Abecarnil is a β-carboline partial benzodiazepine agonist which may be selective for certain subpopulations of benzodiazepine receptors. It has greater affinity for central benzodiazepine receptor sites than diazepam, but low affinity for peripheral benzodiazepine, adrenergic, dopaminergic, opiate and serotonergic receptors.

At present, virtually all published pharmacodynamic data for abecarnil are derived from animals studies. Abecarnil is active in a number of animal models of anxiety and is generally more effective than diazepam. It also attenuated some, but not all, chemically- or electrically-induced seizures in animals (diazepam
antagonised most types of induced seizures) and was protective in genetic models of epilepsy. In most instances, its anticonvulsant activity did not appear to be attenuated during long-term administration. Although some sedation occurs with abecarnil administration to animals, the drug is associated with less sedation, muscle relaxation, ataxia and impairment of memory than are several benzodiazepines. It also produces less potentiation of the effects of ethanol and hexobarbital than diazepam. In animals, the withdrawal syndrome after abecarnil discontinuation or administration of the benzodiazepine antagonist flumazenil is generally reduced or absent compared with benzodiazepines, suggesting that abecarnil has a low dependence potential. Abecarnil appears to have less propensity to induce tolerance than diazepam; it may also have a reduced abuse liability compared with benzodiazepines, as suggested by limited evidence in animals.

The pharmacokinetic profile of abecarnil has yet to be investigated in patients with generalised anxiety disorder. Although pharmacokinetic parameters showed great intra- and interindividual variability in volunteers, the mean oral bioavailability of abecarnil 5 or 10 mg was 39% in older volunteers and 55 to 65% in younger volunteers, and maximum plasma concentrations and AUC values after a single dose or at steady-state were dose-proportional. Abecarnil is predominantly metabolised, with less than about 10% of the drug being excreted unchanged. The main metabolite is the glucuronide conjugate of abecarnil, although 4 metabolites have been identified.

Only one clinical trial assessing the efficacy of abecarnil in the treatment of generalised anxiety disorder has been published in full. Low dosages of the drug (3 to 9 mg/day) were significantly more effective than placebo and produced few serious adverse effects with no significant withdrawal syndrome upon discontinuation of 3 weeks of treatment. However, higher dosages of abecarnil (15 to 30 mg/day, and to a lesser extent 7.5 to 15 mg/day) produced a high incidence of adverse CNS effects [including drowsiness (71 and 51%), a loss of equilibrium (26 and 11%), confusion (24 and 3%), amnesia (15 and 3%), fatigue (15 and 17%), lethargy (18 and 3%), insomnia (15 and 6%) and dizziness (18 and 11%)] which caused discontinuation of treatment in 29% of patients receiving abecarnil 15 to 30 mg/day. Higher drug dosages were also associated with some withdrawal signs upon discontinuation of therapy. In addition, there appeared to be some loss of efficacy with all tested dosages of abecarnil in comparison with placebo during the third week of treatment. Other trials of abecarnil, published collectively in abstract form with little detail, have suggested that 4 to 6 weeks of treatment with the drug had efficacy similar to benzodiazepines and produced a similar number of adverse effects or withdrawal symptoms as placebo when discontinued in a tapered fashion.

In conclusion, experimental evidence to date suggests that abecarnil may be a valuable alternative to currently used agents for the treatment of generalised anxiety disorder, particularly if efficacy is maintained at lower dosages. However, clinical trials, including comparisons with benzodiazepines, will first need to demonstrate the potential advantages (reduced adverse effects, dependence and abuse potential) observed with abecarnil in animal models.