



Effective Health Care

Pharmacological Treatments for Bipolar Disorder I Nomination Summary Document

Results of Topic Selection Process & Next Steps

- The topic, *Pharmacological Treatments for Bipolar Disorder I*, will be addressed by an in-process AHRQ systematic review titled *Treatment for Bipolar Disorder*. Given that the in-process review covers this nomination, no further activity will be undertaken on this topic.
- Agency for Healthcare Research and Quality. Treatment for bipolar disorder. Evidence-based Practice Center Systematic Review Protocol. Rockville, MD: AHRQ; 2014. Available at: <http://www.effectivehealthcare.ahrq.gov/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productid=1926>
- To view a description and status of the research review, please go to: <http://www.effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports/>

Additional Resources

The nomination focused on the harms and benefits of participating in a specific clinical trial. Although an AHRQ EPC product cannot make recommendations to the nominator about this, we have identified the following patient resources that may be useful to the nominator from authoritative sources.

- Clinical Research Trials and You, NIH, <https://www.nih.gov/health-information/nih-clinical-research-trials-you>
- Clinical Trials – Participants, NIH, <http://www.nimh.nih.gov/health/trials/index.shtml>
- A Participant's Guide to Mental Health Clinical Research, National Institute of Mental Health (NIMH), <https://catalyst.harvard.edu/pdf/regulatory/nimh-participants-guide.pdf>
- Learn about Clinical Studies, ClinicalTrials.gov, <https://www.clinicaltrials.gov/ct2/about-studies/learn>
- Inside Clinical Trials: Testing Medical Products in People, U.S. Food and Drug Administration, <http://www.fda.gov/Drugs/ResourcesForYou/Consumers/ucm143531.htm>
- Clinical Trials, MedlinePlus, <https://www.nlm.nih.gov/medlineplus/clinicaltrials.html>

Topic Description

Nominator(s): Individual
Nomination The nominator wants to know whether he/she should participate in the clinical trial,

Summary: “Efficacy, Safety, and Tolerability of an Intramuscular Formulation of Aripiprazole (OPC-14597) as Maintenance Treatment in Bipolar I Patients”. The nominator is interested in the side effects, particularly on weight-gain, and in payment for partaking in clinical trials. He/she is also interested in any improvement that might result from this treatment for bipolar disorder. The nominator would like AHRQ to consider this topic in order to help inform patient decisions about participating in clinical trials.

Staff-Generated PICO

Population(s): Adults (age 18 and over) with bipolar mood disorder I

Intervention(s): Pharmacological treatments, including aripiprazole and other atypical antipsychotics

Comparator(s): Other pharmacological treatments, placebo, usual treatment non-pharmacological treatments

Outcome(s): Time to recurrence of any mood episode, no occurrence of any mood episode, any improvement in patient symptoms or problems from treatment

Key Questions from Nominator: Is it safe to participate in clinical trials, such as OPC 14597 for bipolar mood disorder I, titled “Efficacy, Safety, and Tolerability of an Intramuscular Formulation of Aripiprazole (OPC-14597) as Maintenance Treatment in Bipolar I Patients?”

Revised Key Question:

We identified the clinical trial to which the nominator referred. This randomized, double-blind, placebo-controlled trial is now underway and is no longer recruiting participants. The purpose of this trial is to assess the time to recurrence of any mood episode in subjects with bipolar I disorder who have maintained stability on intramuscularly depot injected aripiprazole for at least 8 weeks. Based on this information, the nominator’s key question was revised to focus more broadly on the pharmacological treatment for bipolar disorder I as follows:

What are the benefits and harms of pharmacological treatments for bipolar disorder I?

Considerations

- The topic meets EHC Program importance criteria. (For more information, see <http://effectivehealthcare.ahrq.gov/index.cfm/submit-a-suggestion-for-research/how-are-research-topics-chosen/>.)
- Bipolar disorder is one of the leading causes of disability among young people, resulting in cognitive and functional impairment and increased mortality due to suicide. People with bipolar disorder have a high prevalence of co-occurring psychiatric and medical conditions, which often complicates treatment or worsens the existing bipolar disorder. Accurate diagnosis and treatment of bipolar disorder can help to prevent and minimize the harmful outcomes associated with this disease.
- Aripiprazole is a commonly used atypical antipsychotic for the treatment of bipolar disorder. However, in our search of the literature, the intramuscular formulation of aripiprazole was specifically noted in only one guideline and one ongoing systematic review identified by our search. A 2011 guideline by the Singapore Ministry of Health stated that among other antipsychotics, aripiprazole may be used

intramuscularly in the acute treatment of agitation in mania.¹ The ongoing systematic review titled *Systematic review of efficacy and safety of second generation antipsychotic long acting injections (SGA LAIs) in maintenance treatment of bipolar disorder*, is examining the efficacy and safety of SGA LAIs, including aripiprazole, for bipolar disorder. The review is anticipated to be completed in June 2016.²

- Topic will be addressed by an in-process AHRQ systematic review titled *Treatment for Bipolar Disorder*. Key questions from this report include:

Key Question 1: What is the efficacy and comparative effectiveness of pharmacologic and nonpharmacologic treatments for adults with bipolar disorder?

- a. How do pharmacologic treatments (monotherapy or combination therapies) affect patient centered outcomes when compared with placebo?
- b. How do pharmacologic treatments (monotherapy or combination therapies) affect patient centered outcomes when compared with other active pharmacologic treatment?
- c. How do behavioral health treatments (psychotherapy, psychosocial interventions) affect patient centered outcomes when compared with usual care?
- d. How do behavioral health treatments (psychotherapy, psychosocial interventions, chronotherapy) affect patient centered outcomes when compared with other active treatment?
- e. How do somatic treatments (electroconvulsive therapy (ECT), transcranial magnetic stimulation (TMS)) affect patient-centered outcomes when compared with other active treatment?
- f. How do comprehensive programs affect patient centered outcomes when compared with usual care?

Key Question 2: What are the harms from pharmacologic and nonpharmacologic treatments for adults with bipolar disorder?

- a. What are the harms from pharmacologic treatments?
- b. What are the harms from behavioral health treatments?
- c. What are the harms from somatic treatments?
- d. What are the harms from comprehensive programs?

Key Question 3: What is the effectiveness of treatments to reduce the metabolic change (metabolic syndrome, glucose dysregulation, weight gain) side effects of first line pharmacologic treatments?

Key Question 4: Which patient characteristics predict the effectiveness and harms of pharmacologic and nonpharmacologic treatments for people with bipolar disorder, including disease-specific characteristics such as bipolar type, phase severity, pediatric onset, new onset, treatment resistant, types of depression, and other comorbidities and patient characteristics such as substance use, other psychiatric comorbidities, medical comorbidities, age, sex, race/ethnicity, socioeconomic status?

¹ Singapore Ministry of Health. Bipolar disorder. Singapore: Singapore Ministry of Health; 2011 Nov. 68 p.

² Asta Prajapati, Jonathan Wilson, Ian Maidment. Systematic review of efficacy and safety of second generation antipsychotic long acting injections (SGA LAIs) in maintenance treatment of bipolar disorder. PROSPERO 2015:CRD42015023948 Available from http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42015023948