DIPARTIMENT TAS-SAĦĦA DEPARTMENT OF HEALTH
MALTA

L-Uffiċċju tal-Uffiċjal Mediku Ewlieni *Office of the Chief Medical Officer*

DH CIRCULAR No. 85/2013
DH 1644/2013

14th May 2013

Attention All: POYC
Medical Practitioners

Re: Clonazepam Tablets

Clonazepam is a highly potent benzodiazepine drug available on the Government Formulary List as 0.5mg and as 2mg tablets.

It is licensed for 'all clinical forms of epileptic disease and seizures in infants, children and adults, especially absence seizures (petit mal) including atypical absence; primary or secondarily generalised tonic-clonic (grand mal), tonic or clonic seizures; partial (focal) seizures with elementary or complex symptomatology; various forms of myoclonic seizures, myoclonus and associated abnormal movements' [SPC].

Clonazepam, like other benzodiazepines, brings about paradoxical effects and drowsiness as well as other long-term effects which include tolerance, dependence, and withdrawal syndrome.

Despite the presence of more appropriate alternatives, clonazepam is currently being used off-license to treat anxiety. This has led to a yearly increase since the department of health exceeded the allocated international quota and in fact this year the department started experiencing shortages. It has been clinically recommended that this medicine be reserved for epileptic patients with restricted prescriber criteria given that for anxiety there are other alternatives.

Withdrawal from benzodiazepine use, especially long-term use, should be gradual because abrupt withdrawal may give rise to symptoms including confusion, toxic psychosis, convulsions, or a condition resembling delirium tremens.

Considering the fact that it is recommended that benzodiazepines are to be used for the shortest time-span possible to treat anxiety, and never exceeding 2–4 weeks due to risks of tolerance and dependence and a lack of long-term effectiveness, it follows that **the benzodiazepine of choice in the treatment of anxiety should be one that facilitates flexible and sensible withdrawal strategies**.

1. The longer the half life of a benzodiazepine is, the smoother withdrawal will be. Smooth withdrawal from benzodiazepines is often difficult to achieve with potent benzodiazepines

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with short half lives. Clonazepam has a short half life compared to diazepam (18-50hours versus ≈200hrs). This makes diazepam a more suitable treatment choice for use in anxiety as it facilitates the prevention of withdrawal symptoms and permits a smoother withdrawal from treatment since it permits a smooth decline in blood concentrations of the benzodiazepine, reslting in less inter-dose fluctuations.

2. Clonazepam is a highly potent benzodiazepine. The 0.5mg dose of clonazepam is equivalent to the 10mg dose of diazepam. Diazepam is available as 5mg and 2mg tablets. The 2mg tablets can be further subdivided into 1mg halves. Diazepam is therefore available in individual units which are much less potent than the weakest unit available of clonazepam, which is of 0.5mg. This makes diazepam a much more versatile benzodiazepine than clonazepam when it comes to withdrawal as the availability of lower potency subunits makes it possible to attain a smooth and tapered withdrawal, hence making diazepam more suitable than clonazepam for use in anxiety. As per SPC, the **total daily dose for diazepam should not exceed 30mg.**

   For the reasons mentioned above, a switchover from clonazepam to diazepam is being recommended for those patients who are being treated with clonazepam for indications excluding the licensed indication.

Thank you
For your attention, please

Dr. Natasha Azzopardi Muscat
Chief Medical Officer

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