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Research paper

## Availability of prescription drugs for bipolar disorder at online pharmacies

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## ABSTRACT

**Background:** There is increasing use of online pharmacies to purchase prescription drugs. While some online pharmacies are legitimate and safe, there are many unsafe and illegal so-called "rogue" online pharmacies. This study investigated the availability of psychotropic drugs online to consumers in the US, using 5 commonly prescribed drugs for bipolar disorder.

**Methods:** Using the search term "buy [drug name]" in the Google, Yahoo and Bing search engines, the characteristics of the online pharmacies found on the first two pages of search results were investigated. The availability of the requested dosage and formulations of two brand (Seroquel XR, Abilify) and three generic drugs (lamotrigine, lithium carbonate and bupropion SR) were determined.

**Results:** Of 30 online pharmacies found, 17 (57%) were rated as rogue by LegitScript. Of the 30 pharmacies, 15 (50%) require a prescription, 21 (70%) claim to be from Canada, with 20 of these having a Canadian International Pharmacy association (CIPA) seal on the website. Only 13 of the 20 sites with a CIPA seal were active CIPA members. There were about the same number of trust verification seals on the rogue and legitimate pharmacy sites. Some rogue pharmacies are professional in appearance, and may be difficult for consumers to recognize as rogue. All five brand and generic drugs were offered for sale online, with or without a prescription. However, many substitutions were presented such as different strengths and formulations including products not approved by the FDA.

**Limitations:** No evaluation of product quality, packaging or purchasing.

**Conclusions:** Psychotropic medications are available online with or without a prescription. The majority of online pharmacy websites were rogue. Physicians should ask about the use of online pharmacies. For those who choose to use online pharmacies, two measures to detect rogue pharmacies are recommended: (1) only purchase drugs from pharmacies that require a prescription, and (2) check all pharmacy verification seals directly on the website of the certifying organization, every time, before purchase.

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## 1. Introduction

Prescription drugs are a critical part of healthcare, and are taken by about half the US population (NCHS, 2014). About 10% of the top 100 prescribed medications are psychotropic drugs, as measured by both number of prescriptions and sales (Brooks, 2014). Drugs for depression, bipolar disorder and schizophrenia are routinely part of the top ten most costly therapeutic drug classes, as reported by pharmacy benefit managers (Catamaran, 2015; Express Scripts, 2014). The traditional expectation is that patients will use a single neighborhood pharmacy to purchase all

their prescription drugs. However, this model is often incorrect, as many patients use multiple pharmacies to purchase drugs. In a national survey of 89,941 patients, 43.2% used multiple pharmacies, with 29.1% of these using 3 or more pharmacies (Look and Mott, 2013). An analysis of 926,956 Medicare Part D claims found that 38.1% of patients used multiple pharmacies, with 25% using them concurrently (Marcum et al., 2014).

In addition to the mix of chain, independent, health system and mail order pharmacies, online pharmacies are an increasing factor in the purchase of prescription drugs. According to the Census bureau in 2013, 74.4% of all US households have Internet access (Census Bureau, 2014), and Forrester estimated in 2015 that 69% of this population regularly buy products online (Forrester, 2015). Although it is difficult to estimate exactly how many Internet users purchase medications online, analysis of the National Cancer

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Institute's Health Information National Trends Survey found that 20% of Internet users in 2012 purchased medications and vitamins online (Desai et al., 2015). In 2012, the FDA surveyed 6090 adults who have made purchases over the Internet and 23% reported buying prescription medicine online (FDA, 2013b). Of those who purchased prescriptions online, 17% purchased from online pharmacies that were not associated with a local pharmacy or health insurance plan (FDA, 2013b).

The primary reason Americans purchase prescription drugs online is financial (Bate et al., 2013; CIPA, 2015b). Half of 1136 adults surveyed in 2014 did not fill prescriptions or skipped doses to save money (Consumer Reports, 2014). Many turn to online Canadian pharmacies to lower the costs of filling prescriptions for brand name drugs, drugs not covered by insurance policies (CIPA, 2015b), and some generic drugs with large recent price increases such as divalproex, clomipramine and carbamazepine (Hirst, 2014; PharmacyChecker, 2014). Although it is illegal to import prescription drugs, FDA personnel may use discretion and allow entry of shipments that contain no more than a 90-day supply for personal use and do not include a controlled substance (FDA, 2015c). The FDA advises consumers to avoid foreign websites, and only purchase online from National Association of Boards of Pharmacy (NABP) approved websites based in the US (FDA, 2015a).

Some online pharmacies are safe, legitimate, fully licensed, follow applicable US regulations, and require a valid prescription for drug purchase. However, there are many illegitimate online pharmacies that pose a serious health risk. Illegitimate online pharmacies may not require a valid prescription, may use incorrect packaging and labeling, may sell drugs with the wrong dose, formulation or ingredients or past expiration date, may offer non-FDA approved drugs, or deliver no product (FDA, 2015a; NABP, 2015a; LegitScript, 2015a; Montoya and Jano, 2007). Research related to the online purchase of psychotropic medications has primarily focused on drug misuse and controlled substances rather than prescribed medications (Orizio et al., 2011; Littlejohn et al., 2005). The purpose of this study was to investigate the availability of five medications routinely prescribed for bipolar disorder to a consumer in the US using online pharmacies. Drugs for bipolar disorder were investigated since long-term polypharmacy is commonly prescribed (Bauer et al., 2013; Weinstock et al., 2014; Centorrino et al., 2010). Also, many patients with bipolar disorder are educated but unemployed (Kogan et al., 2004), and may be interested in buying medications online at lower cost. The online pharmacies were found using standard search engines.

## 2. Methods

### 2.1. Selection of drugs

Five drugs were investigated in this study, two brand and three generic: Seroquel 300 mg XR 100 pills (not available in generic in US), Abilify 20 mg 90 pills (generic aripiprazole approved on April 28, 2015 but not yet available locally), lamotrigine 200 mg 100 pills, lithium carbonate 300 mg 100 pills, and bupropion 150 mg SR 100 tablets (FDA, 2015b). The drugs were selected based on recent prescribing trends for the treatment of bipolar disorder in the US. After FDA approval of many second-generation antipsychotics in the last decade, prescribing of these drugs, and especially of quetiapine and aripiprazole, increased significantly (Hooshmand et al., 2014; Centorrino et al., 2010; Miller et al., 2015; Pillarella et al., 2012). The mood stabilizer lamotrigine is prescribed more frequently than lithium or valproate (Hooshmand et al., 2014; Centorrino et al., 2010; Bauer et al., 2013). Additionally, many patients receive antidepressants despite the controversy (Baldessarini et al., 2007; Goldberg et al., 2009).

Quetiapine, aripiprazole and bupropion are prescribed for other psychiatric indications, and lamotrigine for neurologic indications. In 2014, brand name Abilify and Seroquel XR were part of the top 100 prescribed medications in the US by number of prescriptions (Brooks, 2014). With the exception of quetiapine (Malekshahi et al., 2015), these drugs are not typically purchased by the public for non-medical use or psychiatric self-treatment.

### 2.2. Search strategy

The Google, Yahoo and Bing search engines were used to select the pharmacies included in this study. The searches were performed during the week of July 6, 2015, from an IP address in southern California, about 1285 miles south of the Canadian border. The search term used in the search engines was "buy [drug name]" for the brand name drugs: "buy abilify" and "buy seroquel xr". The unique results from the first two pages returned by the three search engines were investigated, since over 90% of users select a website from the first page of results (Chitika, 2013). The availability of all five drugs was evaluated on every unique pharmacy website.

### 2.3. Pharmacy Certification

There are several private organizations that certify pharmacies. The NABP certifies US pharmacies only through the Verified Internet Pharmacy Practice Sites (VIPPS) program. There are 40 online US pharmacies certified by VIPPS in July 2015, of which 9 are run by pharmacy benefit managers for members only (NABP, 2015b). LegitScript is a private certification agency that approves US pharmacies and is endorsed by NABP. LegitScript monitors 35,610 Internet pharmacies as of July 2015, and provides public access to its database for status lookup (LegitScript, 2015a). PharmacyChecker is another private certification agency but does not allow query of its database (PharmacyChecker, 2015). The Canadian International Pharmacy Association (CIPA) is a trade association of Canadian pharmacies, certifies Canadian websites that comply with Canadian laws, and provides public query to check membership (CIPA, 2015a). For this analysis, CIPA and LegitScript were used to determine Internet pharmacy status.

LegitScript defines an online pharmacy as rogue if it is not in compliance with national laws, does not adhere to accepted standards of pharmacy practice, or engages in deceptive business practices (LegitScript, 2015b). CIPA certified pharmacies appear in LegitScript as unapproved since these are outside the US.

## 3. Results

### 3.1. Search results

There were 38 unique results from 30 online pharmacy websites, and 8 pass through web sites (click on page to reach pharmacy). Characteristics of the 30 pharmacies are shown in Table 1. Of the 30 pharmacies, 15 (50%) required a prescription and 21 (70%) claimed to be from Canada with 20 having a CIPA seal on the website. Of the 20 websites displaying a CIPA seal, only 13 (65%) were active members. Of the 30 pharmacies, 17 (57%) were rated as rogue (16 rogue + 1 not in database) by LegitScript. Six of the 30 sites (20%) appeared unprofessional (e.g., broken links). Additionally, all of 8 pass-through sites (21% of search results), redirected the user to a rogue pharmacy. Of the 30 pharmacies, 25 (83%) showed testimonials that typically focused on customer service issues such as delivery time. While 28 of the 30 sites (93%) mentioned privacy, only 18 (60%) had a specific privacy policy related to confidentiality of medical and financial data. For 10

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