Clonazepam

Introduction
Clonazepam is a benzodiazepine antiepileptic. The 2004 WHO Model Formulary lists it for use in the treatment of: atonic seizures, myoclonic seizures; atypical absence seizures; absence seizures resistant to ethosuximide or valproate; and infantile spasms. In the WHO Model List of Essential Medicines (revised in April 2003), clonazepam is in the complementary list under anticonvulsants/antiepileptics.

Other drugs currently listed in the formulary with related uses include valproate (valproic acid), ethosuximide (complementary list), diazepam, phenytoin, phenobarbital and carbamazepine.

Product and Dosage
Clonazepam is available as a 500 microgram scored tablet. The adult dosage is initially 1mg at night for 4 nights, increased gradually over 2-4 weeks to a usual maintenance dose of 4-8mg daily in divided doses. In older or debilitated patients, the initial dose is 500 micrograms, increased as above. The dose for children aged up to 1 year is initially 250 micrograms increased as above to 0.5-1mg daily in divided doses, in children aged 1-5 years is initially 250 micrograms increased to 1-3mg daily in divided doses and in 5-12 year olds is initially 500 micrograms increased to 3-6mg daily in divided doses.

Evidence of value
According to the Scottish Intercollegiate Guidelines Network (SIGN), clonazepam may be used for refractory myoclonic seizures. However, the guideline does not mention clonazepam as a possible treatment for atonic seizures, atypical absence seizures or absence seizures resistant to ethosuximide or valproate, and recommends valproate and lamotrigine as “drugs of choice for primary generalised seizures”.

Prodigy Guidance recommends clonazepam as “an option” for the treatment of myoclonic seizures, but lists valproate as the “preferred monotherapy”. It states that clonazepam, although effective in the treatment of absence seizures, is not a preferred option because of problems with sedation and tolerance. It lists valproate as the preferred monotherapy for absences, and gives ethosuximide or lamotrigine as alternatives. Prodigy does not mention clonazepam as a possible treatment for atonic seizures.

The British National Formulary (BNF) lists valproate as the drug of choice for myoclonic seizures, but lists clonazepam, along with ethosuximide and lamotrigine as alternatives. It also lists clonazepam, along with phynotoin, valproate, lamotrigine, ethosuximide and phenobarbital, as a drug that may be tried for atypical absence, atonic and tonic seizures.

Adverse Effects
Unwanted effects of clonazepam include drowsiness, fatigue, dizziness, muscle hypotonia, coordination disturbances, hypersalivation in infants,
paradoxical aggression, irritability and mental changes, and rarely, blood disorders and abnormal liver-function tests. The drug is also associated with the development of tolerance. Withdrawal of clonazepam may be difficult because of the risk of dependence. Abrupt withdrawal of benzodiazepines should be avoided, as this may precipitate severe rebound seizures. Dosage should be reduced in stages, over several months, at least.

**Recommendation**

Clonazepam still has a place as a second-line drug for the treatment of refractory myoclonic seizures and should continue to be listed in the WHO Model List of Essential Medicines. There are more suitable alternatives available listed in the Model List for other types of epileptic seizure.


**References**

2. [http://www.who.int/medicines/organization/par/edl/eml/shtml](http://www.who.int/medicines/organization/par/edl/eml/shtml)

**Search Strategy**

The electronic databases, websites, guidelines, systematic reviews and journals searched were:

- Agency for Healthcare Research and Quality
- British Medical Journal
- British National Formulary
- Centre for Reviews and Dissemination
- Clinical Evidence
- Drug and Therapeutics Bulletin
- Guidelines International Network
- Lancet
- Medical Letter
- Medline (OVID)
- MeReC
- National Guideline Clearinghouse
- National Institute of Clinical Excellence
- New England Journal of Medicine
- Prodigy
- The Cochrane Library
- Therapeutics Initiative
- WHO electronic library