Amended scope following consultee information meeting held on 27 March 2003

Health Technology Appraisal

Zaleplon, zolpidem and zopiclone for the management of insomnia

Scope

Objective: To establish the clinical and cost effectiveness of zaleplon, zolpidem and zopiclone, relative to the benzodiazepines, for the management of insomnia, and to produce guidance to the NHS in England and Wales.[1]

Background: Insomnia is a disturbance of normal sleep patterns characterised by difficulty in initiating sleep and/or difficulty maintaining sleep, with frequent nocturnal or early morning awakenings. The sleep disturbance, and associated daytime fatigue causes distress or impairment in social, occupational, or other important areas of functioning. A study published in 1999[2] suggested that the prevalence of insomnia was 22% in the UK population. In the same year there were over 10 million GP prescriptions for hypnotic drugs.

Non-pharmacological treatments for insomnia include sleep hygiene education, stimulus control intervention, sleep restriction, paradoxical intention therapy, relaxation techniques and cognitive behavioural therapy.

Benzodiazepines are the most widely used hypnotics, but are associated with significant adverse effects, especially with high-dose and continuous use, which may be more pronounced in older people. The British National Formulary (Edition 44) lists six benzodiazepines (nitrazepam, flunitrazepam, flurazepam, loprazolam, lormetazepam and temazepam) that currently hold a UK license for short-term treatment of insomnia. Flunitrazepam and flurazepam cannot currently be prescribed on the NHS. It is estimated that approximately of 10% of people with long-term insomnia taking benzodiazepines do so for more than a year[3]. Although extended use of benzodiazepines is common practice, it is outside their current licensed indications and is known to lead to dependency and a withdrawal syndrome on cessation.

The technology: Zaleplon, zolpidem and zopiclone are non-benzodiazepine agents that act at similar receptors (or receptor sub-types) to benzodiazepines. These agents were developed with the aim of overcoming some of the adverse events associated with benzodiazepines. They have a short duration of action and are licensed for short-term use.

Intervention(s)	Zaleplon, zolpidem and zopiclone
Population(s)	Individuals with insomnia
Current standard treatments (comparators)	Benzodiazepines
Other considerations:	The interventions will be appraised within their licensed indications

	If the evidence allows, head to head comparisons between the three drugs listed in the interventions section will be considered. Evidence will particularly be sought on the relative incidence of dependency and withdrawal syndromes. If the evidence allows sub-group analyses will be undertaken and consideration will be given to the dose of the intervention and comparator. It is assumed that individuals participating in clinical trials may also be utilising non-pharmacological strategies. Where the evidence permits this will be taken into consideration. Outcome measures that will be considered include: resolution of symptoms, changes in sleep patterns and architecture, sleep quality, daytime alertness, quality of life, recurrence of insomnia, tolerance, side-effects (including residual daytime sedation and memory impairment) and abuse potential.

[1] The remit from the Department of Health/Welsh Assembly Government was "To appraise the clinical and cost effectiveness of the use of zaleplon, zolpidem and zopiclone in the management of short-term insomnia, compared with medicines in the benzodiazepine class."

[2] Chevalier H, Los F, Boichut D, et al. (1999) Evaluation of severe insomnia in the general population: results of a European multinational survey. *Journal of Psychopharmacology* 13(4 suppl 1): S21-24

[3] Nowell PD, Mazumdar S, Buysse DJ, Dew MA, Reynolds CF, Kupfer DJ. Benzodiazepines and zolpidem for chronic insomnia. A meta-analysis of treatment efficacy. JAMA 1997; 278(24):2170-2177.