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# CENTERSTONE

February 18, 2014

Marilyn Tavenner, Administrator  
Centers for Medicare and Medicaid Services  
7500 Security Boulevard  
Baltimore, MD 21244

RE: Proposed rule seeking to change protected drug classes in Medicare Part C (Medicare Advantage) and Medicare Part D.

Dear Administrator Tavenner,

In January, the Center for Medicare and Medicaid Services (CMS) proposed new regulations for Medicare Part D that, if implemented, we believe, will reduce benefits to beneficiaries as well as interfere with the time honored patient – physician relationship. We wish to express concerns regarding the proposed rule to revise the prescription drug benefit in Medicare Part C (Medicare Advantage) and Medicare Part D. We are specifically concerned regarding Section III.A.14 of the proposed rule which will significantly reverse the agency’s policy towards protected classes of prescription drugs.

As psychiatrists and leaders of community mental health providers with over fifty years’ experience caring for persons with psychosis-related disorders in the community, we believe that antipsychotic medications fully meet the two statutory specifications defined in the past protected classes. These were specifications regarding 1) restricted access to the drugs could result in major or life-threatening clinical consequences, and 2) there is a significant need for access to multiple drugs within a category due to unique chemical actions and pharmacological effects of the drug. From reading the report of your Protected Classes Review Panel, we see that while your panel agrees with us regarding #1, it disagrees regarding #2.

In page four of the Review Panel report, they write:

“The panel concluded, however, that antipsychotics did not meet the non-interchangeability criteria. The APA developed practice guidelines for the treatment of schizophrenia in 2004 and 2009 that discuss initial selection of these agents in broad terms such as “first” and “second” generation antipsychotics. These guidelines do not recommend specific products over one another, and the 2009 updated guidelines note that the distinction between first and second generation antipsychotics appears to have limited clinical utility. These drugs are normally not used in combination with each other for an additive effect, but they are used in combination with other psychiatric medications to treat symptoms such as depression or anxiety, or in combination with non-pharmacological psychosocial treatments. In addition, there is a high discontinuation rate with all of these medications, which would lead one to conclude that there are multiple options for initiation of pharmacological

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therapy in these patients. The Part D program allows beneficiaries and clinicians options to obtain formulary exceptions if one particular agent seems to work better than others for a given patient. As a therapeutic class, antipsychotic agents are noted to cause an increased risk of death in patients who have dementia-related psychosis leading to a black box warning in the FDA-approved labeling for these agents. Unfortunately, CMS' analyses suggest that these agents continue to be prescribed within long term care facilities at an alarming rate. The panel did not determine that additional protections were necessary for antipsychotics based on current protections afforded by our treatment guideline check as well as the nature of the recommendations within the treatment guidelines.”<sup>1</sup>

In reading your panel’s justification for antipsychotics not meeting the non-interchangeability criteria, we believe that their reasoning is based on several assumptions that, from our experience and understanding of current research, seems to be inaccurate justifications against the need for access to multiple drugs within this category.

First of all, we believe that the argument regarding American Psychiatric Association (APA) treatment guidelines is inaccurately rendered and taken out of context. From a chemical perspective, there are significant differences between and within first, second, and third generation antipsychotic medications.<sup>2, 3, 4</sup> Antipsychotics have “the most complex pharmacological mechanisms of any drug class within the field of clinical psychopharmacology” (Stahl, 2103, p. 130).<sup>5</sup> Each drug is unique because they each have very different profiles with regards to their effects on receptors. These medications are not equivalent in their side effects profiles or efficacy.<sup>6, 7</sup> Each medication is different regarding which receptors (dopamine, serotonin, histamine, etc) are targeted and blocked, and there are distinct differences in pharmacodynamic profiles between the various medications. Certain medications cause more weight gain or hyperlipidemia in some patients than others, and some cause life-long extra-pyramidal symptoms (i.e. shaking of hands, etc). In addition, this variation of effect on patients is undoubtedly influenced significantly by factors not yet completely understood, such as each individual person’s genetic makeup.

For example, clozapine, a generic “second generation” atypical antipsychotic medication, is the only antipsychotic medication that has FDA approval to reduce suicidality with schizophrenia.<sup>8, 9</sup> This medication is proven to extend life<sup>10</sup> and reduce hospitalizations for persons with schizophrenia with a history of hospitalizations, and it has been lamented in *Health Affairs* as greatly underutilized as a medication option for persons with schizophrenia.<sup>11</sup> However, it is also an antipsychotic medication that has been shown to cause agranulocytosis, a dangerous and possibly lethal side effect if not properly monitored by a psychiatrist. For individuals that do not develop agranulocytosis, clozapine can be a life-saving (and cost-effective, since it is a generic) treatment choice. For those individuals who do develop agranulocytosis, it should never be prescribed again.

Your review panel noted that using two or more antipsychotic medications simultaneously is not typical best practice. While we agree generally with this comment, each of us has had patients who did require more than one antipsychotic medication at a time. Furthermore, it is unclear how the misuse of multiple medications would be lessened by restricting pharmacy formularies. It would seem that there might be better approaches to deal with that problem.

We also do not understand how the high discontinuation rates for antipsychotics means that there are multiple, equally good options for initiation of pharmacological therapy. From our perspective, this would lead to the opposite conclusion! For our patients, we see high discontinuation rates because there

are highly unique reactions to each of these individual medications. There are obvious genetic underpinnings to the metabolism of these drugs.<sup>12</sup> Different patients can tolerate and use effectively different ones of these drugs. As we do more pharmacogenomics testing in the field of psychiatry, we are now able to see that genetics can impact the tolerability or therapeutic effect for a particular medication for a patient. With pharmacogenomics testing, it can become very obvious why the first several drugs didn't work.

Your review panel cited as a reason for antipsychotics losing their protected status that they are noted to cause an increased risk of death in patients who have dementia-related psychosis and that they are prescribed within long term care facilities at an alarming rate. We agree that antipsychotics are overprescribed to older adults, that they can cause increased risk of death to patients with dementia, and that they are overprescribed in long term care facilities. However, we fail to see how restricting open coverage will do more than dictate *which* 2-3 antipsychotics will be improperly prescribed. Frankly, when looking at prescription patterns for antipsychotics over the past 10 years for the entire US population, one can see that there is a huge uptick in prescribing patterns for all ages, including children ages 0-5.<sup>13, 14, 15, 16</sup> This is very worrisome given the array of side effects for these very potent but very complex medications. However, this similar pattern of increased prescribing can be seen for other psychotropic medications, including ADHD and anxiety medications, which do not have protected status.<sup>17, 18</sup> It is clear that a better understanding of the causes of increased medications should be studied, rather than simply limited the medication choices to the experts who prescribe them. Exceptional behavior, i.e. over utilization of medications by some providers, should not be used to form poor public policy.

At Centerstone, the patients we serve are not in long term care. 80% of the people we serve are on Medicaid patients, and most of our patients that would be impacted by these regulations are "dually eligible," many of them disabled younger in life due to their mental health conditions (bipolar disorder, schizophrenia, among others). As you know, lifetime prevalence of schizophrenia is around 1.1% and bipolar disorder is 2.6% of the general population.<sup>19</sup> Persons with psychosis-related disorders are the sickest of the sick, and only a small subset receives minimally adequate treatment currently.<sup>20</sup> There are a variety of reasons for this lack of adequate treatment, and there are some excellent solutions that have been proposed to address this. We at Centerstone are trying to be part of the solution, working to improve the quality of care we provide through transparent outcomes tracking, utilization of analytics, and incorporation of research-based practices into care. However, we believe adding a restricted formulary for antipsychotics prescription is not part of the solution to improve care for persons with psychosis. We believe that this would actually harm our psychiatric staff's ability to provide the best psychiatric care possible to this fragile population.

While there are some protections talked about in the proposed regulations to aid with transition, these are not clearly laid out. We want to emphasize that forced switching of antipsychotic medications for persons with psychosis related disorders is extremely risky and potentially damaging. We believe that there would be a very real cost in human lives if we are forced to switch medications for people with psychosis related disorders who are reasonably stable. We believe that increased restrictions would result in increased hospitalizations and suicides. Every psychotic relapse, especially with a forced switch from a medication that worked to one that could not be tolerated due to side effects, impacts a person's ability to function, make it to his or her job, sustain relationships, avoid substance abuse, and fight suicidality. Psychoses do not just make people unable to be conscious of reality. They also harm brain functioning, leading to a

sometimes permanent loss in IQ. The dually eligible, the most frail of our patients, would be greatly impacted by these changes and might experience setbacks from which they could not recover.

Being unable to access a drug for these incredibly vulnerable patients after a reasonable number of antecedent trials does not make medical sense. From our perspective, there are already a limited number of choices available, all of which have serious side effects. Our medical staff need the flexibility to work with the patients to identify an antipsychotic that works for them and has side effects that are not intolerable for them. For a patient with Bipolar 1 disorder that is a singer for a living, extreme dry mouth is an intolerable side effect. For a patient who is at risk for diabetes and has prediabetes symptoms, he or she needs a medication with lower incidence of metabolic syndrome. To eliminate a full range of access to these medications, especially injectable medications for persons who, for a variety of reasons (from homelessness to cognitive deficits), cannot take daily medications, is very problematic. We believe that this will lead to a higher level of hospitalization for our patients. Since there are currently so few psychiatric inpatient beds available, we also believe that states would need to ramp up inpatient options. We believe if these changes go into effect, we are going to have fewer patients who have control over their conditions.

We very much appreciate your consideration of these comments. As you can see, we care deeply about ensuring our patients have access to the very best mental healthcare possible.

We strongly oppose this proposed aspect of the rule and respectfully request that in the final rule, antipsychotic medications retain their protected status in Medicare.

Thank you so very much for considering these suggestions. We appreciate your leadership in this matter, and we hope that you take these comments into account as you consider how to best care for the millions of Americans who depend on these medications.

Sincerely,



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