

American Psychiatric Association
1000 Wilson Boulevard
Suite 1825
Arlington, Virginia 22209-3901

September 18, 2015

Re: Practice Guideline on the Use of Antipsychotics to Treat Agitation and Psychosis in Patients With Dementia

To Whom It May Concern,

The Alzheimer's Association appreciates the opportunity to comment on the American Psychiatric Association's (APA) draft Practice Guideline on the Use of Antipsychotics to Treat Agitation and Psychosis in Patients With Dementia.

The Alzheimer's Association is the world's leading voluntary health organization in Alzheimer's care, support, and research. Today, there are more than 5 million Americans living with Alzheimer's disease. Alzheimer's is the sixth leading cause of death in the United States, and the only cause of death among the top 10 without a way to prevent, cure, or even slow its progression. As the Guideline Writing Group (GWG) notes, an overwhelming majority of older persons with dementia experiences psychotic symptoms or agitation. Many related symptoms are the impetus to falls, weight loss, infection, incontinence, and institutionalization, and cause considerable caregiver stress.

Historically, antipsychotic medications have been used appropriately and inappropriately to address some of the behavioral and psychological symptoms of dementia (BPSD), such as agitation, aggression, and hallucinations. The Association continues to support the appropriate use of medications when BPSD pose a greater risk to individuals and families living with dementia than the medications. For the more common occurrences of BPSD, non-pharmacological interventions should be a first-line alternative to pharmacological therapies. We refer APA to the Alzheimer's Association position statement on BPSD.¹ We support APA's efforts to provide clinicians with guidance on a practice with serious consequences for patients and families and agree with most of the statements contained in the draft. We first offer general and cross-cutting comments, which include input from persons in the early stages of a form of dementia. These are followed by responses to specific statements. The Alzheimer's Association has no relevant potential conflicts of interest or significant industry or other financial relationships to disclose.

General Comments

Given the significant impact antipsychotics can have on affected persons, the Alzheimer's Association encourages the GWG to discuss quality of life and patient- and family-centeredness as it relates to antipsychotic choices. Persons with dementia considering whether to take antipsychotic medications are

¹ Alzheimer's Association. (2011). *Challenging Behaviors*, available at http://www.alz.org/documents_custom/statements/Challenging_Behaviors.pdf.

concerned not only about side effects, but how the drugs might dull or alter a person's remaining strengths and capabilities, including the ability to communicate--a basic function that is already complicated by the disease. Persons with dementia and families also acknowledge the potential benefits of appropriately-used antipsychotics. They report that such medications can ease paranoia or anxiety and can alleviate the rage some people experience, keeping them and others safe and allowing them to remain in their homes. These medications may calm an agitated person a few hours, allowing him or her to attend an adult day program, granting a caregiver a few hours of much needed respite.

Persons with dementia who still have some decisionmaking capacity want a say in the circumstances under which they use--or stop use of--antipsychotic medications. Family and/or caregivers should also express concerns and preferences to providers and participate in ongoing discussions. These preferences should be documented, revisited, and respected as part of the treatment plan. This becomes particularly important after the person with dementia can no longer make decisions.

Persons with dementia who reside in nursing homes are typically in the middle to late stages of the disease. These residents have historically been at an increased risk of inappropriate use of antipsychotic medications. The National Partnership to Improve Dementia Care, a public-private partnership, has established a goal of a 30 percent reduction in the use of antipsychotics by the end of 2016. Just as with persons living in the community, nursing home residents and their families and caregivers should be fully informed about the drugs they receive, the potential risks and consequences, and non-pharmacological approaches with an emphasis on person-centered dementia care practices.

The Alzheimer's Association recommends a greater emphasis on the importance of confirming diagnoses prior to considering pharmacologic therapies. The paragraph located at lines 593-606 discusses the considerable degree to which a person's diseases--Lewy Body Dementia, Parkinson's, and other chronic diseases, for example--affect his or her response to an antipsychotic medication. Confirming or excluding diagnoses is a critical early step that will influence treatment choices and should be prioritized accordingly in the report.

While the report suggests that there are few reasonable alternatives to antipsychotics for psychosis or agitation, we note that there is now good evidence for the use of citalopram/escitalopram for agitation. In addition to the studies cited in the draft guideline, a 2002 study by Pollock and colleagues² regarding citalopram shows comparability with perphenazine and superiority to placebo, and a 2014 study by Porsteinsson and colleagues³ shows superiority to placebo. Thus, four head-to-head trials suggest comparability between citalopram/escitalopram and second generation antipsychotics, and two more suggest citalopram is superior to placebo. Consequently, citalopram/escitalopram should be considered as an alternative to antipsychotics for the treatment of agitation.

² Pollock BG, Mulsant BH, Rosen J, Sweet RA, Mazumdar S, Bharucha A, Marin R, Jacob NJ, Huber KA, Kastango KB, Chew ML. Comparison of citalopram, perphenazine, and placebo for the acute treatment of psychosis and behavioral disturbances in hospitalized, demented patients. *Am J Psychiatry*. 2002 Mar;159(3):460-5.

³ Porsteinsson AP, Drye LT, Pollock BG, Devanand DP, Frangakis C, Ismail Z, Marano C, Meinert CL, Mintzer JE, Munro CA, Pelton G, Rabins PV, Rosenberg PB, Schneider LS, Shade DM, Weintraub D, Yesavage J, Lyketsos CG; CitAD Research Group. Effect of citalopram on agitation in Alzheimer disease: the CitAD randomized clinical trial. *JAMA*. 2014 Feb 19;311(7):682-91. doi: 10.1001/jama.2014.93.

Specific Comments

Statement 5, page 6, lines 132-134: We respectfully suggest that this statement specify that, in non-emergency situations, antipsychotics should only be used after non-pharmacological interventions and appropriate pharmacological alternatives have not been effective and symptoms continue to be severe, dangerous, and/or cause significant distress to the patient.

Reference/rationale: As noted above, the Alzheimer's Association believes that non-pharmacological interventions should be first-line alternatives to pharmacological interventions. Those, however, are unlikely to effectively address pain, for example, a possible underlying cause of agitation. Other medications may effectively treat pain and resolve the problem behavior.

Statements 9-11, pages 6-7, lines 145-153: We would like the GWG to consider time frames as suggested points of reference by which to evaluate medication use and tapering and to revisit non-pharmacological interventions, rather than strict time frames.

Reference/rationale: The GWG acknowledges that the time frames recommended for medication use and tapering have not been studied in a randomized fashion and are derived from the expert survey. The report also notes disagreement on the topic among GWG members. In light of this disagreement and in the absence of evidence, the report should suggest time frames as general guidelines, state that clinical judgment should supersede exact time intervals, and encourage providers to consider each individual patient and circumstances.

Statement 13, page 7, lines 157-158: The Alzheimer's Association believes that this statement should recommend that all first generation antipsychotics (FGAs), including haloperidol, should be avoided as first-line agents to treat agitation.

Reference/rationale: The report acknowledges that all FGAs pose a greater risk of mortality than the use of second generation antipsychotics in individuals with dementia. Rather than limiting this statement to haloperidol, APA should recommend avoiding all FGAs in these circumstances in light of the significant risks and limited data.

Thank you for the opportunity to comment. The Alzheimer's Association would be pleased to serve as a resource to APA as it continues to develop these important guidelines. Please contact Laura Thornhill, Manager of Regulatory Affairs, at 202-638-7042 or lthornhill@alz.org if you have questions or if we can be of additional assistance.

Sincerely,



Robert Egge
Executive Vice President, Government Affairs