

Record of Risk Profile Reviews and Updates

Date	Description of Recent Reviews and Updates to Risk Profile
1997 June 18 through 2001 November 26	All Risk Profiles for Compound LY170053 approved before 2001 November 26 are archived in the historical Atom\ICDRisk folder.
2001 November 26	After reviewing the Risk Profile, the clinical research physician determined that changes were needed. Because the Risk Profile had existed only as a MS Word document and was not archived in DocMan, the electronic version of this document was transferred to DocMan on 12 February 2003 to comply with Global SOP requirements.
2002 October 30	Annual review—no changes made.
2003 December 04	After reviewing the Risk Profile, the clinical research physician determined that changes were needed to reflect updates to the olanzapine label and to include several items from the olanzapine core data sheet.

Risk Profile for Olanzapine (LY170053)

Approval Date	04 December 2003
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As of 30 June 2003, more than 12 million patients have taken olanzapine.

Risks and Discomforts Associated with Olanzapine

Very common reports in patients taking olanzapine include sleepiness, weight gain, and an increase in prolactin levels. Common reports include dizziness, lack of energy, an increase in hunger, restlessness, swelling, a decrease in blood pressure when standing up, constipation, dry mouth, high blood sugar, an increase in chemicals in the blood made by the liver, and an increase in lipids, including triglycerides.

Shaking and uncontrolled muscle movements have been reported but have been uncommon in patients who have taken olanzapine for up to 1 year. There is a possibility that these movements may continue after patients stop taking the drug.

Rare cases of Neuroleptic Malignant Syndrome (NMS) have been seen in patients taking olanzapine. Neuroleptic Malignant Syndrome is a serious, potentially life-threatening disorder that includes symptoms such as fever, tight muscles, changes in blood pressure and heart rate, as well as changes in thinking and understanding.

Rare reports of seizures have occurred in patients with a history of seizures or who have other things (which can be explained to you by your doctor) that increase the chance of seizures. There have also been rare reports of liver problems; worsening of high blood sugar; and/or high blood sugar resulting in fruity smelling breath, confusion, dehydration (abnormal loss of body fluids), nausea and vomiting, and coma, which could be life threatening.

Males may have rare problems with the penis staying erect too long.

Very rare cases of inflammation of the pancreas, a potentially life-threatening condition, have been reported in patients taking olanzapine.

Risks in Alzheimer's Patients

In patients with Alzheimer's disease, there have been common reports of unsteady walking and choking when trying to swallow.

Risks in Parkinson's Patients

In patients with Parkinson's disease, worsening of muscle stiffness and shaking, as well as worsening of hallucinations, have been commonly reported.

Risks in Patients Receiving Short-Acting Intramuscular Olanzapine

Common reports of decreased blood pressure, rapid heart rate, and decreased (slower than normal) heart rate have occurred in patients who have received olanzapine by injection into a muscle.

Risks in Patients Receiving Olanzapine in Combination with Lithium or Valproate

Very common reports include weight gain, dry mouth, increased appetite, and shaking and uncontrolled muscle movements. Common reports include speech disorder.

Notes

Do not copy this section into the informed consent document (ICD).

Required Risks

“Required” risks are to be included in all ICDs developed for Lilly-sponsored studies of this compound. Required risks appear in normal font.

Nonrequired Risks

Risks designated as “nonrequired” are to be included in all protocol-specific ICDs, but may be altered or deleted in affiliate-specific or site-specific ICDs. (See the Global Medical **Procedure for Informed Consent**.) Nonrequired risks appear in *italics*. None of the risks above are nonrequired risks.

Special Population Risks

Risks designated for special populations, disease states or regimens are to be included in ICDs only for studies which may enroll these subgroups as participants.

Risks Rationale

The risks mentioned in this document reflect the adverse events contained in the olanzapine core data sheet.

Recent Changes to Risk Profile

Added worsening of high blood sugar to the “Risks and Discomforts Associated with Olanzapine” section to reflect the updated olanzapine label.

Added an increase in prolactin levels, lack of energy, and an increase in lipids, including triglycerides, to the “Risks and Discomforts Associated with Olanzapine” section to more accurately reflect the adverse events contained in the olanzapine core data sheet.

Added a new section “Risks in Patients Receiving Olanzapine in Combination with Lithium or Valproate” to reflect the updated olanzapine core data sheet.

Key for Translation

Nonscientific term	Scientific term
sleepiness	somnolence
having loose stools	diarrhea
having hard or infrequent stools	constipation
shaking and uncontrolled muscle movements	tremor
high blood sugar	hyperglycemia, diabetes
worsening of high blood sugar	exacerbation of pre-existing diabetes
high blood sugar resulting in fruity smelling breath, confusion, dehydration (abnormal loss of body fluids), nausea and vomiting, and coma	diabetic ketoacidosis
restlessness	akathisia
swelling	peripheral edema
lack of energy	asthenia
an increase in prolactin levels	hyperprolactinemia
an increase in lipids	hyperlipidemia
an increase in triglycerides	hypertriglyceridemia
liver problems	hepatitis
inflammation of the pancreas	pancreatitis
loss of consciousness from extremely high blood sugar	diabetic coma
problems with the penis staying erect too long	priapism
decreased blood pressure	hypotension
decreased blood pressure when standing up	orthostatic hypotension
rapid heart rate	tachycardia
decreased (slower than normal) heart rate	bradycardia
unsteady walking	abnormal gait
muscle stiffness and shaking	extrapyramidal syndrome