

# Capravirine



## Drug Description

Capravirine is an imidazole type nonnucleoside reverse transcriptase inhibitor (NNRTI). [1]

## HIV/AIDS-Related Uses

Capravirine is an NNRTI that exhibits potent in vitro antiviral activity against HIV variants with the K103N mutation. Capravirine's in vitro resistance profile suggests that capravirine will reduce plasma HIV RNA levels in NNRTI-experienced patients.

Preliminary data from a phase II trial showed that NNRTI-experienced patients treated with nelfinavir, two nucleoside reverse transcriptase inhibitors (NRTIs), and capravirine had a decrease in plasma HIV RNA from baseline. However, there was no significant difference between the placebo and capravirine groups.[2]

Clinical trials of capravirine were suspended in January 2001 by Pfizer, Agouron Pharmaceuticals' parent company, based on results of an animal toxicology study that demonstrated an unexpected finding of vasculitis. A limited number of patients who had failed previous therapy and were doing well on capravirine were allowed to continue their capravirine regimens. Pfizer resumed clinical trials in December 2001 after reporting that vasculitis had not been observed in people taking capravirine.[3]

## Pharmacology

Capravirine inhibits replication of HIV-1 by interfering with the activity of the viral RNA-dependent DNA polymerase (reverse transcriptase, RT).

Studies of the three-dimensional structure of RT-NNRTI complexes have shown that NNRTIs all bind in a pocket. RT mutations that confer resistance to NNRTIs affect the amino acids that surround this pocket. Most mutations replace a larger amino acid with a smaller one, thereby decreasing RT-NNRTI contact and reducing affinity. Capravirine is larger than other NNRTIs and has three main-chain hydrogen bonding

interactions. This may account for capravirine's greater relative resistance to RT mutations; two mutations are required to confer high-level resistance to capravirine.[4]

In clinical trials, capravirine has displayed linear pharmacokinetics and a half-life of approximately 2 hours. Mean decreases in viral load ranged from 1.23 log<sub>10</sub> for a 700 mg BID dosing regimen to 1.69 log<sub>10</sub> for a 2100 mg BID dosing regimen, compared to a mean decrease of 1.65 log<sub>10</sub> in patients treated with a nelfinavir/zidovudine/lamivudine regimen.[5]

In vitro studies using human liver microsomes demonstrate that CYP3A is the major isoform for capravirine's metabolism; drugs that share this pathway may alter capravirine's pharmacokinetics.[6]

## Adverse Events/Toxicity

Nausea, vomiting, diarrhea, and headache are the most frequently reported side effects of capravirine.[7] Adverse effects occur more frequently at the 2100 mg dose than at the 1400 mg dose.[8]

## Drug and Food Interactions

Twice-daily capravirine in combination with nelfinavir is well tolerated and achieves target drug concentrations. Nelfinavir increases the concentration of capravirine by approximately two-fold.[9]

Capravirine can be taken with food.[10]

## Clinical Trials

For information on clinical trials that involve Capravirine, visit the ClinicalTrials.gov web site at <http://www.clinicaltrials.gov>. In the Search box, enter: Capravirine AND HIV Infections.

## Dosing Information

Mode of Delivery: Oral.[11]

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## Dosing Information (cont.)

Dosage Form: In clinical trials, capravirine has been dosed at 700 mg, 1400 mg, and 2100 mg BID and 700 mg and 1400 mg TID.[12]

Safety and efficacy data suggest that 1400 mg BID may be the optimal dose.[13]

## Chemistry

CAS Name:

5-[(3,5-Dichlorophenyl)thio]-4-(1-methylethyl)-1-(4-pyridinylmethyl)-1H-imidazole-2-methanol carbamate ester[14]

CAS Number: 178979-85-6[15]

Molecular formula: C<sub>20</sub>H<sub>20</sub>Cl<sub>2</sub>N<sub>4</sub>O<sub>2</sub>S[16]

C53.22% H4.47% Cl15.71% N12.41% O7.09% S7.10%[17]

Molecular weight: 451.38[18]

Melting point: 88 C[19]

Physical Description: Crystals from diethylether as hemidehydrate.[20]

## Other Names

S-1153[21]

AG1549[22]

1H-Imidazole-2-methanol, 5-((3,5-dichlorophenyl)thio)-4-(1-methylethyl)-1-(4-pyridinylmethyl)-, carbamate (ester)[23]

## Further Reading

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inhibits replication of known drug-resistant strains of human immunodeficiency virus type 1. Antimicrob Agents Chemother. 1998 Jun;42(6):1340-5.

## Manufacturer Information

Capravirine  
Agouron Pharmaceuticals Inc  
11095 Torreyana Rd  
San Diego, CA 92121  
(888) 847-2237

## For More Information

Contact your doctor or an AIDSinfo Health Information Specialist:

- Via Phone: 1-800-448-0440 Monday - Friday, 12:00 p.m. (Noon) - 5:00 p.m. ET
- Via Live Help: [http://aidsinfo.nih.gov/live\\_help](http://aidsinfo.nih.gov/live_help) Monday - Friday, 12:00 p.m. (Noon) - 4:00 p.m. ET

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## References

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