# INVEGA® (paliperidone ER)
# INVEGA SUSTENNA® (paliperidone palmitate 1-month)
# INVEGA TRINZA® (paliperidone palmitate 3-month)
# INVEGA HAFYERA® (paliperidone palmitate 6-month)
# Drug Interactions with INVEGA, INVEGA SUSTENNA, INVEGA TRINZA, and INVEGA HAFYERA - General

## SUMMARY


- Because paliperidone palmitate is hydrolyzed to paliperidone, results from studies with oral paliperidone should be taken into consideration when assessing drug-drug interaction (DDI) potential.[1]
- Please refer to the local labeling for details regarding the following drugs that have clinically important interactions with INVEGA, INVEGA SUSTENNA, INVEGA TRINZA, and INVEGA HAFYERA[2-4]:
  - Centrally acting Drugs and Alcohol
  - Strong Inducers of CYP3A4/P-glycoprotein (P-gp) - eg, carbamazepine
  - Drugs with Potential for Inducing Orthostatic Hypotension
  - Levodopa and Other Dopamine Agonists
  - Drugs known to Prolong the QTc Interval - avoid use with drugs that also increase QT interval and in patients with risk factors for prolonged QT interval
- No dosage adjustments are required when paliperidone is used concomitantly with valproate.[5]
- A pharmacokinetic interaction between lithium and paliperidone is unlikely.[6]
- Paliperidone is not associated with significant CYP-mediated DDIs but does show moderate-to-strong affinity for P-glycoprotein. Avoid using CYP3A4 and/or P-gp inducers in combination with paliperidone if possible.[7]
- Paliperidone has the potential for inducing orthostatic hypotension. Additive effects may occur when it is coadministered with other therapeutic agents that can also cause orthostatic hypotension. Monitor orthostatic vital signs in patients who have a history of cardiovascular disease, cerebrovascular disease, or conditions that may predispose orthostatic hypotension.[8]
- Paliperidone may antagonize the effect of levodopa and other dopamine agonists. Monitor and manage patients as clinically appropriate.[9]
- Due to the association of antipsychotics with cardiovascular-related adverse events, caution should be exercised when using paliperidone or paliperidone palmitate in patients with pre-existing cardiovascular or cerebrovascular conditions, in those who may be predisposed to dehydration, patients with a family history of QT prolongation, or who are receiving concomitant therapy with a drug that may prolong the QT interval.[9]
- Clinical studies[10-20] and reviews[7,21-23] regarding the DDI potential of INVEGA have been included for your reference.
- Several case studies have reported DDIs with INVEGA and drugs impacting CYP3A4, CYP2D6, and P-gp activity.[24-28]
  - Most recently, a case study of a 34-year-old patient with schizophrenia who developed extrapyramidal side effects (EPSE) suggested that the EPSE may have been due to an interaction between paliperidone and voriconazole, a strong CYP3A4 inhibitor.[29]


## PUBLISHED LITERATURE

**Samtani et al (2009)**[30] presented results from a comprehensive population pharmacokinetic model for INVEGA SUSTENNA analyzing data from 11 clinical trials in patients with schizophrenia. Pooled data from 1,795 patients and 18,530 pharmacokinetic samples with valid concentration time points were used to develop the model. Comedication effects were evaluated for drugs used by ≥10% of the patient population. The analysis illustrated that medications from the drug classes represented by lorazepam, acetaminophen, diazepam, olanzapine, and ibuprofen had negligible and non-significant

effects on paliperidone pharmacokinetics. Medications known to interact with CYP2D6, CYP3A4, or drug transporters were not evaluated in this study because they were not used by sufficient number of patients.

## LITERATURE SEARCH

A literature search of MEDLINE®, EMBASE®, BIOSIS Previews®, and DERWENT Drug File (and/or other resources, including internal/external databases) pertaining to this topic was conducted through 10 June 2024.

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