

November 23, 2020

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Re: Formulary Coverage of Selective Serotonin Reuptake Inhibitors

Dear Dr. Brennan and Dr. Chaguturu:

The undersigned organizations write to request that CVS Caremark allow stable patients to remain on their current selective serotonin reuptake inhibitor (SSRI) medication. According to the “2021 Standard Control Formulary Removals and Updates,” CVS Caremark intends to exclude coverage of four SSRI products (Paxil, Paxil CR, Pexeva, and Viibryd) from its formularies as of January 1, 2021.<sup>1</sup> As a result, individuals with depression, a condition that impacts highly vulnerable patients, could lose access to their medically necessary treatments and could experience significant adverse effects, including worsening depression and risk of suicide. This change is especially troubling amidst the COVID-19 pandemic, which has caused a sharp increase in depression symptoms and suicide ideations.

## I. Depression Is a Serious Mental Health Condition

Depression is a significant mental health condition that affects mood and behavior as well as physical functions, such as ability to eat, sleep, work, study, and enjoy friends and activities.<sup>2</sup> Untreated or undertreated depression can result in serious problems and can render an individual disabled in his or her work life, family life, and social life.<sup>3</sup>

Finding the right treatment for the individual patient is vital, and once an individual with depression achieves stability with an antidepressant, he or she must be able to remain on his or her medication. It can take several weeks for a patient to see improvement from an antidepressant, such as an SSRI, and not all antidepressants work the same way in each patient.<sup>4</sup> A patient may need to switch to different SSRIs in the same class. Some SSRIs may be more successful than others for the particular patient because not all medications even within the same class affect patients in the same manner.<sup>5</sup>

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<sup>1</sup> <https://payorsolutions.cvshealth.com/sites/default/files/cvs-health-payor-solutions-2021-cvs-caremark-formulary-updates-drug-list.pdf>

<sup>2</sup> <https://www.healthline.com/health/clinical-depression#whats-mdd>.

<sup>3</sup> <https://www.webmd.com/depression/guide/untreated-depression-effects#2>

<sup>4</sup> <https://www.healthline.com/health/mdd/switching-antidepressants>

<sup>5</sup> <https://www.healthline.com/health/mdd/switching-antidepressants>

## **II. Removal of an SSRI Product from Coverage Can Jeopardize Patient Health**

We are concerned that a decision to exclude coverage of SSRI products from CVS Caremark's formulary could result in nonmedical switching. Nonmedical switching occurs when an insurer requires a stable patient to switch from his or her current, effective medication to an alternative drug by excluding the original medication from coverage, elevating the drug to a higher cost tier, or otherwise limiting access to a treatment or increasing the patient's out-of-pocket costs. The patient is forced to switch to a "therapeutically equivalent" medication based on the actions of the payer rather than for medical reasons. Therapeutically equivalent drugs do not need to be chemically equivalent, bioequivalent, or generically equivalent.<sup>6</sup> They can be entirely different medications. We do not oppose switching a plan enrollee from a brand medication to a generic version that exhibits the same level of safety and effectiveness. However, we are opposed to policies that force stable plan enrollees to switch to a therapeutically equivalent medication for nonmedical reasons.

### **A. SSRIs Are Not Interchangeable**

Currently, the U.S. Food and Drug Administration (FDA) has approved branded SSRIs for seven products for the treatment of depression.<sup>7</sup> While the FDA has determined that all SSRI products are effective, these medications are not interchangeable, meaning that they do not "produce the same clinical results as the reference product in any given patient."<sup>8</sup> For example, vilazodone combines two mechanisms in a single drug—an SSRI with 5HT1A receptor partial agonist actions, or a serotonin partial agonist reuptake inhibitor (SPARI), whereas other SSRIs do not.<sup>9</sup> As such, studies have shown that patients who discontinue one SSRI product and are switched onto another may not be able to tolerate or may not successfully respond to the latter SSRI product.<sup>10</sup>

While CVS Caremark may continue to cover alternative SSRI products, given the lack of interchangeability between these products, stable patients who are switched could experience negative health outcomes and unnecessary risks that could be avoided. Data has shown that each subsequent switch from one SSRI to other tends to "yield less favorable outcomes as treatment-resistant depression increases."<sup>11</sup> According to the Sequenced Treatment Alternatives to Relieve Depression (Star\*D) trial, with each cumulative course of treatment, rates of remission in depression patients decreased.<sup>12</sup> Yet, patients who are unable to achieve remission of depression may face a higher risk of relapse, more rapid relapse, increased rate of recurrence, shorter course of well intervals, fewer symptom-free weeks, and increased risk of suicide.

Switchers also have had higher rates of all-cause and depression-related hospitalizations

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<sup>6</sup> <http://www.gabionline.net/biosimilars/general/glossary-of-key-terms>

<sup>7</sup> <https://www.fda.gov/drugs/information-drug-class/selective-serotonin-reuptake-inhibitors-ssris-information> (Those products are citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline, vilazodone.)

<sup>8</sup> <https://pubmed.ncbi.nlm.nih.gov/10520974/#:~:text=The%20SSRIs%20appear%20to%20be,be%20treated%20effectively%20with%20another.>

<sup>9</sup> <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3736894/>

<sup>10</sup> <https://pubmed.ncbi.nlm.nih.gov/10520974/#:~:text=The%20SSRIs%20appear%20to%20be,be%20treated%20effectively%20with%20another.>

<sup>11</sup> <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3736894/>

<sup>12</sup> <https://ps.psychiatryonline.org/doi/full/10.1176/ps.2009.60.11.1439>

and emergency room visits.<sup>13</sup> Additionally, in patients with depression and baseline sexual dysfunction, some SSRIs have been shown to be effective in treating sexual dysfunction whereas others have made sexual dysfunction worse.<sup>14</sup> Other patients who were switched experienced higher rates of weight gain with one product over another.

## B. Switching Can Result in Discontinuation or Serotonin Syndrome

Also troublesome is that a patient must discontinue one SSRI before switching to another. If discontinuation is abrupt, the patient can develop discontinuation syndrome, which includes adverse reactions such as nausea, sweating, dysphoric mood, irritability, agitation, dizziness, sensory disturbances (e.g., paresthesia), tremor, anxiety, confusion, headache, lethargy, emotional lability, insomnia, hypomania, tinnitus, and seizures.<sup>15</sup> Some patients can experience these symptoms up to a year after discontinuing their SSRI.<sup>16</sup> Switching SSRIs too rapidly can result serotonin syndrome, which can products mild symptoms (e.g., nervousness, agitation, tremor, diaphoresis, shivering, mydriasis, hyperreflexia, and diarrhea) to more severe symptoms (e.g., tachycardia, hyperthermia, hypertension, myoclonus, muscular rigidity, delirium, convulsions, organ system failure, and even death).<sup>17</sup>

It is recommended that seven to 14 days pass between discontinuation of one SSRI and the initiation of another.<sup>18</sup> Within that period, the patient's dose must be tapered down. However, oftentimes, when an insurer or pharmacy benefit manager implements a formulary change, pharmacists switch patients' medications without informing the patients' prescriber, and quite commonly, without telling the patient.<sup>19</sup> As such, the prescriber may not receive the opportunity to taper the patient off of one SSRI and onto another, thereby increasing chances of discontinuation syndrome.

## C. Switching Can Result in Breaks in Continuity of Care

Once a new SSRI is initiated, it can take another week or two to titrate up on the new dose and a total of six to eight weeks on the new medication to determine whether the new SSRI is effective.<sup>20</sup> Dosing is not equivalent among SSRIs either, so even if a patient was well-treated on a particular dose of one SSRI, he or she may need a higher dose of another SSRI, meaning the prescriber may need to experiment with different doses before the patient can attain remission. As such, a patient's depression may not be well controlled for several weeks, if not months. In that time, symptoms may worsen rather than improve. The switch can result in "delayed or more seriously compromised clinical management of depression[, which] may result in continued morbidity[, and] which in turn may lead to higher consumption of medical resources."<sup>21</sup>

<sup>13</sup> <https://pubmed.ncbi.nlm.nih.gov/20504111/>

<sup>14</sup> [https://journals.lww.com/intclinspsychopharm/fulltext/2015/07000/Sexual\\_dysfunction\\_during\\_treatment\\_of\\_major.6.aspx](https://journals.lww.com/intclinspsychopharm/fulltext/2015/07000/Sexual_dysfunction_during_treatment_of_major.6.aspx)

<sup>15</sup> <https://www.aafp.org/afp/2006/0801/p449.html>; <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5449237/>

<sup>16</sup> <https://www.karger.com/Article/Fulltext/492693>

<sup>17</sup> <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6734608/>

<sup>18</sup> [https://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366\(19\)30032-X/fulltext?dgcid=raven\\_jbs\\_etoc\\_email#](https://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366(19)30032-X/fulltext?dgcid=raven_jbs_etoc_email#); <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4919171/>

<sup>19</sup> [https://nclnet.org/common\\_therapeutic\\_drug\\_substitutions/](https://nclnet.org/common_therapeutic_drug_substitutions/)

<sup>20</sup> <https://www.jmcp.org/doi/pdf/10.18553/jmcp.1999.5.2.138>

<sup>21</sup> <https://www.jmcp.org/doi/pdf/10.18553/jmcp.1999.5.2.138>

#### **D. SSRI Switches Do Not Produce Cost-Savings**

Additionally, studies have shown that SSRI switches do not produce cost savings for the patient or plan. According to one study, patients with depression who were switched to a different SSRI for nonmedical reasons after being stable on their current SSRI used more resources and had higher healthcare costs within three months of the switch than patients who remained on their current medication.<sup>22</sup> Another study found that switchers had higher medical costs, drug costs, and total healthcare costs compared to patients who were not switched.<sup>23</sup> More specifically, researchers found that patients who were switched to another SSRI “consumed the highest amount of resources, resulting in a 76% (\$3,000) increase in total health care expenditures compared to patients who received a consistent and adequate single agent at a single dose.”<sup>24</sup>

#### **C. Patients with Depression Need to Maintain Stability Especially Amidst the COVID-19 Pandemic**

Rates of depression and suicidal ideation have significantly increased during the COVID-19 pandemic. According to a recent study published in the *Journal of the American Medical Association* (JAMA), depression symptom prevalence is over three times higher during the pandemic than before.<sup>25</sup> A CDC survey from June 2020 found that over 30 percent of respondents reported symptoms of anxiety disorder or depressive disorder and almost 11 percent reported suicidal ideations.<sup>26</sup> Elevated levels of suicidal ideations were also reported.<sup>27</sup> The JAMA study noted that a combination of social distancing, economic stress, barriers to mental health treatment, pervasive national anxiety, and a spike in gun sales are creating “a perfect storm” for suicide mortality.<sup>28</sup> As a result, the CDC have encouraged individuals experience symptoms of depression to seek treatment, and other experts have stressed that patients should stick with their current treatment plan, including their current medication.<sup>29</sup> As such, now is not the time to switch patients from their current medication to a different treatment that could be less effective in the individual patient or cause adverse events.

#### **D. Nonmedical Switching Creates an Additional Administrative Burden for Health Care Providers**

CVS’s nonmedical switching policy creates additional, unnecessary administrative hurdles that many providers may not be able to currently meet. To ensure that stable patients remain on their current medication, health care providers will be required to request a formulary exception or a prior authorization for medical necessity. This process is burdensome, time-consuming, and especially troublesome during the COVID-19 pandemic when many health care providers have

<sup>22</sup> <https://pubmed.ncbi.nlm.nih.gov/20504111/>

<sup>23</sup> <https://pubmed.ncbi.nlm.nih.gov/20504111/>

<sup>24</sup> <https://www.jmcp.org/doi/pdf/10.18553/jmcp.1999.5.2.138>

<sup>25</sup> <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2770146/>

<sup>26</sup> <https://www.cdc.gov/mmwr/volumes/69/wr/mm6932a1.htm>

<sup>27</sup> <https://www.cdc.gov/mmwr/volumes/69/wr/mm6932a1.htm>

<sup>28</sup> <https://www.psychcom.net/covid-19-suicide-rates>

<sup>29</sup> <https://www.cdc.gov/coronavirus/2019-ncov/daily-life-coping/managing-stress-anxiety.html>;

<https://medicine.umich.edu/dept/psychiatry/michigan-psychiatry-resources-covid-19/specific-mental-health-conditions/depression-managing-stress-during-covid-19-pandemic>

furloughed or fired their administrative staff. Many health care practices have had to shut their doors during the pandemic due to state social distancing orders.<sup>30</sup> Additionally, patients' health care utilization has significantly decreased due to both social distancing orders and fear of exposure to COVID-19. As a result, health care providers have had to reduce their administrative staff.<sup>31</sup> According to a survey released in September 2020, 42 percent of physicians have had to lay off or furlough staff.<sup>32</sup> Without administrative staff, there is no one to complete exception and prior authorization requests, meaning that stable patients who need to stay on their current medication may not be able to do so due to a lack of providers' lack of capacity to complete administrative tasks.

### **III. Conclusion**

We recommend that CVS Caremark allow stable patients to remain on their current SSRIs in the 2021 plan year. Patients with depression can suffer symptoms that significantly impact their major life activities. Amidst the COVID-19 pandemic, depression symptoms have been amplified. As such, stable patients should not be subjected to the added difficulty of losing access to medications that have helped them achieve remission.

We would like to schedule a meeting or call with you to discuss this matter further and request that you provide us with your availability. You can reach us at (202) 559-0380 or [policy@aimedalliance.org](mailto:policy@aimedalliance.org).

Sincerely,

Aimed Alliance  
Anxiety and Depression Association of America (ADAA)  
The American Foundation for Suicide Prevention  
Center for U.S. Policy  
The Depression and Bipolar Support Alliance  
The Flawless Foundation  
HealthyWomen  
Mental Health America  
National Alliance on Mental Illness (NAMI)  
The National Eating Disorders Association  
The National Federation of Families

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<sup>30</sup> <https://www.washingtonpost.com/outlook/2020/04/24/pandemic-could-put-your-doctor-out-of-business/?arc404=true>

<sup>31</sup> [https://www.herald-dispatch.com/business/small-doctor-practices-struggle-to-survive-amid-coronavirus-pandemic/article\\_f8004973-5d2a-57d8-8257-1e63f34abe6e.html](https://www.herald-dispatch.com/business/small-doctor-practices-struggle-to-survive-amid-coronavirus-pandemic/article_f8004973-5d2a-57d8-8257-1e63f34abe6e.html)

<sup>32</sup> [https://www.herald-dispatch.com/business/small-doctor-practices-struggle-to-survive-amid-coronavirus-pandemic/article\\_f8004973-5d2a-57d8-8257-1e63f34abe6e.html](https://www.herald-dispatch.com/business/small-doctor-practices-struggle-to-survive-amid-coronavirus-pandemic/article_f8004973-5d2a-57d8-8257-1e63f34abe6e.html)