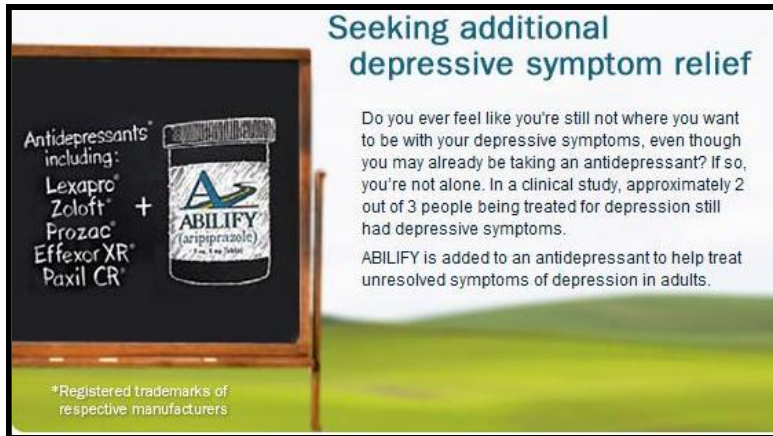


E-mail stream

We need to get it right.

Should we be using a drug to treat depression where the incidence of akathisia (dyskinesia) is more twice the expected remission rate for depression with the drug?

Abilify is a relatively new drug indicated for the treatment of depression. It is a serotonin and dopamine agonist.

The image is a promotional graphic for Abilify. On the left, a chalkboard lists several antidepressants: Lexapro, Zoloft, Prozac, Effexor XR, and Paxil CR, with a plus sign next to a small image of an Abilify pill bottle. The text on the chalkboard reads "Antidepressants including: Lexapro, Zoloft, Prozac, Effexor XR, Paxil CR + ABILIFY (aripiprazole)". To the right of the chalkboard, the headline reads "Seeking additional depressive symptom relief". Below the headline, the text asks, "Do you ever feel like you're still not where you want to be with your depressive symptoms, even though you may already be taking an antidepressant? If so, you're not alone. In a clinical study, approximately 2 out of 3 people being treated for depression still had depressive symptoms." Below this, it states, "ABILIFY is added to an antidepressant to help treat unresolved symptoms of depression in adults." At the bottom left of the graphic, a small note says "\*Registered trademarks of respective manufacturers".

The screen shot above is from [www.abilify.com](http://www.abilify.com). It notes that approximately 2 of 3 people being treated for depression do not have symptoms fully under control (i.e. they are still depressed). In the peer reviewed writing I did, published February 2009, it is noted at the placebo effect in double blind studies of depression treatment with reuptake inhibitors is 30% to 45%, and the following is true:

1. Only 7% to 13% of patients get relief of symptoms greater than placebo with reuptake inhibitors.
2. No patients over 65 years of age get symptoms relief greater than placebo in the treatment of depression with reuptake inhibitors.

The Abilify ad, in asserting that 2 of 3 patients treated with reuptake inhibitors for depress still have symptoms is consistent with the peer reviewed literature on the subject current treatment with reuptake inhibitors. If they have symptoms they are still depressed.

But just how good is Abilify (Aripiprazole)?

At the bottom is a double blind placebo controlled study of the efficacy of Abilify. Depression remission rates with Abilify were 9.2% greater than placebo, about the same as reuptake inhibitors versus placebo. 15.0% of patients achieved some clinical response greater than placebo in treatment of depression. The incidence of akathisia (dyskinesia) with Abilify was 21.7% greater than placebo meaning the incidence of developing Akathisia (dyskinesia) was over twice the incidence of those getting remission of depression with Abilify. In plain English, when you start a patient on Abilify the odds of developing akathisia (dyskinesia) are over twice as likely than getting remission of depression symptoms.

Double blind studies have consistently demonstrated that reuptake inhibitors in the treatment of depression lead to relief of symptoms better than placebo in only 7% to 13% of patients. The reuptake inhibitors deplete neurotransmitters further as noted by the Nation Institute of Drugs Abuse model. The only way to prevent reuptake inhibitors from depleting neurotransmitter during use is by giving balanced amino acid precursors simultaneously. In the last 5 years we have had no treatment failures reported in treating depression with amino acids when the protocols are followed properly. The key here is “following the protocol properly”. Patients who quit treatment, physicians that do not follow through to the last step of the depression protocol, etc. do have treatment failure but the failure is from not following the protocol properly.

I think it is a fair assertion that giving drugs where the response is only 7% to 13% greater than placebo that deplete neurotransmitters and/or cause akathisia (dyskinesia) with other side effects at a rate that is much greater than the expectation of relief of symptoms is not optimal.

**FROM:** The Efficacy and Safety of Aripiprazole as Adjunctive Therapy in Major Depressive Disorder: A Second Multicenter, Randomized, Double-Blind, Placebo-Controlled Study Marcus, Ronald N. MD; McQuade, Robert D. PhD; Carson, William H.MD; Hennicken, Delphine MS; Fava, Maurizio MD; Simon, Jeffrey S.MD; Trivedi, Madhukar H. MD; Thase, Michael E. MD; Berman, RobertM. MD

**CONCLUSION:** Remission rates were significantly greater with adjunctive aripiprazole than placebo (25.4% vs 15.2%;  $P = 0.016$ ) as were response rates (32.4% vs 17.4%;  $P < 0.001$ ). Adverse events occurring in 10% of patients or more with adjunctive placebo or aripiprazole were akathisia (4.2% vs 25.9%), ... and fatigue (3.7% vs 10.1%).

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