-4]

Priligy® (Janssen Cilag AB, Sollentuna, Sweden), the medicinal product whose active ingredient is dapoxetine, a short-acting selective serotonin reuptake inhibitor, has been granted marketing authorization for the treatment of premature ejaculation in men aged 18 to 64 years in seven European Union countries, Mexico, South Korea, and New Zealand while marketing authorization applications are currently under review by health authorities in other countries (March 2010). Each film coated tablet of Priligy contains dapoxetine hydrochloride equivalent to 30 mg or 60 mg dapoxetine.[5]

The Internet site “BetterSexTech.com” claims to sell “Dapoxetine HCL/60mg pills”. [6] The site provides promotional statements about how dapoxetine enhances the sexual experience (e.g., better control and satisfaction) and also refers to findings from published studies.[7] The site does not indicate that the recommended starting dose of Priligy for all patients is 30 mg, as stated in the Summary of Product Characteristics.[5] A sample of their product, Staying Power RX, was purchased directly from the Internet site for the purpose of analyzing its chemical contents.

## Method

Four tablets of Staying Power RX were analyzed with quantitative and qualitative analytical techniques such as infrared, Raman, and mass spectroscopy, and high performance liquid chromatography (HPLC) with UV detection to determine not only the identity and amount of active pharmaceutical ingredients, but also its impurity profile using the same official test methods used for quality control release of Priligy tablets. A full scan mass spectrum of the sample product matched the electrospray mass fragmentation pattern of the dapoxetine reference standard, confirming the presence of dapoxetine molecular ion  $[M+H]^+$  base of exact mass: 306.28 in the Staying Power RX sample.

## Results

Figure 1 shows high performance liquid chromatogram (HPLC) peaks at a UV detection wavelength of (293 nm) found in the sample tablets and a selectivity batch of dapoxetine containing its full known impurity profile. The retention times and area under the peaks for known dapoxetine peak indicate the presence of dapoxetine at  $\pm 100\%$  (99.4 % w/w Eq.) of the label claim of 60 mg. However, an unknown “impurity” peak in the sample product present at approximately 13.1% w/w did not coincide with any of the known impurities in the dapoxetine selectivity batch chromatogram.

The identity of the unknown impurity in the sample product was determined by performing LC-MS-MS analysis as shown in Figure 2. Based on its mass spectrum, the impurity appeared to be sildenafil. A standard of sildenafil was used to determine its exact amount in the Staying Power RX tablets and found to be equivalent to 5.6 mg of sildenafil, the active ingredient in a medication used for the treatment of ED.[8] Neither the Staying Power RX product packaging nor the Internet site selling the product disclosed that sildenafil is contained as

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3 an ingredient of this medication,[6] whose presence in the samples of Staying Power RX may  
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5 pose risks for the user in whom sildenafil is contraindicated.  
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## 8 **Discussion**

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10 Counterfeit drugs are inherently dangerous and are a growing problem. The dangers of  
11 counterfeit medications are often underestimated by physicians, as well as patients. Jackson et al  
12 (2010) described the scope of the problem with counterfeit PDE5i medications and the safety  
13 risks associated with illicit medications.[3] Men often use the Internet to obtain PDE5i  
14 medication, which means increased direct risks associated with receiving counterfeit medication,  
15 and more indirect risks related to circumventing the healthcare system. These risks include the  
16 possibility of unknown impurities, dosage variability, dosage mislabeling which may lead to  
17 accidental overdose, and incorrect or incomplete descriptions of product composition create a  
18 substantial risk for drug-drug interactions. An example of such risks was highlighted in a report  
19 on counterfeit medication used in Singapore for ED; it is thought that 150 patients were  
20 hospitalised with severe hypoglycaemia, and 4 subsequently died, as a result of taking a product  
21 containing sildenafil that was contaminated with a sulphonylurea, glyburide.[9, 10]  
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38 We described a counterfeit medication sold on the Internet for the treatment of PE for  
39 which analyses demonstrate undisclosed PDE5i. Not only did the medication contain the  
40 contaminate, but the Internet site only sold a 60 mg dose and did not indicate that the  
41 recommended starting dose of the medication for all patients is 30 mg. This highlights the risk  
42 associated with circumventing the healthcare system and consultation with the physician. A  
43 recent report that dapoxetine was isolated as an adulterant in a health supplement used for sexual  
44 performance enhancement further illustrates the growing problem with counterfeit drugs.[11]  
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3 Weiss (2006) has discussed pros and cons of ordering medications online, provided  
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5 guidances on how to best use Internet pharmacies, and recommended that patients be advised to  
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7 purchase medications on the Internet only with great caution.[12] Proactive discussions by  
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9 physicians regarding sexual conditions and their treatment could lessen the chance of patients  
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11 choosing the Internet to purchase what may be potentially deleterious medications.  
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### Author Contributions

All authors contributed to the conceptual development of the manuscript and critically reviewed drafts and approved the final version for submission. Richard Klep oversaw the collection, analysis, and interpretation of data, and preparation of the figures. John Dean and Joseph Aquilina contributed to the literature review and writing of the text. All authors listed met ICMJE authorship criteria and no person not named as an author qualified for authorship on this manuscript.

### Acknowledgements

Johnson & Johnson funded the purchase and analysis of the chemical contents of the sample of the Staying Power RX product. Bradford Challis, PhD, an employee of Johnson & Johnson, provided editorial assistance.

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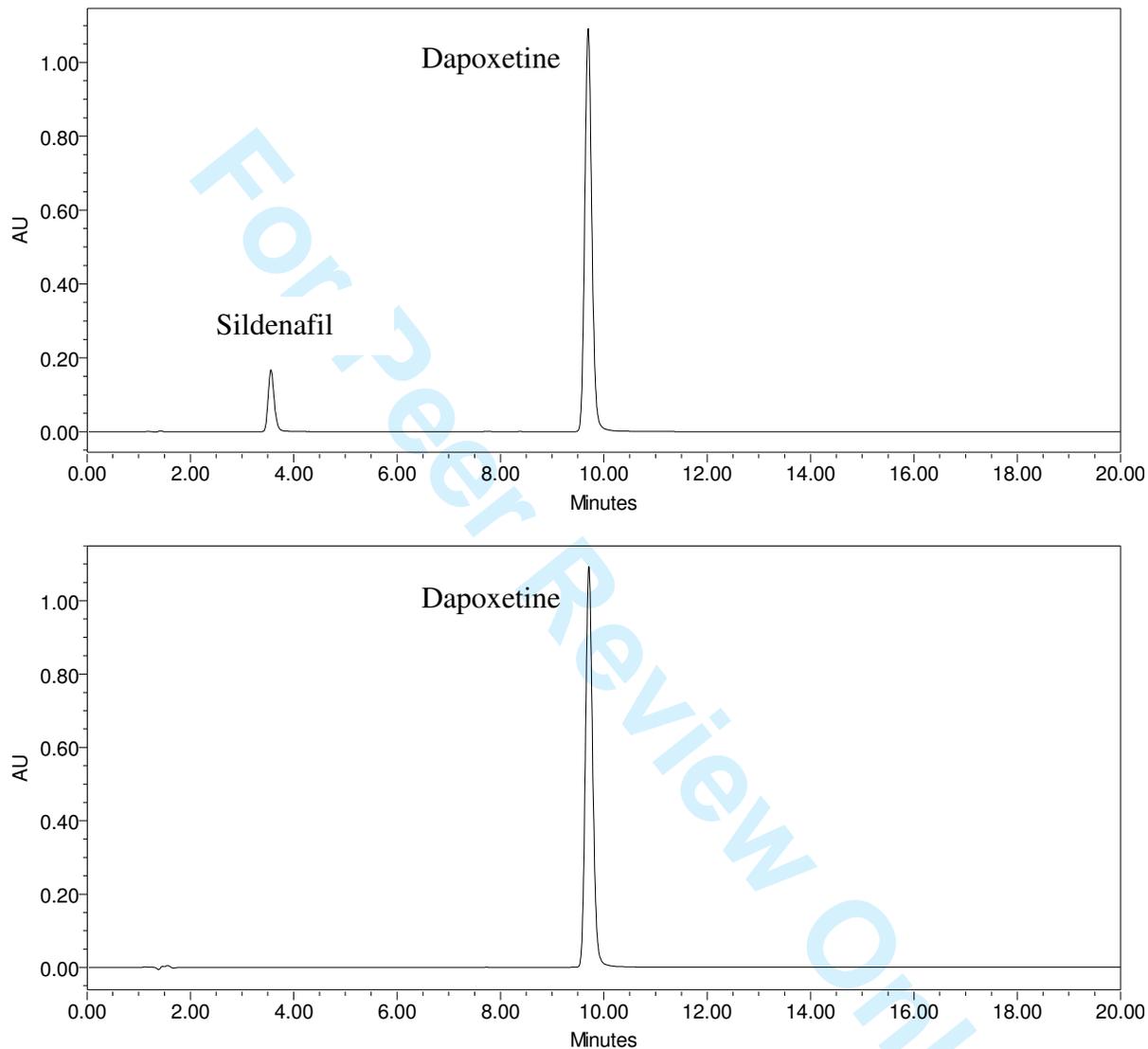
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**Figure 1.** HPLC chromatograms of Staying Power RX (top panel) and dapoxetine reference (bottom panel).



**Figure 2.** UV spectrum (top), product ion MS spectrum (middle), and electrospray mass spectrum (bottom panel) of Sildenafil (exact mass = 474.2049) determined in sample of Staying Power RX.

