Quazepam
A Preliminary Review of its Pharmacodynamic and Pharmacokinetic Properties, and Therapeutic Efficacy in Insomnia

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Summary

Quazepam is a trifluoroethyl benzodiazepine hypnotic with a half-life of 27 to 41 hours, which has been shown to induce and maintain sleep in the short to long term (up to 4 weeks) treatment of patients with chronic or transient insomnia.

Although its hypnotic efficacy has been well characterised against placebo, there are few clinical studies in comparison with established hypnotics, particularly over long term administration. However, preliminary evidence suggests that quazepam 15 to 30mg is as effective as flurazepam and triazolam in usual therapeutic doses, and causes minimal rebound insomnia following its withdrawal, unlike rapidly eliminated benzodiazepines such as triazolam. The lack of rebound phenomena is likely to be attributable to the 'carryover' effects occurring after discontinuation of quazepam, which has pharmacologically active metabolites with half-lives of elimination similar to or longer than that of the parent drug. Probably because of the long half-lives of quazepam's metabolites, daytime sedation, fatigue and lethargy are the most frequently reported side effects. These side effects are most intense with the 30mg dose and least with the 7.5mg dose, which has not been studied extensively.

Hence, quazepam is an effective hypnotic which may be particularly suitable for short or medium term use in patients in whom withdrawal effects or rebound insomnia may be especially bothersome. Further definition of certain characteristics of its profile - such as its long term use and potential for development of tolerance or dependence, effects on psychomotor skills, efficacy of the 7.5mg dose, and suitability in elderly patients and patients with chronic organic diseases - will assist in more clearly defining its ultimate place in therapy.

Pharmacodynamic Studies

In comparison with baseline established by the administration of placebo, quazepam in doses of 7.5 to 45mg decreases sleep latency and percentage of stage 1 sleep, and facilitates sleep maintenance as measured by reductions in number of awakenings, wake time after sleep onset and total wake time, and prolonged total sleep time. These effects are usually apparent following a single dose. The percentage of sleep spent in stage 2 increases, whereas that of rapid eye movement (REM) sleep and slow wave sleep (stages 3 and 4) is shortened.

Comparative parallel group sleep laboratory studies reveal that the profile of sleep induction and maintenance with quazepam 15 and 30mg is similar to that of flurazepam. Unlike the more rapidly eliminated benzodiazepines triazolam and temazepam, the hypnotic effects of quazepam persist throughout the first night or more of drug withdrawal. Thus, rebound insomnia has not been shown to occur with quazepam, in contrast to the