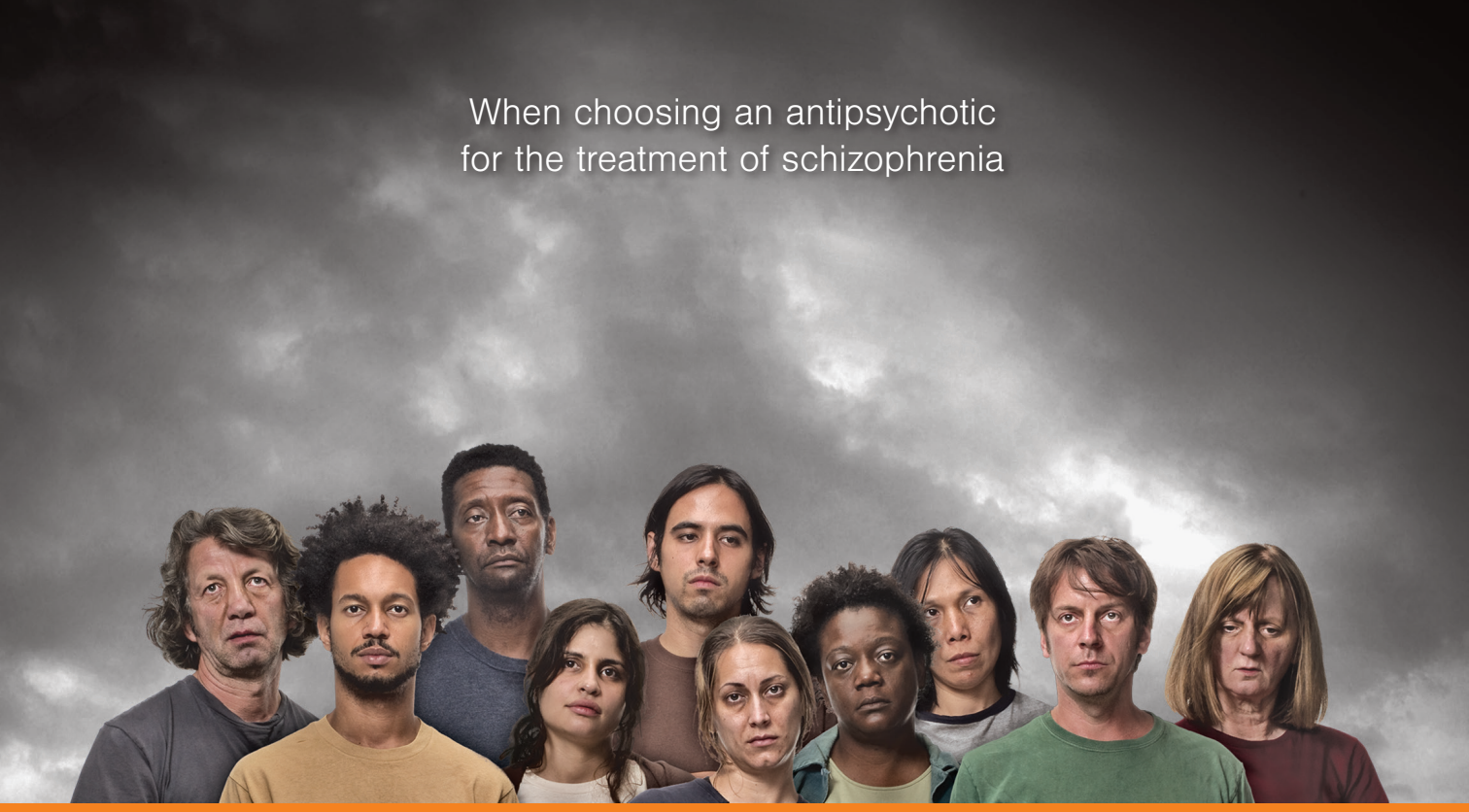
When choosing an antipsychotic
for the treatment of schizophrenia



You Consider Efficacy for Their Minds
You Consider Safety and Tolerability for Their Bodies

LIFT HERE

## But Is There Even More to Consider When Prescribing an Antipsychotic?

When choosing an antipsychotic
for the treatment of schizophrenia

# INVEGA Demonstrated
# Powerful Efficacy With Safety and Tolerability


**Please see Important Safety Information and brief summary of full Prescribing Information for INVEGA on following pages.**

MANY PHYSICIANS HAVE DISCOVERED THE ADDITIONAL FEATURES OF INVEGA

## Pharmacokinetic Metabolism and Excretion

- CYP450 isozymes play a limited role in the overall metabolism of INVEGA

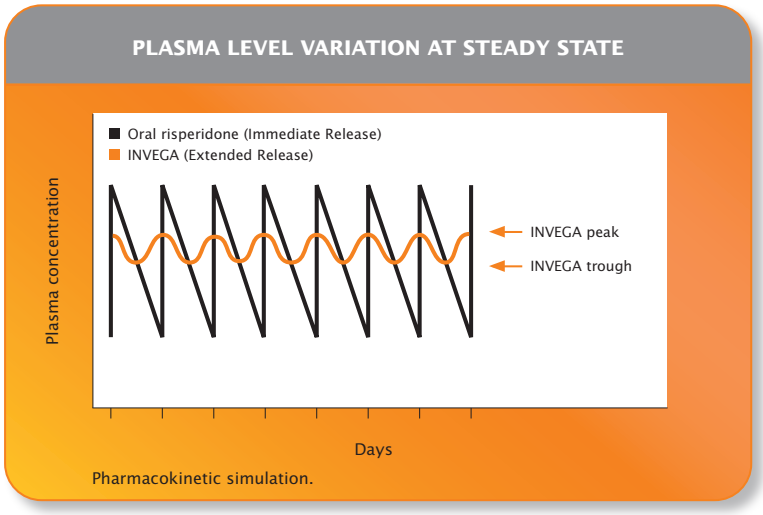
- Less than 10% of the dose is metabolized by each of the 4 identified metabolic pathways*
- Primarily excreted unchanged via the kidneys

*Dealkylation, hydroxylation, dehydrogenation, and benzisoxazole scission.

**Renal Impairment:** Dosing must be individualized according to the patient's renal function status. The maximum recommended dose of INVEGA is 6 mg for patients with mild renal impairment and 3 mg for patients with moderate to severe renal impairment (see Dosing for Special Populations).

## Innovative Drug Delivery

- Innovative OROS® extended-release technology for reduced peak/trough fluctuations†[1]




†Correlation to clinical effect has not been established.

INVEGA™
PALIPERIDONE
*Extended-Release Tablets*

STRENGTH FOR THE WHOLE PERSON

INVEGA™ (paliperidone) extended-release tablets are indicated for the acute and maintenance treatment of schizophrenia.

## IMPORTANT SAFETY INFORMATION FOR INVEGA

**Increased Mortality in Elderly Patients with Dementia-Related Psychosis**

**Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo. Analyses of 17 placebo-controlled trials (modal duration of 10 weeks) in these patients revealed a risk of death in the drug-treated patients of between 1.6 to 1.7 times that seen in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. 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. INVEGA™ (paliperidone) is not approved for the treatment of patients with dementia-related psychosis.**

**Commonly observed adverse events:** The most commonly observed adverse events, occurring at an incidence of ≥5% and at least 2 times placebo, were akathisia and extrapyramidal disorder.

**QT Prolongation:** INVEGA causes a modest increase in the corrected QT (QTc) interval. INVEGA should be avoided in combination with other drugs that are known to prolong the QTc interval, in patients with congenital long QT syndrome or a history of cardiac arrhythmias. Certain circumstances may increase the risk of torsades de pointes and/or sudden death in association with the use of drugs that prolong the QTc interval.

**Neuroleptic Malignant Syndrome (NMS):** NMS, a potentially fatal symptom complex, has been reported with the use of antipsychotic medications, including INVEGA. Clinical manifestations include muscle rigidity, fever, altered mental status and evidence of autonomic instability (see full Prescribing Information). Management should include immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy, intensive symptomatic treatment and medical monitoring, and treatment of any concomitant serious medical problems.

**Tardive Dyskinesia (TD):** TD is a syndrome of potentially irreversible, involuntary, dyskinetic movements that may develop in patients treated with antipsychotic medications. The risk of developing TD and the likelihood that dyskinetic movements will become irreversible are believed to increase with duration of treatment and total cumulative dose. Elderly patients appeared to be at increased risk for TD. Prescribing should be consistent with the need to minimize the risk of TD. The syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn.

**Hyperglycemia and Diabetes:** Hyperglycemia, some cases extreme and associated with ketoacidosis, hyperosmolar coma or death has been reported in patients treated with atypical antipsychotics (APS). Patients starting treatment with APS who have or are at risk for diabetes should undergo fasting blood glucose testing at the beginning of and during treatment. Patients who develop symptoms of hyperglycemia should also undergo fasting blood glucose testing.

**Gastrointestinal:** INVEGA should ordinarily not be administered to patients with pre-existing severe gastrointestinal narrowing. Rare instances of obstructive symptoms have been reported in patients with known strictures taking nondeformable formulations. INVEGA should only be used in patients who are able to swallow the tablet whole.

**Cerebrovascular Adverse Events (CAEs):** CAEs, including fatalities, have been reported in elderly patients with dementia-related psychosis taking atypical antipsychotics in clinical trials. INVEGA is not approved for treating these patients.

**Seizures:** INVEGA should be used cautiously in patients with a history of seizures.

**Hyperprolactinemia:** As with other drugs that antagonize dopamine $D_2$ receptors, INVEGA elevates prolactin levels and the elevation persists during chronic administration.

**Suicide:** The possibility of suicide attempt is inherent in psychotic illnesses and close supervision of high-risk patients should accompany drug therapy.

**Orthostatic Hypotension:** INVEGA may induce orthostatic hypotension associated with dizziness, tachycardia, and in some patients, syncope, especially during the initial dose-titration period. Monitoring should be considered in patients for whom this may be of concern. INVEGA should be used with caution in patients with known cardiovascular disease, and conditions that would predispose patients to hypotension.

**Potential for Cognitive and Motor Impairment:** INVEGA has the potential to impair judgment, thinking, or motor skills. Patients should be cautioned about operating hazardous machinery, including motor vehicles, until they are reasonably certain that INVEGA does not affect them adversely.

**Maintenance Treatment:** Physicians who elect to use INVEGA for extended periods should periodically re-evaluate the long-term risks and benefits of the drug for the individual patient.

**Drug Interactions:** Given the primary CNS effects of INVEGA, INVEGA should be used with caution in combination with other centrally acting drugs and alcohol.

**Weight Gain:** The proportion of subjects having a weight gain of ≥7% body weight were comparable to placebo (5%) for 3 mg (7%) and 6 mg (6%). A higher incidence was seen for 9 mg (9%) and 12 mg (9%).

**Renal Impairment:** Dosing must be individualized according to the patient's renal function status. The maximum recommended dose of INVEGA is 6 mg for patients with mild renal impairment and 3 mg for patients with moderate to severe renal impairment (see Dosing for Special Populations).

**Reference: 1.** Conley R, Gupta SK, Sathyan G. Clinical spectrum of the osmotic-controlled release oral delivery system (OROS®), an advanced oral delivery form. *Curr Med Res Opin*. 2006;22(10):1879-1892.



**Please see brief summary of full Prescribing Information for INVEGA on following pages.**