



# Pharmacokinetics of Risperidone: Clinical Summary

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Risperidone is a second-generation antipsychotic metabolized by the enzyme cytochrome P450 2D6 (CYP2D6). It is available as long-acting injection (depot injection) as well as oral formulations. This clinical summary highlights pharmacokinetic features relevant to mental health prescribers.

## Formulations

- Oral formulations:
  - Tablets
  - Orally disintegrating tablets
  - Liquid formulation
- Long-acting injection: risperidone microspheres (Risperdal Consta)

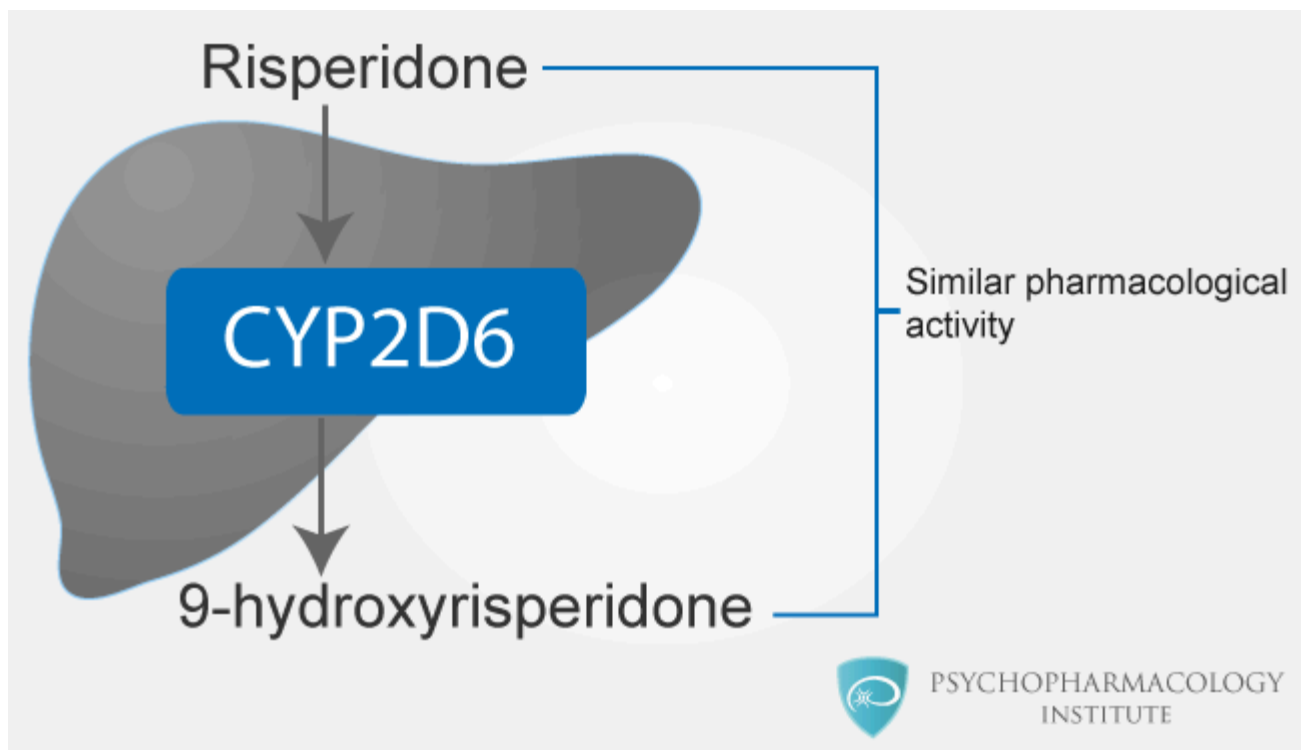
## General pharmacokinetics

### Distribution

- Volume of distribution: 1-2 L/kg.
- Risperidone binds to albumin and alpha1-acid glycoprotein.
- Plasma protein binding:
  - For risperidone: 90%
  - For 9-hydroxyrisperidone: 77%



## Metabolism



### *Risperidone metabolism by CYP2D6*

- CYP 2D6 is the enzyme that catalyzes hydroxylation of risperidone to 9-hydroxyrisperidone.
- The metabolite 9-hydroxyrisperidone has similar pharmacological activity as risperidone.
- CYP 2D6 is subject to genetic polymorphism:
  - Extensive metabolizers convert risperidone rapidly into 9-hydroxyrisperidone
  - Poor CYP 2D6 metabolizers convert risperidone much more slowly.
  - Pharmacokinetics of risperidone and 9-hydroxyrisperidone combined after single and multiple doses are similar in extensive and poor metabolizers.

## Pharmacokinetics of Oral Formulations

### Absorption

- Orally disintegrating tablets and oral solution are bioequivalent to tablets.
- Rapidly absorbed after oral administration.
- Peak plasma levels achieved within 1 hour.
- Linear pharmacokinetics.
- Time to reach steady state ( between 4 and 5 half-lives for all drugs):
  - For risperidone:
    - 1 day in extensive metabolizers.
    - 5 days in poor metabolizers.
  - For 9-hydroxyrisperidone:



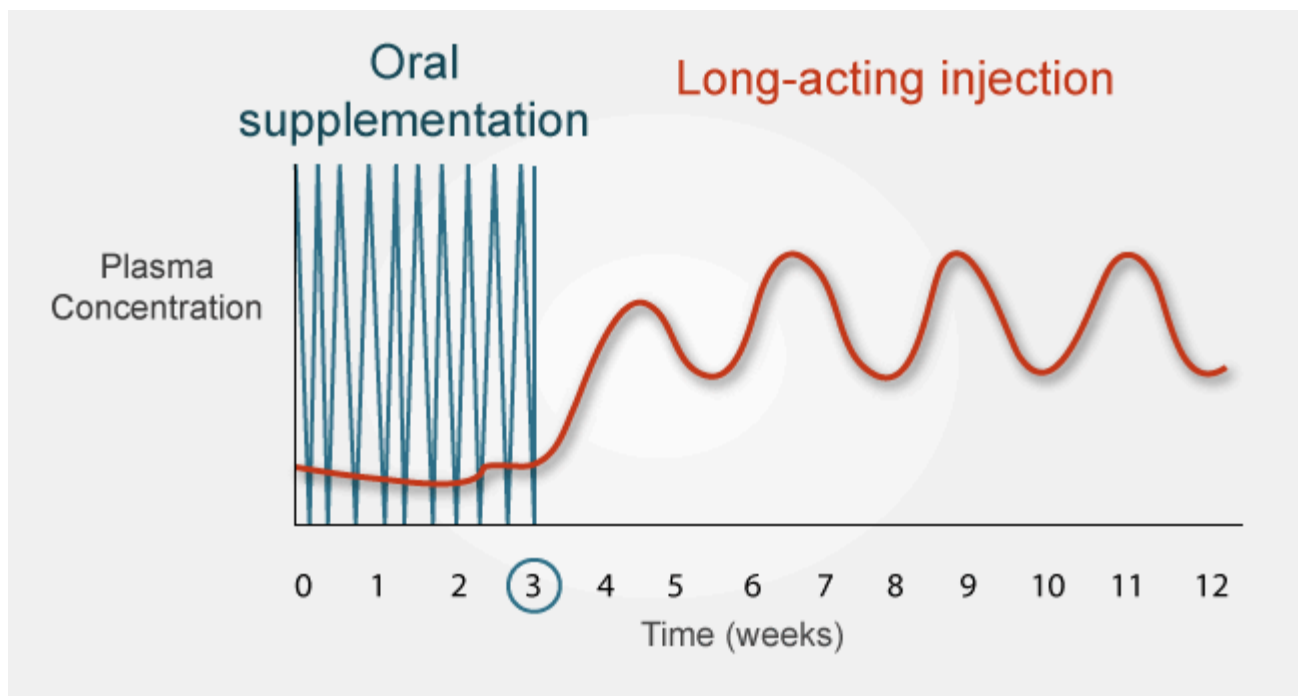
- 5-6 days, measured in extensive metabolizers.
- Food effect: risperidone can be administered with or without meals.

### Excretion

- Apparent half-life of risperidone:
  - 3 hours in extensive metabolizers
  - 20 hours in poor metabolizers
- Apparent half-life of 9-hydroxyrisperidone:
  - 21 hours in extensive metabolizers
  - 30 hours in poor metabolizers

### Pharmacokinetics of Long-Acting Injection (Risperidone Microspheres)

- Risperidone microspheres release considerable amounts of drug 3 weeks after injection.
- Long-acting risperidone should be supplemented with oral risperidone for 3 weeks.



- Apparent half-life of risperidone plus 9-hydroxyrisperidone is 3 to 6 days (related to the erosion of the microspheres and subsequent absorption of risperidone).



## Related Information on Risperidone

- [Mechanism of Action of Risperidone](#)
- [Risperidone Indications: FDA-Approved and Off-Label Uses](#)

## References

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