period should be limited to 2 weeks when brotizolam, midazolam, or triazolam are used.[16]

Tolerance to the hypnotic effects of benzodiazepines develops rapidly, with sleep latency and pattern returning to pretreatment levels within a few weeks of starting treatment.

A number of other drugs have been used as alternatives to the benzodiazepines. Zaleplon, zopiclone, and zolpidem act on the same receptors or receptor subtypes as the benzodiazepines although structurally they are unrelated. Their short duration of action makes them more suitable for patients who have trouble falling asleep. The CPMP has recommended that treatment with zolpidem should be limited to a maximum of 4 weeks.[16] It remains to be proven whether these drugs offer any advantages over the benzodiazepines. Indeed, the CSM considers that zopiclone has the same potential for adverse psychiatric reactions, including dependence, as benzodiazepines.[17] NICE[18] in the UK found no compelling evidence of any clinically useful differences between these drugs and the shorter-acting benzodiazepines in terms of effectiveness, adverse effects, or potential for dependence or abuse, and recommends that patients who do not respond to zaleplon, zopiclone, zolpidem, or benzodiazepines should not be switched between these hypnotics; patients may be switched if adverse effects directly related to a specific drug occur.

The use of cloral hydrate and its derivatives as hypnotics is now very limited. They have been used as alternatives to benzodiazepines in the elderly, although there is no convincing evidence of any special value in these patients. They used to be considered useful hypnotics for children but such use is rarely justified.

Clomethiazole has also been used as an alternative to benzodiazepines in the elderly. Nasal and conjunctival irritation may be troublesome, and the danger of overdosage and risk of dependence should be considered.

Some antihistamines have hypnotic properties and a number, including alimemazine, diphenhydramine, doxylamine, and promethazine, are marketed for insomnia. They may cause troublesome antimuscarinic effects and those with longer half-lives may cause hangover effects. Promethazine is also popular for use in children, but such use is not usually justified (see Sudden Infant Death Syndrome under Adverse Effects of Promethazine, p.588, for further details).

Barbiturates are no longer recommended as hypnotics because of their adverse effects. The CSM[19] has advised that barbiturates should only be used for insomnia that is severe and intractable when there are compelling reasons to, and then only in patients already taking barbiturates. It was also advised that attempts should be made to wean patients off barbiturate hypnotics. Similarly, compounds such as ethchlorvynol, glutethimide, and methaqualone are not recommended.

Alcohol is not recommended because it has a short weak hypnotic action, and rebound excitation can result in early morning insomnia. Its diuretic effects can interrupt sleep and chronic use can lead to rapid development of tolerance and addiction.

Tryptophan, sometimes in the form of dietary supplements, has enjoyed some popularity in the treatment of insomnia. Its efficacy is difficult to substantiate and, since the publication of reports linking tryptophan with the eosinophilic-myalgia syndrome, preparations indicated for insomnia have been withdrawn from the market in many countries.

Melatonin, a hormone believed to be involved in the maintenance of circadian rhythms, may be useful in the treatment of insomnias such as those due to **jet lag**[20] or other disorders (where it might act by resetting the body clock), and in the elderly. However, its benefits have been questioned,[21] and certainly evidence for a direct hypnotic effect is less conclusive; its sleep-inducing properties are usually only seen after very high, supraphysiological concentrations have been attained.[5,6] Ramelteon, a melatonin receptor agonist, is used as a hypnotic in some countries.

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Sleep-associated movement disorders. Parasomnias are motor disorders, with or without autonomic features, that occur during sleep or are exaggerated by sleep. Some of the main parasomnias include nightmares, night terrors, sleepwalking (somnambulism), nocturnal enuresis (p.2180), bruxism (teeth grinding), head banging, and aggression during sleep. Other common movement disorders associated with sleep are restless legs syndrome and periodic limb movements in sleep. Parasomnias are common but rarely require treatment with drugs other than the symptomatic treatment of sleep-related medical problems. The management of some of these conditions is discussed briefly below.

The **restless legs syndrome** is characterised by an unpleasant creeping sensation deep in the legs with an irresistible urge to move them. Symptoms begin during relaxation in the evenings and in bed, and interfere with the ability to fall asleep. The aetiology of this condition is obscure and treatment has been largely empirical.[1-11] Drug treatment may not always be necessary and non-pharmacological methods such as good sleep hygiene should be tried initially.[1,3,7,8,12] There have been reports of efficacy with a wide range of treatments, although few have been well studied. Dopaminergic therapy has emerged as a common first-line treatment, a long-acting agonist, such as cabergoline, pergolide, pramipexole, or ropinirole, being preferred in order to avoid the complications associated with levodopa.[5,6,8-12] Anticonvulsants, such as carbamazepine, clonazepam, and gabapentin may be of use in those intolerant of dopamine agonists or in those who require additional medication.[5,8-11] Other drugs that have been reported to be of benefit include some opioids, clonidine, and the benzodiazepines.[5,7-12] Iron supplementation may be effective if the syndrome is associated with iron deficiency.[2-4,7-12] Many patients with restless legs syndrome exhibit **periodic limb movements in sleep**,[2,3] characterised by repetitive periodic leg and foot jerking during sleep. Treatments tried are similar to those for the restless legs syndrome; clonazepam and levodopa are amongst the drugs shown to be of benefit.

Some **parasomnias** have responded to treatment with benzodiazepines.[13,14] These include bruxism, head banging, aggression during sleep, night terrors, and sleepwalking.

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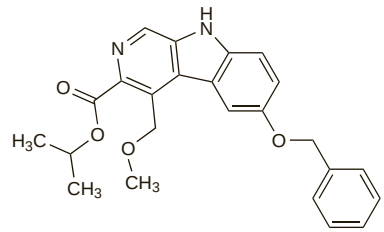
Abecarnil *(rINN)*

Abécarnil; Abecarnilo; Abecarnilum; ZK-112119. Isopropyl 6-(benzyloxy)-4-(methoxymethyl)-9*H*-pyrido(3,4-*b*)indole-3-carboxylate.

Абекарнил

$C_{24}H_{24}N_2O_4$ = 404.5.

CAS — 111841-85-1.



Profile

Abecarnil is a beta-carboline compound reported to be a partial agonist at benzodiazepine receptors. It has been studied for its anxiolytic and anticonvulsant actions in anxiety disorders and alcohol withdrawal syndrome.

◊ References.

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Acamprosate Calcium *(BANM, USAN, rINNM)*

Acamprosate calcique; Acamprosate de Calcium; Acamprosato de calcio; Acamprosatum calcicum; Akamprosaattikalsium; Akamprosát vápenatá sůl; Akamprosatkalcium; Akamprosato kalcio druska; Akamprozát-kalcium; Calcii Acamprosatum; Calcium Acetylhomotaurinate. Calcium 3-acetamido-1-propanesulphate.

Кальций Акампрозат

$C_{10}H_{20}CaN_2O_8S_2$ = 400.5.

CAS — 77337-76-9 (acamprosate); 77337-73-6 (acamprosate calcium).

ATC — N07BB03.