

Drugs

Antipsychotics

FDA ALERT [6/16/2008]: FDA is notifying healthcare professionals that both conventional and atypical antipsychotics are associated with an increased risk of mortality in elderly patients treated for dementia-related psychosis.

In April 2005, FDA notified healthcare professionals that patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death. Since issuing that notification, FDA has reviewed additional information that indicates the risk is also associated with conventional antipsychotics.

Antipsychotics are not indicated for the treatment of dementia-related psychosis.

This information reflects FDA's current analysis of data available to FDA concerning these drugs. FDA intends to update this sheet when additional information or analyses become available.

To report any unexpected adverse or serious events associated with the use of these drugs, please contact the FDA MedWatch program using the contact information at the bottom of this page.

FDA is requiring the manufacturers of conventional antipsychotic drugs to add a *Boxed Warning* and *Warning* to the drugs' prescribing information about the risk of mortality in elderly patients treated for dementia-related psychosis similar to the *Boxed Warning* and *Warning* added to the prescribing information of the atypical antipsychotic drugs in 2005.* See the last page of this document for a list of conventional and atypical antipsychotic drugs.

Considerations for Healthcare Professionals

- Elderly patients with dementia-related psychosis treated with conventional or atypical antipsychotic drugs are at an increased risk of death.
- Antipsychotic drugs are not approved for the treatment of dementia-related psychosis. Furthermore, there is no approved drug for the treatment of dementia-related psychosis. Healthcare professionals should consider other management options.
- Physicians who prescribe antipsychotics to elderly patients with dementia-related psychosis should discuss this risk of increased mortality with their patients, patients' families, and caregivers.

Background Information and Data

Previously, in April 2005, FDA informed healthcare professionals and the public about the increased risk of mortality in elderly patients receiving atypical antipsychotic drugs to treat dementia-related psychosis ([April 2005 Public Health Advisory and Information for Healthcare Professionals](#)). At that time, the analyses of 17 placebo-controlled trials that enrolled 5377 elderly patients with dementia-related behavioral disorders revealed a risk of death in the drug-treated patients of between 1.6 to 1.7 times that seen in placebo-treated patients. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infectious (e.g. pneumonia) in nature. Based on this analysis, FDA requested that the manufacturers of atypical antipsychotic drugs include information about this risk in a *Boxed Warning* and the *Warnings* section of the drugs' prescribing information.

Recently, two observational epidemiological studies^{1,2} were published that examined the risk of death in patients who were treated with conventional antipsychotic drugs.

Gill et al.¹ performed a retrospective cohort study in Ontario, Canada of 27,259 adults, 66 years of age or older, with a diagnosis of dementia between April 1997 and March 2002. The investigators compared the risk for death with use of an atypical antipsychotic versus no antipsychotic and the risk for death with use of a conventional antipsychotic versus an atypical antipsychotic. They found that atypical antipsychotics were associated with increased mortality as compared to no antipsychotic use as early as 30 days and persisting until study end at 180 days. The investigators found that conventional antipsychotic use showed a marginally higher risk of death compared with atypical antipsychotic use. The causes of death were not reported in this study.

Schneeweiss et al.² performed a retrospective cohort study in British Columbia, Canada of 37,241 adults, 65 years of age or older, who were prescribed conventional (12,882) or atypical (24,359) antipsychotic medications for any reason between January 1996 and December 2004. The investigators compared the 180-day all cause mortality with use of a conventional antipsychotic versus an atypical antipsychotic. They found that the risk of death in the group of patients treated with conventional antipsychotic medications was comparable to, or possibly greater than, the risk of death in the group of patients treated with atypical antipsychotic medications. The causes of death with the highest relative risk were cancer and cardiac disease.

FDA considers that the methodological limitations in these two studies preclude any conclusion that conventional antipsychotics have a greater risk of death with use than atypical antipsychotics. FDA has determined, however, that the overall weight of evidence, including these studies, indicates that the conventional antipsychotics share the increased risk of death in elderly patients with dementia-related psychosis that has been observed for the atypical antipsychotics. The prescribing information for all antipsychotic drugs will now include the same information about this risk in a *Boxed Warning* and the *Warnings* section.

*FDA is requiring the manufacturers to make these changes to the prescribing information for these drugs under its new authority to require safety label changes provided in Title IX of the FDA Amendments Act of 2007 (creating new section

505(o)(4) of the Federal Food, Drug, and Cosmetic Act).

References

1. Gill SS et al. Antipsychotic drug use and mortality in older adults with dementia. *Ann Intern Med.* 2007;146:775-786
2. Schneeweiss S et al. Risk of death associated with the use of conventional versus atypical antipsychotic drugs among elderly patients. *CMAJ.* 2007;176:627-632.

Conventional Antipsychotic Drugs

Compazine
(prochlorperazine)
Haldol (haloperidol)
Loxitane (loxapine)
Mellaril (thioridazine)
Moban (molindone)
Navane (thiothixene)
Orap (pimozide)
Prolixin (fluphenazine)
Stelazine (trifluoperazine)
Thorazine (chlorpromazine)
Trilafon (perphenazine)

Atypical Antipsychotic Drugs

Abilify (aripiprazole)
Clozaril (clozapine)
FazaClo (clozapine)
Geodon (ziprasidone)
Invega (paliperidone)
Risperdal (risperidone)
Seroquel (quetiapine)
Zyprexa (olanzapine)
Symbyax (olanzapine and fluoxetine)

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