

Report of the Benzodiazepine Committee

AUGUST 2002



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DEPARTMENT
OF HEALTH AND
CHILDREN
AN ROINN
SLAINTE AGUS LEANAÍ



Foreword by Minister Michéal Martin

I established the Benzodiazepine Committee in June 2000 and asked it to examine the current prescribing and use of benzodiazepines and to consider recommendations on good prescribing and dispensing practice, paying particular attention to the management of drug misusers.

This comprehensive Report, which marks the fruition of extensive work and consultations undertaken by the Benzodiazepine Committee represents a major step towards addressing inappropriate benzodiazepine use in this country. It sets out in some detail the facts about benzodiazepine usage in Ireland and makes recommendations across a number of areas. It also includes Good Practice Guidelines to assist clinicians in adopting best practice in what is a complex and difficult area.

The Report emphasises in particular the positive results of awareness raising, both among health professionals and among the general public, in relation to the appropriate use of benzodiazepines.

Finally, I would like to record my appreciation of the work of the members of the Benzodiazepine Committee in producing this comprehensive, informative and useful Report.

A handwritten signature in black ink that reads "Michéal Martin". The signature is written in a cursive, flowing style.

Michéal Martin T.D.

Minister for Health and Children

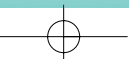
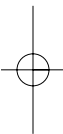
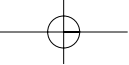
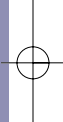
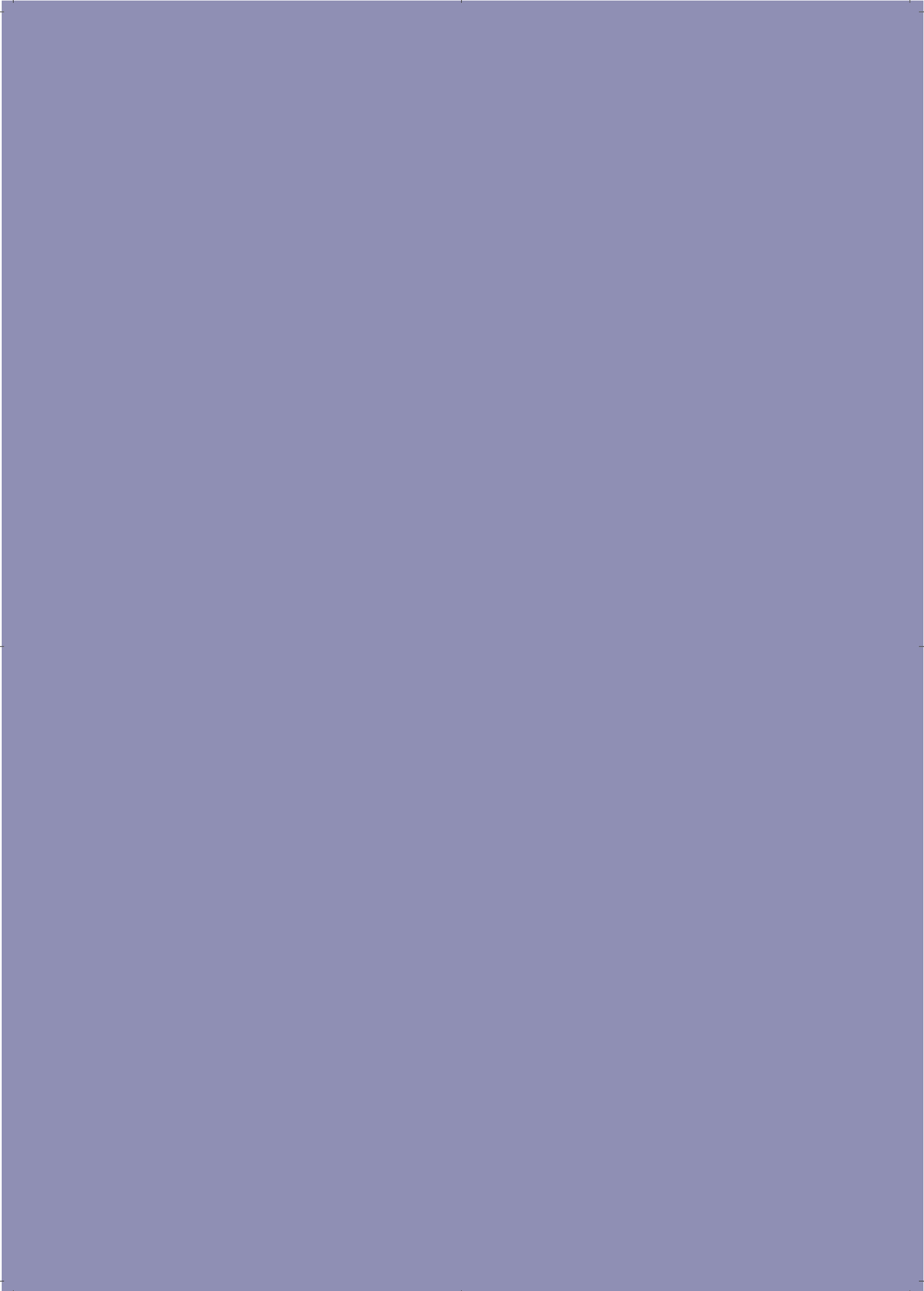
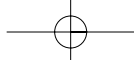


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CHAPTER ONE

Introduction

1.1 Terms of Reference and Work of Committee

The Benzodiazepine Committee was established by Mr Micheál Martin, T.D., Minister for Health and Children in June, 2000. Its terms of reference were:

- ❖ to examine the current prescribing and use of benzodiazepines;
- ❖ to consider recommendations on good prescribing and dispensing practice, paying particular attention to the management of drug misusers;
- ❖ to make recommendations as appropriate.

The membership of the Committee was as follows:

- Mr Martin Gallagher, Assistant Chief Executive, East Coast Area Health Board (Chair)
- Professor Colin Bradley, Department of General Practice, University College Cork
- Mr John Byrne, Vice President, An Bord Altranais
- Dr Sean Conroy, Regional Manager, Western Health Board
- Mr John Corr, Community Pharmacist, Coolock, Pharmaceutical Society of Ireland and Irish Pharmaceutical Union
- Dr Ide deLargy, Irish College of General Practitioners
- Dr Neville De Souza, Specialist in Public Health, South Eastern Health Board
- Mr Tony Geoghegan, Director, Merchants Quay Project
- Mr Tom Gilson, JADD (Jobstown Assisting Drug Dependency)
- Dr Kieran Harkin, GP Unit, South Western Area Health Board
- Ms Mary Jackson, Assistant Principal, Department of Health and Children
- Dr Howard Johnson, Specialist in Public Health, ERHA
- Dr Eamon Keenan, Consultant Psychiatrist, South Western Area Health Board
- Mr Tom McGuinn, Chief Pharmacist, Department of Health and Children
- Dr John O'Connor, Consultant Psychiatrist, Irish Division, Royal College of Psychiatrists
- Dr Denis O'Driscoll, Liaison Pharmacist, South Western Area Health Board
- Dr Dermot Walsh, Inspector of Mental Hospitals
- Ms Louise Kenny, Higher Executive Officer, Department of Health and Children (Secretary)

In order to assist it in its work, the Committee placed advertisements in the medical press inviting submissions on the issue of benzodiazepines, and interested groups, such as Local Drugs Task Forces and health boards, were also requested to make submissions. A total of 22 written submissions was received and a further three oral presentations were made to the Committee. Those who provided submissions are listed at Appendix 1, and a synopsis of the main points of the oral submissions is presented in Appendix 2.

The Committee as a whole met on 14 occasions, and a sub-committee which was charged with the task of developing good practice guidelines for clinicians met on 4 occasions.

1.2 What are Benzodiazepines?

Definition

Benzodiazepines are defined as ‘a large family of drugs used as hypnotics, anxiolytics, tranquillizers, anticonvulsants, pre-medication, and for intravenous sedation. They differ in their duration of action, metabolites and lipid solubility. Short acting ones are used as hypnotics, longer acting ones as hypnotics and tranquillizers, and those with high lipid solubility act rapidly if given intravenously. They act as a specific central nervous system receptor or by potentiating the action of inhibitory neuro transmitters. They have advantages over other sedatives by having some selectivity for anxiety rather than general sedation’.¹

Background information

Benzodiazepines were developed in the 1950’s and are among the most widely used prescription medicinal products in the world. They can generally be divided into :

- 1) anxiolytics (anti-anxiety drugs) which include diazepam (Valium®), alprazolam (Alprox®, Calmax®, Gerax® and Xanax®), bromazepam (Lexotan®), chlordiazepoxide (Librium®), clobazam (Frisium®) and chlorazepate (Tranxene®);

and

- 2) hypnotics (sleep-inducing drugs) which include flunitrazepam (Rohypnol®); flurazepam (Dalmane®), loperazolam (Dormonox®), lormetazepam (Noctamid®), nitrazepam (Mogadon®, Somnite®) and temazepam (Normison®, Nortem®, Tenox®).

This division is not absolute, however, because many of the anxiolytics can also act as hypnotics.

Benzodiazepines have a wide range of usage and are valuable, and sometimes life saving, across a wide range of clinical conditions when appropriately used. The major clinical advantages are in the treatment of certain anxiety states, insomnia, panic, epilepsy, muscle spasms and pre-surgical stress. Their use has generally been perceived as being safe and of low toxicity. Nearly all the disadvantages of benzodiazepines have resulted from inappropriate long-term use, and it is this use that has earned them a poor reputation, particularly as drugs of dependence. Adverse effects include psychomotor impairment, especially in the elderly and occasionally paradoxical excitement. With long-term use, tolerance, dependence and withdrawal effects can become major disadvantages.

1.3 Why was this Committee Established?

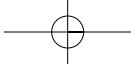
Concerns have been expressed over many years about the potential for misuse of benzodiazepines amongst a range of users. For instance, the External Review of Drug Services for the Eastern Health Board (January 2000) ², while generally positive about the expansion of methadone treatment provision for problem opiate users in the Dublin area, expressed specific misgivings about the high rate of benzodiazepine use amongst this client group, as indicated by urinalysis data. The reviewers concluded that these "high rates of benzodiazepine positivity indicate a major problem of polydrug misuse which requires urgent and concerted attention" (p.8). Research has also linked the use of benzodiazepines to a range of problems, including an increased risk of falls, in the elderly population. This research suggests that the elderly are especially vulnerable to adverse effects of hypnotic drugs. Rates of metabolism of benzodiazepines that are oxidised (e.g. diazepam, nitrazepam) decline with age. ^{4,3} Elderly patients are also more susceptible to central nervous system (CNS) depression and may develop confusional states and ataxia, leading to falls and fractures. ⁵ They are also sensitive to respiratory depression and prone to sleep apnoea and other sleep disorders. ⁶ Finally, it has been recognised for a considerable period of time that benzodiazepine anxiolytics and hypnotics can cause drug dependence when taken on a long-term basis, even in prescribed therapeutic doses.

Whilst the major medical bodies, including the Royal College of Psychiatrists, the Royal College of Physicians, and the Irish College of General Practitioners have advised that benzodiazepines should not be prescribed for more than 2 to 4 weeks, there is evidence that there are still many long-term prescribed users of these drugs in Ireland. It would appear that these patients receive little support or advice from their doctors, and generally it would also appear that some medical practitioners are not well informed about benzodiazepine withdrawal symptoms or methods of withdrawal.

A feature of some concern revealed by an examination of prescribing patterns to patients in the General Medical Services Scheme is that the estimated standard prescription quantity for all benzodiazepine hypnotic drugs appears to be a one month's supply. Since benzodiazepines are indicated for short-term relief (two to four weeks), and tolerance to their effects may develop within three to fourteen days of continuous use, it would appear that in many cases the prescribing of these drugs is excessive and perhaps has become a matter of routine.

1.4 Anticipated Outcome of this Report

From the perspective of the Committee, the most desirable outcome would be the preservation of the benzodiazepines as versatile and valuable drugs in clinical medicine through the fostering of rational prescribing practices of these drugs for all groups of patients. In this way, the prevalence of inappropriate use of the benzodiazepines would be greatly reduced, leading to a significant reduction in the number of patients becoming dependent on them and also to reduced consumption by known opiate misusers.

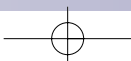
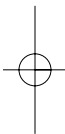
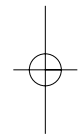


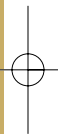
1.5 Limitations of Report

While the full implementation of the recommendations in this report will create a greater awareness of good practice in relation to prescribing of benzodiazepines among GPs and the general public, the Committee recognises the limitations of any single initiative in tackling the overall problem of drug use in Irish society.

Action on benzodiazepines is only one of the 100 actions identified in the national Drugs Strategy 2001 – 2008 "Building on Experience" which sets targets and key performance indicators under the four pillars of education and prevention, supply reduction, treatment and rehabilitation, and research. A multi-faceted approach is needed which includes strategic development of social inclusion and national anti-poverty initiatives.

Close monitoring and attainment of key performance indicators over the coming years and integrated, multi-sectoral action at national, regional and local levels will be crucial to the overall success in reducing the demand for drugs and the problem of drug misuse.







CHAPTER TWO

Benzodiazepine Usage in Ireland and Europe

2.1 Estimating the prevalence of benzodiazepine usage

While accurate statistics on benzodiazepine usage in Ireland are not readily available, the Committee considered it important to study such data as were available so as to identify trends and reach conclusions about inappropriate use of these drugs – whether in the general population or amongst the sub-population of opiate users.

Two studies (Studies 1 and 2 below) examined benzodiazepine use, based on data from the General Medical Services (GMS) Scheme. Study 1 looked at the GMS for the country as a whole, while Study 2 looked at benzodiazepine use in the GMS population within the Eastern Regional Health Authority area. A further study (Study 3) examined the use and prescribing of benzodiazepines in the drug misusing population.

Use of Defined Daily Doses (DDDs) in drug utilization studies

In the examinations carried out on the statistics provided by the General Medical Services Scheme it was decided to use Defined Daily Doses (DDDs) as the unit of measurement. This is the unit that is normally used in drug utilisation studies and is the assumed average maintenance dose per day for a drug used for its main indication in adults. These units are updated annually by the World Health Organisation. In practice, drug consumption is usually expressed in terms of the number of DDDs per 1000 of the population concerned. It thereby provides a rough estimate of the proportion of the population treated daily with the drugs. For example, the figure 10 DDDs per 1000 inhabitants per day would indicate that the amount used in terms of one normal adult dose per day would be given to 1% of the population on average.

2.2 Benzodiazepines in the National General Medical Services Scheme: Study 1

A review was carried out of the usage of benzodiazepines and related drugs, zaleplon, zolpidem and zopiclone in the General Medical Services Scheme over the years 1995 to 2000. Zaleplon (Sonata®), zolpidem (Stilnoct®) and zopiclone (Zileze®, Zimoclone®, Zimovane®, Zopitan®, Zorclone®) are not benzodiazepines, but are hypnotics which appeared to be in increasing use. There were some suggestions that these drugs were also being sought for abuse purposes so it was decided to include them as part of this review.

This national scheme currently covers approximately 31% of the population. Usage of the various drugs concerned was established for the years 1995, 1996, 1998, 1999 and 2000 on the basis of statistics made available by the General Medical Services (Payment) Board. (Data for 1997 were incomplete and were therefore excluded).

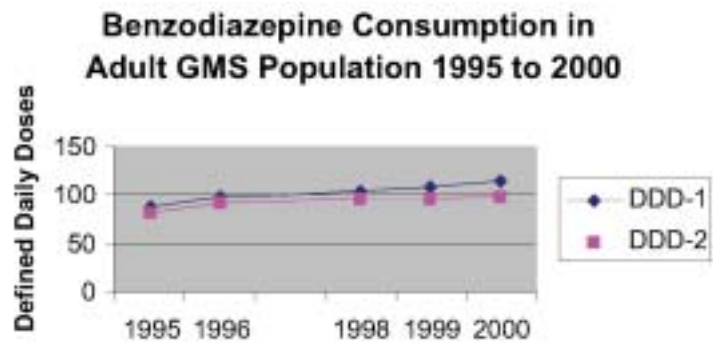
The amount of each drug used was then expressed in terms of the number of Defined Daily Doses (DDD) per 1000 of the adult (over 15 years) GMS population per day. These population statistics are published annually by the GMS (Payments) Board. The outcome of this examination is included in Table 1.

Table 1

Benzodiazepine usage in GMS Adult Population

International Non-Proprietary Name	Defined Daily Doses (DDDs) per day per 1000 of the adult GMS population				
	(1995)	(1996)	(1998)	(1999)	(2000)
<i>Alprazolam</i>	5.255	5.710	7.302	8.010	9.274
<i>Bromazepam</i>	3.718	3.774	4.040	4.136	4.210
<i>Brotizolam</i>	0.306	0.258	0.001	0.000	0.000
<i>Chlorodiazepoxide</i>	0.891	1.028	0.932	0.887	1.624
<i>Clobazam</i>	1.537	1.481	1.407	1.332	1.418
<i>Clorazepate</i>	2.260	2.183	2.264	1.688	1.873
<i>Diazepam</i>	16.362	21.627	23.118	23.248	23.814
<i>Flunitrazepam</i>	6.916	6.687	5.326	4.594	4.323
<i>Flurazepam</i>	10.216	10.383	11.041	10.749	10.757
<i>Loprazolam</i>	0.158	0.192	0.092	0.005	0.001
<i>Lorazepam</i>	2.775	2.689	2.649	2.685	2.759
<i>Lormetazepam</i>	4.098	4.811	5.979	6.362	6.487
<i>Medazepam</i>	0.063	0.005	0.000	0.000	0.000
<i>Midazolam</i>	0.014	0.015	0.025	0.021	0.027
<i>Nitrazepam</i>	4.944	10.389	9.872	9.424	9.127
<i>Prazepam</i>	1.277	1.232	1.219	1.209	1.247
<i>Temazepam</i>	16.696	15.269	15.131	15.405	15.215
<i>Triazolam</i>	4.861	5.507	6.487	6.740	7.095
<i>Zaleplon</i>	0.000	0.000	0.000	0.035	0.343
<i>Zolpidem</i>	0.000	0.000	0.000	2.414	3.657
<i>Zopiclone</i>	5.001	5.623	8.748	10.306	12.687
Totals (of DDDs/1000/day)	87.346	98.862	105.636	109.251	115.939

This Table suggests that in 2000, 11.6% of the adult GMS population were using benzodiazepines. It also suggests that the usage of benzodiazepines is increasing gradually from 87 DDDs in 1995 to 116 DDDs in 2000. This trend remains when the non-benzodiazepines are removed, as shown in Figure 1.

Figure 1

DDD-1 refers to the benzodiazepines with zaleplon, zolpidem and zopiclone and DDD-2 refers to the benzodiazepines alone.

The GMS information available for the years 1995 to 2000 relates, as already explained, to that portion of the population which is eligible for the General Medical Services scheme. In December 2000 this represented 1,148,095 persons out of an estimated population of 3,786,900. As of that date, it was estimated that adults and children over 15 years of age made up 877,863 of all the GMS eligible persons. In calculating the number of DDDs, the adult population figures as of December in each year were used. It was decided that children under 15 years of age should be omitted from these calculations on the basis that their usage of these drugs would be minimal and that their omission would provide a more realistic estimation of benzodiazepine usage.

Table 2**Prescribing frequency and estimation of DDDs per prescription**

Year	Prescribing Frequency	Prescribing Frequency/Adult Population	Estimated Number of DDDs per prescription
1995	1,268,669	1.341	25.130
1996	1,430,461	1.529	25.226
1997	1,460,358	1.599	N/A
1998	1,473,731	1.641	26.163
1999	1,526,325	1.707	26.126
2000	1,605,053	1.828	26.365

Table 2 shows that when the prescribing frequencies - the term used to refer to the total number of prescriptions for the year - in the General Medical Services scheme are taken into account, there is a continuing increase in the prescribing rate for benzodiazepines over the years from 1995 to 2000. While this parallels the increase in the quantities used over the same years as disclosed in Table 1, it is apparent that there is overall a continuing increase in the usage of these drugs in the scheme.

An attempt has also been made to determine the number of DDDs on each prescription. This was based on the total number of DDDs for each year being divided by the total number of prescriptions for the year (i.e. the prescribing frequency). The result of this exercise is set out in the right hand column of Table 2. It would appear from this that the average number of DDDs per prescription is 26 : in other words, 26 days supply. Based on the arrangements for the GMS, it would seem clear that most of these prescriptions are being written for a month's supply and that this has virtually become the standard practice for the prescribing of benzodiazepines in that scheme.

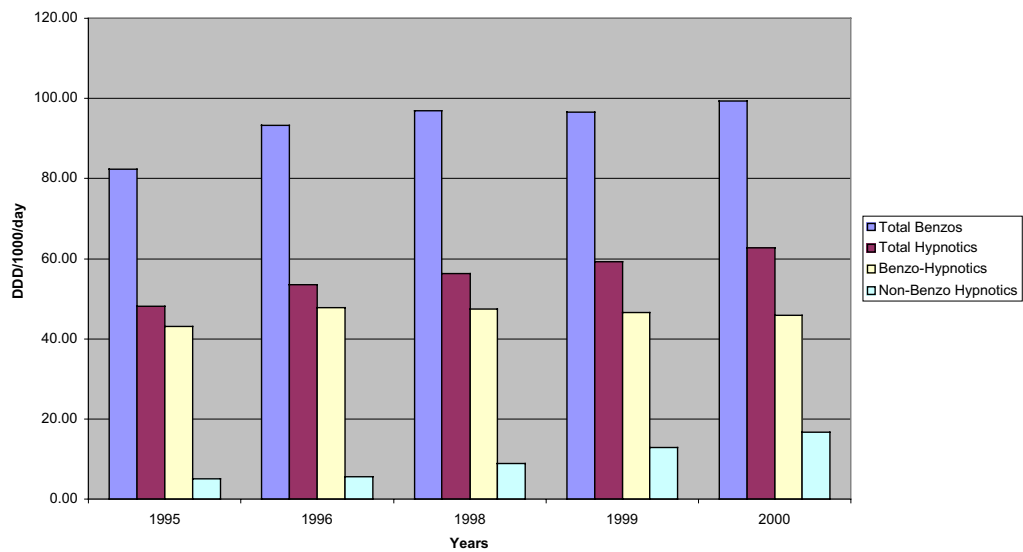
Benzodiazepines for the treatment of insomnia (hypnotics)

It has been suggested that those benzodiazepines for the treatment of insomnia (i.e. hypnotics) are those that are most likely to be misused. The substances and products in this category are flunitrazepam (Rohypnol®), flurazepam (Dalmane®), loperazolam (Dormonox®), lormetazepam (Noctamid®), nitrazepam (Mogadon®, Somnite®) and temazepam (Normison®, Nortem®, Tenox®). As previously mentioned, while zaleplon (Sonata®), zolpidem (Stilnox®) and zopiclone (Zileze®, Zimoclone®, Zimovane®, Zopitan®, Zorclone®) are not benzodiazepines, some submissions pointed out that they were being abused so it was decided to examine their use with other benzodiazepines. The information in Table 1 above was used as the basis of this examination.

Detailed data on the use of hypnotics – both benzodiazepine and non-benzodiazepine hypnotics - are presented in Appendices 3, 4 and 5 and are summarised below in Figure 2. In general, it is clear that there has been a gradual increase in both the frequency of prescribing and the usage of hypnotics over the years 1995 to 2000. Most of the increase, however, can be accounted for by the increase in use of drugs in the non-benzodiazepine category (such as zopiclone) where there has been a considerable increase in their usage, quantities and frequencies.

Figure 2

Various Benzodiazepine Consumptions 1995 - 2000



While the usage of benzodiazepine hypnotics is not increasing significantly, neither has it decreased. The limited changes that have occurred in the case of flunitrazepam and temazepam most likely have their origin in the changes in the controls that were introduced in 1993 when these drugs were moved from Schedule 4 to Schedule 3 of the Misuse of Drugs Regulations, 1988 (S.I. No.328 of 1988). There was a consequential increase in the usage of nitrazepam and lormetazepam. The drug loprazolam was discontinued over this period.

Conclusions and Recommendations

GMS data can provide useful information on patterns of use, and the Committee recommends that the GMS should therefore review and report at regular intervals on the prescription and use of benzodiazepines, on the basis of the claims for reimbursement that are submitted monthly to the General Medical Services (Payments) Board. Reports should also be prepared by the Board and provided to the GP / Primary Care Unit doctors and as appropriate to the individual practitioners, particularly where there may be concerns arising from the continuous use by patients of benzodiazepines. The GMS (Payments) Board should also be requested to take whatever steps are necessary to ensure that "repeat prescription forms", and the repeat prescription facilities that are currently installed on some of the computer software in use for the writing of GP prescriptions, are not available or used for the issue of multiple prescriptions for benzodiazepines in the course of a single consultation. In this context it was noted that the patient packs that are being made available to the market for many of these products are for a months supply and that this is a matter that might be considered by the Irish Medicines Board.

An attempt was made to compare the usage of benzodiazepine drugs in the General Medical Services scheme with that in the community generally. Because of the absence of reliable information on usage in the community, it was not possible to establish figures with any great confidence. However, the evaluations that were carried out suggested that for 2000, between 60% and 70% of the total benzodiazepine usage in the community took place in the General Medical Services scheme. This is an area that may merit further study.

2.3 Benzodiazepines in the General Medical Services Scheme in the Eastern Regional Health Authority : Study 2

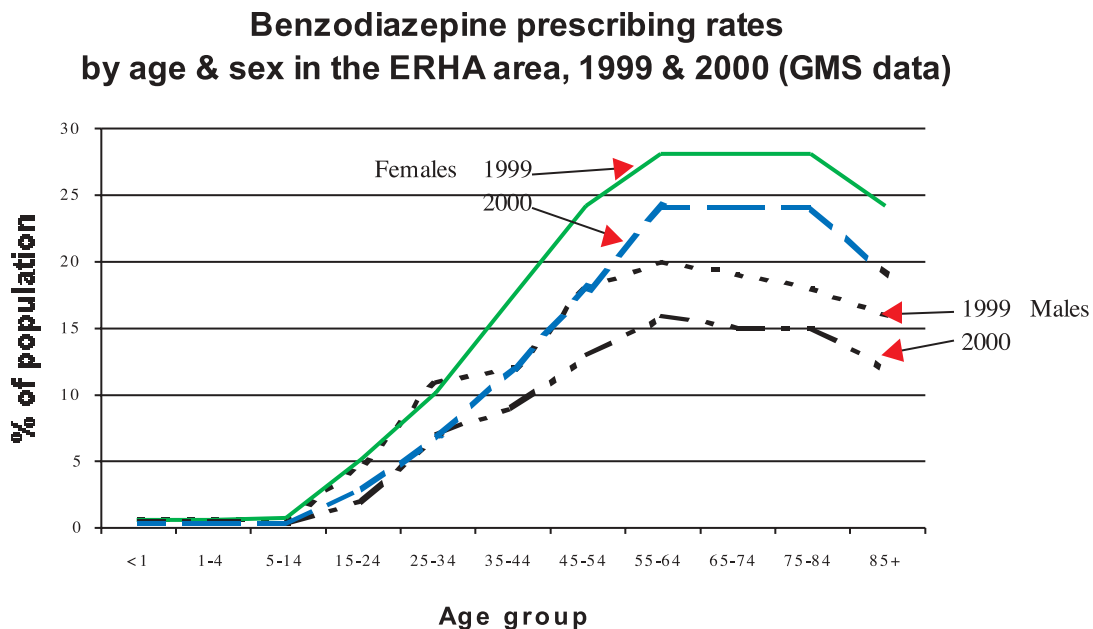
Another study was carried out by the Health Information Unit, Department of Public Health, Eastern Regional Health Authority which analysed GMS data for two six month periods (January to June 1999 and January to June 2000).

The Eastern Regional Health Authority (Eastern Region) covers the counties of Dublin, Kildare and Wicklow. The Region has a total population of approximately 1.3 million persons (1996 Census), of which approximately 26% are eligible under the General Medical Services (GMS) scheme. Data on the drug prescribing patterns of general practitioners (GPs) participating in the scheme are recorded by the GMS Payments Board (GMSPB).

Records with Anatomical Therapeutic Classification (ATC) codes N05BA (psycholeptics containing benzodiazepine derivatives) or N05CD (hypnotics and sedatives containing benzodiazepine derivatives) were included. Overall benzodiazepine prescribing rates by age and sex were calculated for each time period, together with age and sex standardised prescribing ratios for each GP. Prescribing patterns in the Eastern Region was used as the reference population. The GMS population during the month of April in each year was used as the denominator.

During the six month period in 1999, there were approximately 200,000 claims for benzodiazepines made by 47,000 patients. During a similar time period in 2000, there were approximately 197,000 claims for benzodiazepines made by 46,000 patients. In both years, these patients made approximately 4.3 claims per six month period for the drug.

In 1999, 13.6% of the total GMS population were prescribed a benzodiazepine derivative at least once over the six months period, compared to 9.9% in 2000. The prescribing rates for males in 1999 and 2000 were 10.6% and 7.4% respectively, compared to 15.8% and 11.8% for females in the two periods respectively. As shown in Figure 3, the use of benzodiazepines increased with age, reaching a peak in the late 60s and early 70s, with higher usage being found amongst females of all age groups.

Figure 3

In 1999, there were 494 GPs participating in the GMS scheme in the ERHA region. Of these, 90 (18%) had higher than expected prescribing ratios for benzodiazepines, with 31 (6%) prescribing at least 50% more than the average, and 9 (2%) prescribing at least twice the average.

In 2000, there were 492 GPs participating in the GMS scheme. Of these, 85 (17%) had higher than expected prescribing ratios for benzodiazepines, with 23 (5%) prescribing at least 50% more than the average, and 5 (1%) prescribing at least twice the average.

The study found that benzodiazepines were commonly prescribed in the GMS population, being taken by approximately 1 in 10 persons overall and up to 1 in 5 in the older age groups. Benzodiazepine prescribing was higher for females.

Approximately 5% of the GPs were found to be prescribing benzodiazepines at a rate at least 50% higher than that of their peers. However, the influence of potential confounding factors such as differences in patients and specialist referral patterns, practice size, or appropriate treatment based on high case detection rates are unknown.

It is of concern that approximately up to 70% of the clients would appear to be taking benzodiazepines on an ongoing basis (i.e. 4.3 claims per six month period, presuming each claim is for a one month period).

Whilst the results of the study should be interpreted with caution, there are indications that the overall benzodiazepine prescribing rates may be reducing slowly over time.

2.4 Benzodiazepine prescribing and misuse among the drug using population in the ERHA Area: Study 3

The use and prescribing of benzodiazepines in the drug using population was also examined.⁷ The results of all urinalysis carried out in June 2000 were examined, looking specifically at those which were positive for benzodiazepines. The urinalysis results within certain drug treatment clinics were compared to the numbers of individuals in receipt of benzodiazepine drugs at the clinic. At the time of the study there were 55 treatment locations in the health boards in the Eastern Regional Health Authority area. 22 of these were larger addiction centres and 33 were satellite clinics.

Figure 4 shows the results for the larger addiction centres (where drugs are dispensed on site). There is a wide discrepancy between the two sets of figures indicating either a lack of communication between the clinics and community GP's or else widespread abuse on the black market.

Figure 4

The percentage testing positive for benzodiazepines in selected addiction centres compared to the percentage prescribed

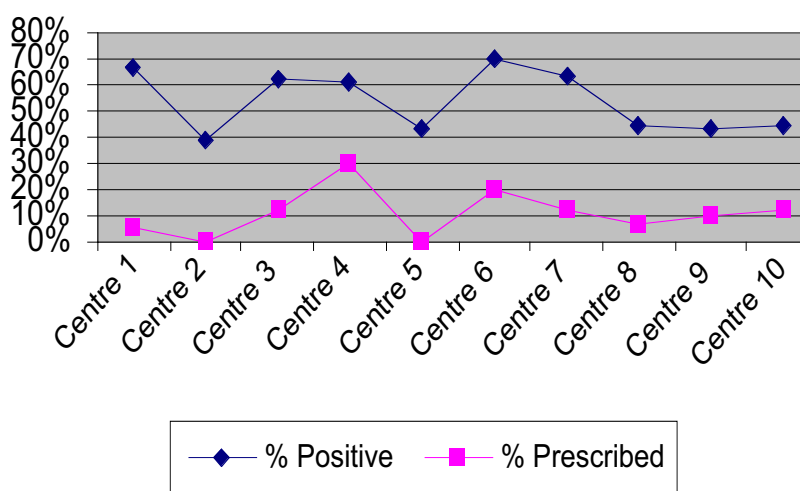


Figure 5 shows the situation at satellite clinics where the overall level of those testing positive for benzodiazepines is less than at addiction centres. It should also be noted that those attending these clinics are more stable than those attending the addiction centres. Those satellite clinics with high levels of individuals being prescribed benzodiazepines have generally only small numbers attending.

Figure 5

Satellite Clinics : % testing positive for benzodiazepines compared to % of benzodiazepines prescribed

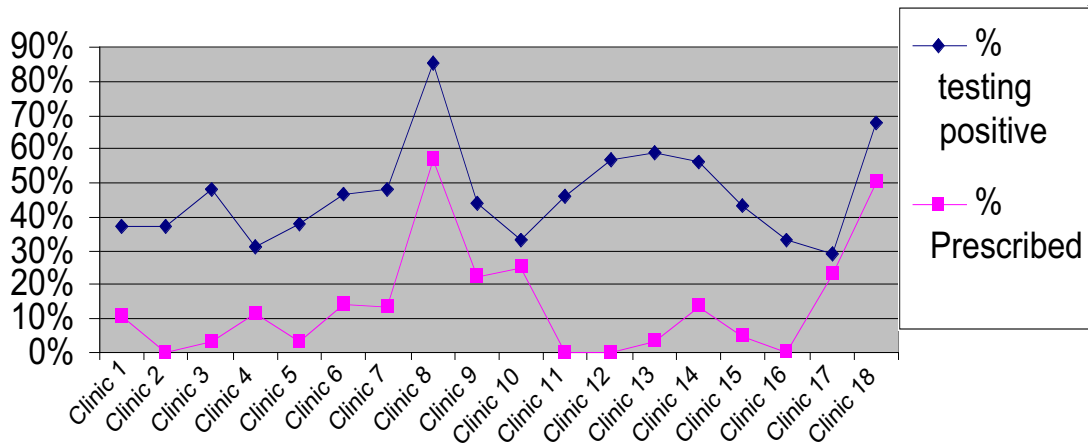
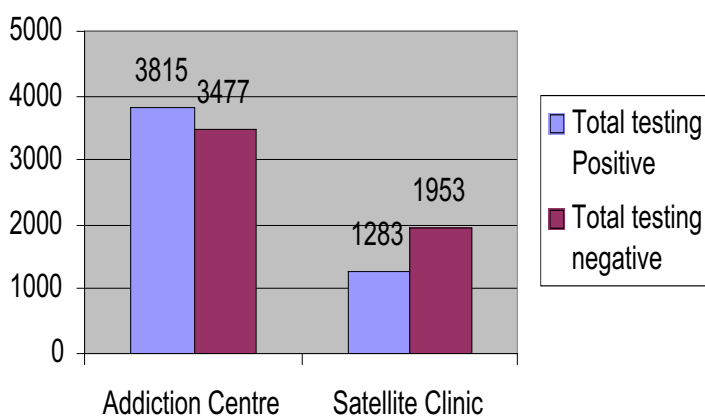


Figure 6 gives an overall situation of the results of urinalysis at the different health board services.

Figure 6

Total number of samples testing positive and negative for Benzodiazepines



A 1999 study⁸ of drug users admitted to a detoxification unit for benzodiazepine withdrawal identified equal abuses of diazepam, flunitrazepam and flurazepam. Self-report from drug users identifies diazepam as the most widely abused benzodiazepine on the black market.

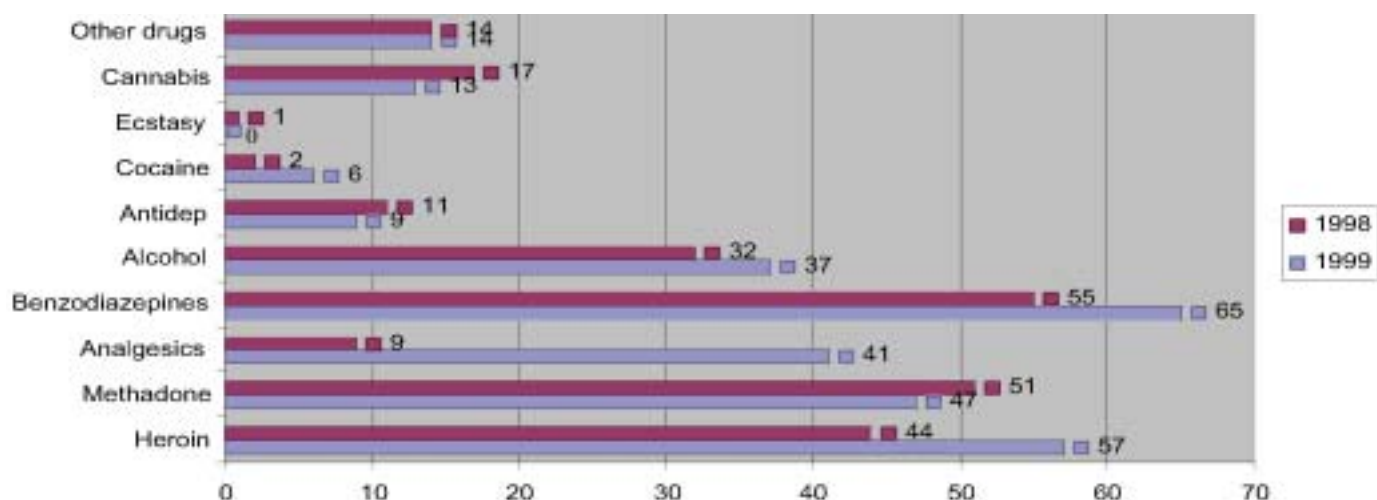
Some other sources of data were used to build a more complete picture of the patterns of abuse in the drug using population. These include the National Drug Treatment Reporting System (NDTRS)⁹ and Opioid related deaths as reported by the Dublin City Coroner.¹⁰

The NDTRS figures for 1997 and 1998 were examined and showed 4910 contacts in 1997 and 6043 contacts in 1998. In both cases 70% of the contacts were male. Heroin was most commonly reported as the main drug of abuse for both years with 3422(70%) in 1997 and 4297(71%) in 1998. Only 60(1.2%) individuals in 1997 and 96(1.6%) individuals in 1998 reported benzodiazepines as their main drug of abuse. A higher percentage reported benzodiazepines as a second drug of abuse in both years, 254(4.2%) in 1997 and 1036(17.1%) in 1998. It is worth noting the increase of individuals reporting benzodiazepines as a second drug of abuse between the two years.

The report on inquests held by the Dublin City Coroner in relation to opioid related deaths in 1998 and 1999 provides further evidence of the problem of benzodiazepine misuse in this population. A breakdown of the drugs implicated in opioid related deaths is given in Figure 7 below. In 1998, 663 inquests were held and 77 were extracted as opiate related. In 1999 645 inquests were held and 86 extracted. When the drugs implicated in these deaths are examined it can be seen that in both years the most common drug group involved was benzodiazepines.

Figure 7

Drugs implicated in Opioid related deaths



2.5 Mortality in the general population and Benzodiazepines

The Central Statistics Office provided information on deaths under ICD9, code 304.1 for the years 1995 – 1999, which suggested that benzodiazepines had been consumed by a number of persons on the mortality registers in that period.

It would be necessary to examine deaths in more detail by getting primary information from families, certifying general practitioners, pathologists, coroners and police to decide precisely what has been the exact contribution of benzodiazepines to the deaths. It is likely that in some cases there is a combination of benzodiazepine misuse, coupled with opiate dependence. (This information has already been highlighted by the Dublin City Coroner's study described above). However, further work is required in order to improve reporting on all drug related deaths and to clarify whether the drugs in question were actually the cause of death.

The Committee recommends that reporting of drug related deaths is improved so that statistical information clearly identifies whether drug dependence and/or drug misuse were the actual cause of death.

2.6 Benzodiazepine Prescribing within the Prison Services

Currently benzodiazepines within the prison are prescribed both by the general practitioners and the psychiatrists. The prison service is committed towards a greater integration of community and prison health care to ensure that individuals in prison have the same access to the range of health care services available in the community. Therefore, prescribing of benzodiazepine drugs in the prison should reflect the prescribing in the community as outlined in this report. As part of this process a co-ordinator of Drug Treatment Services in Prisons in the ERHA has been appointed. This should help to ensure that the good practice guidelines for benzodiazepine prescribing are put in place by clinicians involved in the delivery of both drug misuse and psychiatric services to prisoners.

2.7 Conclusion from Irish Studies

The above studies suggest that benzodiazepine prescribing and misuse of these drugs, particularly amongst the drug misusing population, are significant health issues in Ireland, with approximately 1 in 10 persons in the GMS population being prescribed these drugs. Diazepam is the drug preferentially misused by drug users and is the most widely prescribed in the medical card services scheme.

The studies, however, must be interpreted with caution. Study 1 uses Defined Daily Doses as its measure of use, while Study 2 uses prescriptions dispensed. Both studies are limited to examination of persons in the General Medical Services scheme.

While study 1, which includes the national GMS population indicates that benzodiazepine prescribing is increasing, study 2, which is based on ERHA area population only, suggests that prescribing rates are decreasing. This may be related to Study 1 having used DDDs (a measure prescribing volume) whereas Study 2 relates to the proportion of the population in receipt of prescriptions regardless of amounts.

It is difficult to interpret the data with a large degree of reliability as it relates only to the GMS population, even though it is suggested that between 60% and 70% of benzodiazepine prescribing occurs in this scheme. Study 2 indicates that a large proportion of benzodiazepine use occurs in the older age groups and amongst females in particular. Also, information from the Department of Psychiatry of the Elderly at St James's Hospital, Dublin states that many elderly patients have been taking benzodiazepines on a long term basis and are physiologically and psychologically dependent. All studies suggest that benzodiazepine prescribing tends to be for long periods of time, which would appear to be in conflict with best practice.

The exact rate of prescription and misuse in the private sector remains unknown. However, anecdotal evidence suggests that the prescribing of benzodiazepines may be decreasing in the private sector.

It is clear, from Study 3 that benzodiazepine misuse amongst opiate users is a problem. Evidence presented by the oral and the written submissions suggests that drug misusers will misuse a 'cocktail' of other drugs in order to top up, even when these people are on a methadone maintenance programme.

The Committee recommends that ongoing evaluation and monitoring be carried out into the use and misuse of Benzodiazepines in Ireland, particularly in the private sector and among older people.

2.8 Use of Flunitrazepam in Date Rape

Reports of Flunitrazepam (rohypnol) being used in cases of date rape were considered by the Committee.

Rohypnol (Flunitrazepam) has been classified as a Schedule 3 controlled drug in this country since 1993, when it was reclassified under the Misuse of Drugs Acts, 1977 and 1984 (S.I. No. 342 of 1993) in response to reports of misuse. Unauthorised possession is an offence. The Regulations require that doctors prescribing rohypnol abide by the special prescription writing requirements and rohypnol should be stored in a controlled drugs cabinet in accordance with the Safe Custody Regulations, 1982. Rohypnol may only be obtained on foot of a prescription from a medical practitioner and there is a need for a greater awareness among medical practitioners of the problems which can arise when rohypnol or other controlled drugs are prescribed in an inappropriate fashion.

There have been ongoing queries about the links between rohypnol and date rape. The anecdotal evidence received by the Department of Health and Children relates mainly to newspaper reports. The Department has not received confirmed reports from general practitioners, the Rape Crisis Centre or others linking rohypnol with date rape.

The period of time in which rohypnol is detectable in the body is quite short and may range from only 12 to 72 hours, depending on the amount consumed and individual circumstances, making it difficult to confirm its presence in biological samples.

One commercial manufacturer has included a coloured dye in its formulation in an effort to address this problem. Its formulation also makes it difficult for this drug to be dissolved in most liquids. However, not all Flunitrazepam (Roche – Rohypnol) available in the drug assisted sexual assault context may be from a licit source and so may not be formulated in this way.

The State Laboratory is currently undertaking a study of the samples referred to it for analysis during 2001 in relation to cases of alleged sexual assault or suspected ‘spiked drink’ cases.

Despite the lack of evidence of a link between flunitrazepam and date rape in this country, the Committee acknowledged public concern with the issue and the necessity for ongoing monitoring of the situation.

The committee concluded that at present the main abuse of this drug is by opiate addicts, who ‘top up’ their use of other drugs with rohypnol, to get a greater ‘high’. It had been suggested in a submission that rohypnol did not show up in urine samples of people tested on methadone maintenance. This was the case a number of years ago, however current testing in drug treatment clinics can make a positive diagnosis of use of a wide range of benzodiazepines, including rohypnol.

2.9 Benzodiazepine usage in Europe

The Pompidou Group of the Council of Europe provides a forum for the exchange of information and development of initiatives on drug related issues among its 33 member states. A questionnaire was issued to members in 2000, the results of which gave an overview of information available on benzodiazepines in those countries which made returns and which was considered at a meeting of experts in January 2001. The Report ⁷ of this meeting details the results.

The aim of this questionnaire was to identify sources of information on benzodiazepine consumption, the prevalence of abuse, the harmful effects caused and the strategies implemented to reduce demand.

There were very few replies to this questionnaire. The replies received indicated that only a few countries had been able to identify sources of information on illegal consumption. Methods used for collecting information included: registration and surveying of people under treatment, arrests and seizures, health surveys carried out among the population in general and in schools, and specific surveys among drug addicts. Methods used for collecting information on legal consumption included: checks on and analysis of benzodiazepines prescriptions, checks on pharmacies and suppliers, checks on imports and exports of benzodiazepines, and surveys carried out in pharmacies and in the pharmaceutical industry.

No country was able to provide figures on the prevalence of abuse or on illegal consumption. However, a few countries provided some general information on prevalence.

The survey also showed that benzodiazepine abuse caused considerable harm; flunitrazepam and diazepam were among the most prominent of the substances cited. Among the illegal drug-using population, opiate users suffered the most serious harm.

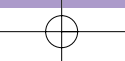
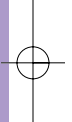
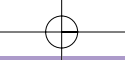
The shortage of information on the legal and illegal use of benzodiazepines was primarily accounted for by the fact that the information simply was not available, there were no systematic data collection procedures or the existing information sources were incomplete or difficult to exploit.

2.10 Summary

These results show that Ireland is not unique in experiencing problems with benzodiazepine drugs and like other countries adequate data is not available to give a clear picture of the situation.

The Decisions arrived at from the meeting have subsequently been adopted, as resolution 44/13 by the Commission on Narcotic Drugs. This Resolution is at Appendix 6.

The Committee welcomes this Resolution 44/13 and recommends that Ireland take the recommendations of the resolution into account in the development of policies for the appropriate use of benzodiazepines.





CHAPTER THREE

Good Practice Guidelines

3.1 Rationale for the Development of Good Practice Guidelines

In view of the worrying evidence on benzodiazepine use in Ireland presented in Chapter 2, it was considered of paramount importance to develop and disseminate guidelines for good clinical practice in this sphere. A number of submissions suggested that benzodiazepines should be regulated by way of a protocol similar to the statutory Methadone Protocol of 1998, but the Committee took the view that this would be impractical because of the high level of legitimate medical usage of these drugs. Instead, a sub-committee was established for the purpose of devising good practice guidelines and exploring how close monitoring systems of benzodiazepine prescription and use might be instituted.

In carrying out its task, the sub-committee drew extensively on a 1997 publication from the Royal College of Psychiatrists, *Benzodiazepines: Risks, Benefits or Dependence*, and on detailed information provided by the Irish Medicines Board. The full text of the guidelines is contained in Appendix 7.

3.2 Summary of Recommendations of Good Practice Guidelines for Clinicians

The main recommendations for practitioners contemplating the prescribing of benzodiazepines are as follows:-

Before initiating prescribing

Take a full history, including an alcohol and licit and illicit drug history ;
inform the patient of the side-effect profile of benzodiazepines and offer an information leaflet;
consider and treat, if possible, any underlying causes of the condition for which benzodiazepines may be prescribed;
consider referral to other services;
consider alternative therapies;
consider delaying prescribing until a subsequent visit.

When prescribing for the first time

Initiate with the lowest recommended dose but this may need to be adjusted depending on patient's response;
do not prescribe for longer than 4 weeks;
use phased dispensing where possible;
ensure that agreements between doctor and patient are documented;
record all details of medication prescribed and duration of treatment;
ensure that clear, effective and speedy communication concerning benzodiazepine usage takes place between prescribing professionals both within and between services.

For patients dependent upon benzodiazepines or patients in receipt of continuing prescribing

Issue small quantities at a time (usually not more than one week);
review regularly (usually monthly);
use a long acting benzodiazepine in dosages no higher than diazepam 5 mg three times daily or equivalent;
ensure that all patients are made aware of the risks of long term benzodiazepine use and document this communication;
use signed consent forms where appropriate;
encourage all patients with dependency to withdraw and offer them a detoxification programme at regular intervals (at least annually) and document all communication;
seek specialist advice before prescribing to patients who have become dependent as a result of substance abuse.

The guidelines also contain recommendations for withdrawal from benzodiazepines. Specific advice is also given in relation to the prescribing of benzodiazepines to special patient groups such as: substance misusers, elderly patients, patients who are in hospitals or institutions, and pregnant and breastfeeding women.

A number of submissions recommended that alternative therapies should be considered rather than the prescribing of benzodiazepines. The sub-committee fully endorsed this view and recommended that where possible practitioners should consider this option. Appendix 1 of the Guidelines outlines types of alternative therapies that may be offered.

The Committee recommends that these Good Practice Guidelines on Benzodiazepines for Clinicians are disseminated to all practitioners, including hospital practitioners and implemented in full.

It is recognised that the time required for the full implementation of these guidelines might be lengthy.

The Irish College of General Practitioners is supportive of the Guidelines but point to the lack of supports such as psychologists, nurses, counsellors etc. as being a barrier to their full implementation. The Committee acknowledges these concerns.

The Primary Health Care Strategy which was published by the Minister for Health and Children in November 2001 recognises the need for the appointment of a range of community based support services e.g. counsellors, nurses etc. to support primary care practitioners. However, it will take time for these supports to come on stream. It is expected however that the implementation of the recommendations contained in this strategy will have a positive effect in the overall implementation of the Good Practice Guidelines.

3.3 Interim measures

While awaiting the publication of the good practice guidelines, it was felt that interim measures be put in place with regard to benzodiazepine usage amongst the drug-using community, in particular those who were attending drug treatment clinics in the Eastern Regional Health Authority area. A proposal was developed by the Committee to reduce sources of multi-prescribing to known drug users. The objective was to identify either the clinic practitioner or the patient's general practitioner as the doctor who would take the "lead role" in prescribing benzodiazepines or psychotropic drugs. However, in most cases the clinic should take responsibility for prescribing these drugs. Identifying and improving communications with a patient's general practitioner is essential to this process. Following consultation with the three area health boards in the Eastern Region, the Chairman of the Committee wrote to the area health board Chief Executives in April 2001 advising them of the new arrangements to be put in place.

The Committee considers that the operation of these measures is a fundamental requirement to limiting the use of benzodiazepines for drug misusers. *The Committee recommends that contacting a client's general practitioner should be part of the contract that is made between a client being admitted to treatment and the health board.*

The Committee recommends that clinic doctors communicate with the client's general practitioner regarding the prescribing of benzodiazepines and other psychotropic substances. In most cases the clinic should, with the agreement of the general practitioner take responsibility for the prescribing of these substances and so prevent double or multi-prescribing to known drug users.

3.4 Good Practice in Hospitals and Nursing Homes

The main focus of this report is prescribing practice in the primary health care system. However, in the course of compiling the report it was clear that a number of GPs have been faced with the dilemma of referral of a patient from a hospital or institutional setting who had a prescription for benzodiazepines. In a number of cases a medical consultant may have initiated these prescriptions.

The Committee recommends that all hospital and other institutional healthcare providers examine their benzodiazepine prescribing practice to ensure that patients are not initiated unnecessarily on these drugs and that an assessment of the need for continued prescription of these drugs would be undertaken in the case of each patient, prior to discharge.

3.5 Education and Awareness

Some submissions received by the Committee suggested that further education was required, both for medical practitioners and the general public, into the addictive potential of benzodiazepines. It was also suggested that practitioners should devote more time to listening to the concerns and worries of their patients, and it was argued that the prescribing of drugs can sometimes be an easy option for busy doctors.

In this context, the Committee reviewed attempts to reduce benzodiazepine use in the Netherlands as outlined by Dr Fransje W Vander Waals in her presentation to the Pompidou Group meeting on benzodiazepines in January 2001. Following the publication of a report on this topic by the Health Council of the Netherlands in 1998, a number of studies were initiated. One such study looked at creating awareness amongst the public, especially in doctor's surgeries and pharmacies. In clinics, all chronic benzodiazepine users received special correspondence informing them about their benzodiazepine use and about their effects and side effects. One third of users received an information letter giving details of these effects; one third the information letter and an invitation to come to the clinic for a consultation; and one third the information letter, an invitation for a consultation and an invitation for special counselling. Results showed that between 15% and 20% of patients stopped benzodiazepine use after receiving adequate information.

This initiative clearly shows the benefits of education and awareness. The Committee examined sources of such education materials including leaflets aimed at doctors, pharmacists and the general public.

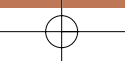
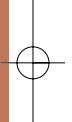
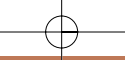
With regard to education and awareness the Committee recommends that:

- *information leaflets be developed for doctors on how to recognise the symptoms of drug misuse in patients;*
- *guidelines on good practice and the detection of prescription fraud be developed for pharmacists in consultation with the relevant professional bodies;*
- *patient information leaflets be developed and appropriate awareness material be made available for display in health centres, doctor's surgeries, hospitals, drug treatment clinics and pharmacies;*
- *further education courses for existing general practitioners, nurses, pharmacists and other practitioners should include a module on benzodiazepine prescribing.*

With regard to good practice the Committee recommends that:

Clinicians adhere to the good practice Guidelines on Benzodiazepines for Clinicians and in particular that :

- *practitioners should critically and urgently review their current level of benzodiazepine prescribing and in many cases this should lead to considerable reduction;*
- *prescribing benzodiazepines to opioid users (and other drug users) should be seen as exceptional rather than a routine clinical decision;*
- *patients dependent on opioids should be advised that the taking of benzodiazepines can greatly increase the risk of overdose - this message should be conveyed as a matter of routine by all those who have contact with drug misusers.*





CHAPTER FOUR

Current Legislation and Controls, and Proposals for Legislative change and improved Monitoring

4.1 Current Controls

Benzodiazepines are controlled drugs contained in Schedules 3 and 4 to the Misuse of Drugs Regulations, 1988 (S.I.No.328 of 1988). Most benzodiazepines, with the exception of flunitrazepam and temazepam, are contained in Schedule 4 of these regulations. The current main control over the prescription and supply of these Schedule 4 drugs are set out in the Medicinal Products (Prescription and Control of Supply) Regulations, 1996 (S.I. No. 256 of 1996) where they are contained in Schedule 1, Part A.

In the case of flunitrazepam and temazepam, which are in Schedule 3 to the Misuse of Drugs Regulations 1988, unauthorised possession is an offence and strict prescription, safe custody and prescription writing requirements are in force under the Misuse of Drugs Acts.

Control under the Medical Products (Prescription and Control of Supply) Regulations, 1996

The nature of the controls under these 1996 regulations is such that the medicinal products concerned may only be supplied on foot of medical prescriptions. These may not be repeated by pharmacists without a further prescription being supplied, or a prescription with specific directions (either in the prescriber's own handwriting or typed script) being presented thus enabling a repeat supply to be made.

When the repeat prescription forms were made available under the General Medical Services scheme, they were not intended to be used for the prescribing of those drugs in Schedule 1A to the previous 1993 regulations. In the case of benzodiazepines however, there was a determined effort made to avail of the use of these forms for the purpose of prescribing and dispensing. As a result of these efforts, a provision was introduced into the Medicinal Products (Prescription and Control of Supply) Regulations, 1996 (which replaced the 1993 regulations) to require that, in the case of a repeatable prescription for a Schedule 1A product, *"such prescription shall not be repeatable unless the intervals of supply or the number of occasions of supply has been written thereon in the prescriber's own handwriting or prescriber's own typed script"*. It had been suggested at the time that a significant number of these prescriptions that were being issued on repeat prescription forms, were being issued in error and that urgent steps had to be taken to invalidate them, unless of course it was the prescriber's express intention that a repeat supply was to be made.

Despite the introduction of these prescription-writing requirements for benzodiazepines, there is today considerable evidence that repeat prescriptions for these drugs are being issued. Furthermore, some of the software programmes in use have been written in a manner so as to facilitate the issue of forward dated prescriptions.

Accordingly, the practice of repeat prescribing of benzodiazepines has been continued and, because of the manner in which the prescriptions are issued and subsequently presented for dispensing, these repeat prescriptions are not identifiable in the normal manner. ***It is therefore proposed that the forward dating of prescriptions for benzodiazepines should be prohibited and that consideration be given to the extension of this prohibition to all controlled drugs.***

4.2 Legislation arising out of Ireland's International Obligations

Ireland is a Party to the UN Convention on Psychotropic Substances 1971. The lists of substances that are subject to international control under this Convention is regularly updated to take account of ongoing trends in drug abuse involving psychotropic substances. The following additional benzodiazepine and benzodiazepine-type substances are now required to be subjected to control under the Misuse of Drugs Acts by virtue of this Convention: aminorex, brotizolam, mesocarb and zolpidem. Furthermore, this country has been invited to implement the two UN ECOSOC resolutions (1987/30 and 1991/44) to all those substances that are included in Schedules III and IV to the Convention on Psychotropic Substances 1971, which includes all benzodiazepines.

Arising from the addition of these substances to the 1971 UN Convention and the undertaking given on behalf of the Government that this country would implement the two ECOSOC resolutions, the following legislative changes are to be made to the controls under the Misuse of Drugs Acts at an early date:

- (a) aminorex, brotizolam, mesocarb and zolpidem are to be added to the Schedule of controlled drugs;
- (b) all benzodiazepines are to be subjected to import and export control under the Act and unauthorised possession is to be made an offence;
- (c) prescription-only control under the Act will be applied to all these drugs as they currently apply to Schedule 2 and 3 drugs;
- (d) the existing repeat prescription facility that was applicable to these drugs will cease to be available; this will be replaced by an "instalment" prescription facility as for other controlled drugs, where further supplies are to be made. In this case the first instalment must be dispensed not later than fourteen days after the writing of the prescription and no instalment is supplied later than five months after the date on the prescription;
- (e) in view of the requirement to include zolpidem in the controls under the Misuse of Drugs Acts, consideration is being given to extension of controls to the other hypnotic drugs of this nature, namely zaleplon and zopiclone;
- (f) In the absence of specific record keeping requirements being applied to benzodiazepines supplied in pharmacies, consideration is being given to –
 - (i) the making available, for the purpose of supervision under the Misuse of Drugs Acts, of any records kept in pharmacies in electronic form in respect of the dispensing of medical prescription which relates to the supply of controlled drugs; and

- (ii) requiring persons keeping open shop under the Pharmacy Acts to keep their dispensed benzodiazepine prescriptions separate from all other prescriptions in order to facilitate inspection and monitoring.

4.3 Proposals for Legislative Changes and Improved Monitoring

Hand writing requirements under the Misuse of Drugs Acts

In 1993, when flunitrazepam and temazepam were moved from Schedule 4 of the Misuse of Drugs Regulations to Schedule 3, the full prescription writing requirements were applied to prescriptions written for those drugs. In its deliberations the Committee was of the view that this strict prescription writing requirement should be applicable to all prescriptions for benzodiazepines thereby reducing the possibility that the prescriptions might be altered by their recipients.

The Committee noted that, in the case of those benzodiazepines where the full prescription writing requirements were necessary, the degree of the compliance with those requirements was poor and that special difficulties were created by the use of computers for the generation of these prescriptions. The Committee also noted the high volumes of prescriptions for these drugs that are being used in current medical practice in this country.

While the Committee was strongly of the view that the full prescription writing requirements should be applicable to these drugs, it was also prepared to accept computer generated prescriptions for these drugs without the necessity for those elements that are required to be handwritten to be handwritten. This was on the basis that any unauthorised alterations that were likely to be made to these prescriptions after they had been properly issued would be identifiable by a dispensing pharmacist.

Monitoring of Prescribing and Use of Benzodiazepines

The Committee discussed a number of possibilities for the monitoring of all prescriptions (GMS and private) issued for benzodiazepines having regard to the extent to which these medicinal products are in current use and the difficulties that such measures may present to the medical and pharmaceutical professions.

Special Prescription Form

Various submissions received suggested that the introduction of a special prescription form for benzodiazepines be introduced with a view to appropriate monitoring. The Committee discussed the possibility of using such a special form as the basis for monitoring the prescribing and dispensing of these drugs. It became clear, in the course of these discussions that the introduction of such a form for benzodiazepines alone, without being applied to all controlled drugs would present some difficulties. It was also considered that there would be little benefit in introducing such a form if appropriate monitoring arrangements were not to be put in place at the same time. The essentials of such monitoring would be on the basis that all prescription forms which had been dispensed would be forwarded to a single centre for evaluation with a view to the detection of inappropriate prescription and use.

Some evidence¹¹ suggests that the tightening of controls for benzodiazepines could have the effect of reduced prescribing of benzodiazepines but a switch by clinicians to prescribing alternative drugs, which at best might be less appropriate but at worst might be more dangerous. It might also lead to under prescribing of a useful medication in certain circumstances that may not be as beneficial to a patient.

Electronic monitoring through pharmacy computers

It was also considered that some form of electronic monitoring should be introduced on the basis that most pharmacies have computers and that there is a trend for the electronic transmission of data for payment to the General Medical Services (Payments) Board. An effective electronic monitoring system would of course be dependent upon the availability of a suitably validated software programme. The Committee acknowledges that currently the capacity of pharmacists to forward all prescriptions to a central agency for monitoring purposes is problematic. Not all pharmacies have the same computer systems in place and not every prescription is submitted for reimbursing purposes.

The Committee discussed both options outlined above and was unable to arrive at a consensus view as to which system would be the most beneficial. Both proposals have merit. A committee established by the GMS(P)B is currently examining ways to monitor all controlled drugs. It was considered that the recommendations of this Committee would have some bearing on the recommendations of the Benzodiazepine Committee.

The committee recommends that a monitoring system for all benzodiazepine prescriptions (GMS and private) should be introduced as quickly as possible; discussions should take place with the appropriate bodies with regard to the introduction of such a monitoring system at an early date and that cognisance be taken of the recommendations of the GMS Committee on Controlled Drugs.

Developments in IT electronic prescribing in the future may open up new opportunities for the monitoring and control of these drugs. It would be essential that due regard be also taken of the recommendations of the National Health Information Strategy.

The Committee supports the measures outlined at 4.2 and recommends that regulations to bring these into effect be introduced as soon as possible. It further recommends that forward dating of prescriptions for benzodiazepines should be prohibited.

4.4 Legislative Controls Under the Misuse of Drugs Acts

Committee of Inquiry and Issuing of Temporary Direction

The fact that all medicinal products containing benzodiazepines are classified as controlled drugs under these Acts means that the supervisory provisions apply equally to these drugs, as they apply to those drugs in Schedule 1 or 2 to the Misuse of Drugs Regulations 1988. In effect, those provisions relating to the investigation of cases where the Minister believes that a practitioner is or has been administering or supplying or authorising the administration or supply of any controlled drugs, remain available. The possibility therefore remains that a Direction as provided for under the Acts may issue in respect of a practitioner prohibiting him prescribing, administering or supplying or authorising the administration or supply of such controlled drugs as may be specified in the Direction.

The Chief Medical Officer in the Department of Health and Children has regularly given advice to general practitioners on best practice, and has also warned them about the need for caution in the prescribing of benzodiazepines. Where GPs do not heed this advice and prescribe controlled drugs in what is deemed to be an irresponsible fashion, the Misuse of Drugs Acts, 1977 and 1984 confer powers on the Minister in relation to monitoring the activities of these medical practitioners. The Acts provide *inter alia* for the setting up of Committees of Inquiry and the issuing of Special Directions by the Minister in particular cases; this provision will now be looked at in some detail.

Under the Misuse of Drugs Acts the Minister for Health and Children may issue a Direction which would prohibit a general practitioner from prescribing specified controlled drugs. Once the Minister has issued the Direction he is then required to set up a Committee of Inquiry to investigate the matter within a specified time (28 days). The Minister may, however, extend this time, if necessary. The Committee is comprised of three persons of whom one (who shall be the Chairman) shall be nominated by the Minister. One shall be a member of the respondent's profession who is also a member of the registration authority, and one shall be a person appointed from a panel of members of the respondent's profession who is not a member of the registration authority concerned, nominated by such other organisations as are in the opinion of the Minister representative of the profession to which the respondent belongs. The Committee is required to consider the evidence presented by the Minister and any counter arguments presented by the doctor in defence. If it finds in the Minister's favour, the Minister can then issue a Special Direction against the doctor prohibiting him or her from prescribing some/all controlled drugs, and the Minister must also notify the Medical Council of the outcome.

Over the years, these powers have been availed of on only a few occasions, due mainly to the difficulty in collecting evidence to enable a judgement to be made by the Minister. In many circumstances where there appeared to be a *prima facie* case for an inquiry, prescriptions appeared to have been dispensed in many pharmacies, and - in the absence of a single monitoring centre - evidence could not readily be gathered on the prescribing practice. The availability of information from a monitoring centre, such as that recommended above, would enable the powers available under the Act for this purpose to be used more frequently, and as such would become a deterrent to the over prescription of these drugs.

The Committee recommends that the small number of doctors who may be prescribing inappropriately, putting their patients and others at risk, should be identified, investigated and dealt with accordingly – utilising the Ministerial Committee of Inquiry, strengthened by the new monitoring systems already recommended here.

The Committee also recommends that any pharmacist, who would become aware that a particular doctor may be prescribing benzodiazepines inappropriately, should be encouraged and if necessary, should be obliged by legislation to draw this matter to the attention of the authorities who would be in a position to take appropriate action.

4.5 Role of Professionals

Powers of the Medical Council

The Fitness to Practice Committee of the Medical Council also has powers in relation to regulating the prescribing of GPs. It can independently inquire, on foot of a complaint, into the prescribing practice of a GP, and it may also prohibit or curtail the prescribing of practitioners who are deemed to be unfit to practice by virtue of being ill themselves (e.g. through misuse of drugs or alcohol) or prescribing in an irresponsible fashion.

Medical Audit

Under the terms of the Methadone Protocol, GPs who are involved in prescribing methadone to drug misusers must firstly participate in training before they commence prescribing. Once they begin to prescribe they agree to undergo regular medical audit. Training and audit procedures have been jointly agreed by the Irish College of General Practitioners and health boards and proper medical audit procedures should ensure that the practice of GPs adheres to approved standards and that the quality of care provided to patients is in keeping with best practice.

While the brief of this Committee is in relation to benzodiazepines, it notes that the ICGP carries out regular audits, at least annually, of all GPs contracted by health boards to provide treatment services to drug misusers under the Methadone Protocol. It further notes that the audit of these GPs includes an examination of benzodiazepine prescribing practice.

The Committee recommends that the Irish College of General Practitioners and Health Boards investigate how a system of medical audit/peer review could be introduced, whereby all doctors' prescribing practices, including benzodiazepine prescribing, would be reviewed on a regular basis, and appropriate support and advice provided as required.

The Role of the GP Unit or Primary Care Unit

The GP Unit, or the Primary Care Unit as it is called in some health boards, can also act as a conduit of feedback on individual prescribing patterns to general practitioners. The GP Unit can offer assistance in interpreting data on prescribing and advice on modifying prescribing behaviour.

This audit feedback mechanism requires the provision of data by the GMS (Payments) Board to the GP units.

The Committee recommends that GP Units play a proactive role in providing advice and support to GPs on best prescribing practice.

The Role of the Pharmacy, and Communication between General Practitioners and Pharmacists in relation to Fraud

Community Pharmacists are ideally placed to recognise anomalous or inappropriate prescribing and to monitor and detect fraudulent prescriptions.

The issue of fraudulent benzodiazepine prescription was raised in only a few submissions, but the Committee was aware that this practice goes on to some extent in this country. One submission from a general practitioner who worked in the National Health Service in the UK proposed a system of interagency communication to tackle the problem of prescription fraud. This would involve a pharmacist notifying the health board of a bogus or fraudulent prescription, together with information on known aliases and a description of the alleged forger. The health board, in turn, would advise the doctor, whose prescriptions were forged, to write all prescriptions for a certain period thereafter in red ink. The health board would also inform all pharmacies and doctors in the area of the problem and provide the relevant details. The health board would also inform the Gardaí who may be in a position to take appropriate action.

Another example of effective communication that was considered is a cascading system. When a pharmacist suspects that he/she has received a fraudulent prescription the health board is notified by the pharmacist (possibly to the Community Care Pharmacist or Drugs/AIDS liaison pharmacist) providing the relevant information. A decision is made by the health board on whether or not to proceed with the cascade. If it is decided to proceed, the health board would make a telephone or fax communication with one pharmacist in the area. This pharmacist in turn would contact two more pharmacists with the relevant information. In effect when a pharmacist receives one call he/she makes two calls. In this way all the pharmacists in one area are made aware very quickly of information in relation to the circulation of fraudulent prescriptions.

The Committee considered that the action that is undertaken in the UK in relation to such fraudulent activities might also be a useful way to respond to this issue in the Irish setting. It also considered that the cascading system could be useful in providing effective communication in this area.

The Committee therefore recommends that all health boards in co-operation with the Pharmaceutical Society of Ireland, the Gardaí and other bodies as appropriate put in place a system of communication to address the question of fraudulent prescriptions.

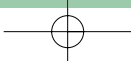
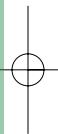
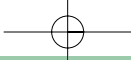
The Committee also looked specifically at the role of the pharmacist with regard to the monitoring and detection of fraudulent prescriptions. It was noted that some pharmacies stamp all prescriptions immediately on presentation whether subsequently dispensed or not. This practice alerts other pharmacists receiving the same prescription that there is a query about the undispensed prescription, and the Committee regarded it as a simple but useful mechanism for dealing with suspicious prescriptions, particularly in circumstances when pharmacists are obliged to return them when they most likely will be presented in another pharmacy.

The Committee therefore recommends that, as a first step in identifying potential fraudulent prescriptions for benzodiazepines, all prescriptions should, as a matter of policy be stamped immediately on presentation at pharmacies.

It is recommended in an earlier chapter that Good Practice Guidelines for Pharmacists in relation to benzodiazepines be developed. However, it is noted that general dispensing guidelines for pharmacists already exist. It is believed that the role of the pharmacist should include assisting in the detecting and monitoring of cases of multi-scripting.

There is a proposal within the ERHA that the Community Care Pharmacists would increase, their supervisory and advisory roles to include an element of peer review of pharmacists handling of prescriptions for benzodiazepines. The Committee supports this and believes that the development of such a role should be established in close co-operation with the Pharmaceutical Society of Ireland.

The Committee recommends that Community Care Pharmacists in all health boards should increase their supervisory and advisory role to include peer review of benzodiazepine dispensing practices, in close co-operation with the Pharmaceutical Society of Ireland.





CHAPTER FIVE

Summary of Recommendations

1. The General Medical Services (Payments) Board should review and report at regular intervals on the prescription and use of benzodiazepines on the basis of the claims for reimbursement which are submitted to it on a monthly basis.
2. Reports should be prepared by the General Medical Services (Payments) Board and provided to GP / Primary Care Units and as appropriate to individual practitioners, particularly where there may be concerns arising from the continuous use by patients of benzodiazepines.
3. The General Medical Services (Payments) Board should also be requested to take whatever steps are necessary to ensure that "repeat prescription forms", and the repeat prescription facilities that are currently installed on some of the computer software in use for the writing of GP prescriptions, are not available or used for the issue of multiple prescriptions for benzodiazepines in the course of a single consultation.
4. Reporting of drug related deaths should be improved so that statistical information clearly identifies whether drug dependence and/or drug misuse were the actual cause of death.
5. Ongoing evaluation and monitoring should be carried out into the use and misuse of benzodiazepines in Ireland, particularly in the private sector and among older people.
6. Patient packs that are being made available to the market for many benzodiazepine products are for a month's supply: this issue should be raised with the Irish Medicines Board with a view to reducing pack sizes.
7. Ireland should take into account Resolution 44/13 of the Commission on Narcotic Drugs in the development of policies for the appropriate use of benzodiazepines.
8. Good Practice Guidelines on Benzodiazepines for Clinicians should be disseminated to all practitioners including hospital practitioners and implemented in full. Where possible, alternative therapies to the prescribing of benzodiazepines should be considered by clinicians.
9. The provision of details of a client's general practitioner should be part of the contract between a client and a health board clinic for the treatment of drug misuse.
10. Clinic doctors should communicate with clients' general practitioners involved in the treatment of drug misusers regarding the prescribing of benzodiazepines. In most cases the clinic should, with the agreement of the general practitioner, take responsibility for the prescribing of benzodiazepines and so prevent double or multi-prescribing to known drug users.

11. All hospital and other institutional healthcare providers should examine their benzodiazepine prescribing practice to ensure that patients are not initiated unnecessarily on these drugs and that an assessment of the need for continued prescription of these drugs would be undertaken in the case of each patient, prior to discharge.
12. With regard to education and awareness, the Committee recommends that:
 - ❖ information leaflets be developed for doctors on how to recognise the symptoms of drug misuse in patients;
 - ❖ guidelines on good practice and on the detection of prescription fraud be developed for pharmacists in consultation with the relevant professional bodies;
 - ❖ patient information leaflets be developed and appropriate awareness material be made available for display in health centres, doctors' surgeries, hospitals, drug treatment clinics and pharmacies;
 - ❖ further education courses for existing general practitioners, nurses, pharmacists and other practitioners should include a module on benzodiazepine prescribing.
13. With regard to good practice, the Committee recommends that clinicians adhere to the Good Practice Guidelines on Benzodiazepines for Clinicians with particular emphasis on the following :
 - ❖ practitioners should critically and urgently review their current level of benzodiazepine prescribing and in many cases this should lead to considerable reduction;
 - ❖ prescribing benzodiazepines to opioid users (and other drug users) should be seen as an exceptional rather than a routine clinical decision;
 - ❖ patients dependent on opioids should be advised that the concurrent taking of benzodiazepines can greatly increase the risk of overdose: this message should be conveyed as a matter of routine by all those who have contact with drug misusers.
14. Forward dating of prescriptions for benzodiazepines should be prohibited and consideration should be given to the extension of this prohibition to all controlled drugs.
15. A monitoring system for all benzodiazepine prescriptions issued (GMS and private) should be introduced as quickly as possible; discussions should take place with the appropriate bodies with regard to the introduction of such a monitoring system at an early date and cognisance should be taken of the recommendations of the GMS Committee on Controlled Drugs.
16. The Department of Health and Children should draw up legislation at an early date to comply with Ireland's international obligations as outlined in section 4.2

17. In developing new legislation consideration should be given to:
 - ❖ the extension of controls to Zaleplon and Zopiclone;
 - ❖ the making available, for the purpose of supervision under the Misuse of Drugs Acts, of any records kept in pharmacies in electronic form in respect of the dispensing of medical prescriptions which relate to controlled drugs;
 - ❖ requiring persons keeping open shop under the Pharmacy Acts to keep their dispensed benzodiazepine prescriptions separate from all other prescriptions in order to facilitate inspection and monitoring.
18. The due process of law should be used to prevent irresponsible prescribing of benzodiazepines, and the necessary resources should be made available in the Department of Health and Children to ensure that the small number of doctors who are prescribing inappropriately – thereby putting their patients and others at risk should be identified, investigated and dealt with appropriately.
19. Any pharmacist, who would become aware that a particular doctor may be prescribing benzodiazepines inappropriately, should be encouraged and if necessary, should be obliged by legislation to draw this matter to the attention of the authorities who would be in a position to take appropriate action.
20. The Irish College of General Practitioners and the health boards should investigate how a system of medical audit/peer review could be introduced whereby all doctors' prescribing practices, including benzodiazepines would be reviewed on a regular basis and support and advice provided as required.
21. GP /Primary Care Units should play a proactive role in providing advice and support to GPs on best prescribing practice.
22. All health boards in co-operation with the Pharmaceutical Society of Ireland, the Gardaí and other bodies as appropriate should put in place a system of communication to address the question of fraudulent prescriptions.
23. As a first step in identifying potential fraudulent prescriptions for benzodiazepines, all prescriptions should be stamped on presentation at a pharmacy.
24. Community Care Pharmacists in all health boards should increase their supervisory and advisory role to include peer review of benzodiazepine dispensing practices, in close co-operation with the Pharmaceutical Society of Ireland.

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11. Michael Weintraub, MD, Satish Singh, MB,BS(hons); Louise Byrne, Kumar Maharaj, RPH; Laurence Guttmacher, MD:- *Consequences of the 1989 New York State Triplicate Benzodiazepine Prescription Regulations*.

Appendix 1

BENZODIAZEPINE REVIEW

Submissions Received

1. Dr Raymond Walley M.B B.Ch B.A.O M.R.C.G.P., Glasnevin Ave, Medical Centre, Dublin 11
2. Brian Mc Loughlin, Chairperson, Bray Local Drugs Task Force
3. Seamus de Burca, CEO, Mid Western Health Board, Limerick
4. Maurice Farnan, Area Co-ordinator, Tallaght Local Drugs Task Force
5. Jean Flanagan, Registered Nurse, Cuan Dara Detoxification Unit, Cherry Orchard Hospital, Dublin 10
6. Clodagh O'Sullivan RPN, Nursing Officer, Substance Abuse Service
Dolores Barragary, RPN, RGN, Addiction Counsellor, Substance Abuse Service
The Lodge, St Vincents Hospital, Fairview, Dublin 3
7. Sheila Stone, Co-ordinator, Dublin 12 Local Drugs Task Force
8. Professor Colin Bradley, Professor of General Practice, UCC
9. Dr Paul Quigley, Northern Area Health Board, Domville House, Ballymun, Dublin 9
10. Pat Madden, Programme Manager, Southern Health Board
11. Andrew Barber, President, Hospital Pharmacists Association, Ireland.
12. Dr Paul Scully, Senior Registrar in Psychiatry, St Patricks Hospital, Dublin 8
13. Mairead Lyons, Co-ordinator, Ballyfermot Local Drugs Task Force, Dublin 10
14. Julie Cruickshank, Co-ordinator, North Inner City Drugs Task Force, Dublin 1
15. Geoff Day, Assistant CEO, North Eastern Health Board, Kells, Co Meath
16. CityWide, 175 North Strand Road, Dublin 1
17. Dr. Joan Gilvarry, Irish Medicines Board, Earlsfort Centre, Earlsfort Terrace, Dublin 2
18. Maria Fox, Education Officer - Drugs and Alcohol, Mid Western Health Board
19. The Adult Psychiatric Service - Area 7, St Vincents Hospital, Convent Ave,
Richmond Road, Dublin 3
20. John Whyte, Interim Co-ordinator, Canal Communities Local Drugs Task Force
21. Professor Brian Lawlor MD., FRCPI, FRCPsychy., St James's Hospital, Dublin 8
22. Mark Rogers, Managing Director, Roche Pharmaceuticals, Clonskeagh, Dublin 14.

Appendix 2

Oral Presentations

1. Representatives of the North Inner City Local Drugs Task Force
2. Dr Paul Quigley, Northern Area Health Board

During the oral presentations the Committee heard first hand reports of benzodiazepine use amongst drug users and use by those on methadone maintenance programmes. GPs, voluntary and community groups clearly indicated the physical effects of benzodiazepines on individuals they encountered in their services. They spoke of personality changes, inability to engage with others, difficulty in having a conversation. It emerged that the abuse of benzodiazepines is now occurring at an early age and that these drugs are often sourced from the person's home where a relative may have been prescribed benzodiazepines by their general practitioner. This particular phenomenon had also been put forward in a number of written submissions. One other issue which came across both in this oral presentation and through written submissions was that other drugs, which were not benzodiazepines, such as tricyclic depressants, were being misused. It was suggested that should controls be put in place for benzodiazepines that drug misusers would find alternative drugs to use in conjunction with whatever other drugs they may be taking.

Professional Bodies consulted

Royal College Psychiatrists of Ireland
Irish College of General Practitioners
Royal College of Physicians
Pharmaceutical Society of Ireland
The Medical Council

Appendix 3**Benzodiazepines for the treatment of insomnia**

International Non-Proprietary Name	DDD per day per 1000 for the adult GMS population	DDD per day per 1000 for the adult GMS population	DDD per day per 1000 for the adult GMS population	DDD per day per 1000 for the adult GMS population	DDD per day per 1000 for the adult GMS population
	1995	1996	1998	1999	2000
Flunitrazepam	6.92	6.69	5.33	4.59	4.32
Flurazepam	10.22	10.38	11.04	10.75	10.76
Loprazolam	0.16	0.19	0.09	0.00	0.00
Lormetazepam	4.10	4.81	5.98	6.36	6.49
Nitrazepam	4.94	10.39	9.87	9.42	9.13
Temazepam	16.70	15.27	15.13	15.40	215.21
Zaleplon	0.00	0.00	0.00	0.04	0.34
Zolpidem	0.00	0.00	0.00	2.41	3.66
Zopiclone	5.00	5.62	8.75	10.31	12.69
Totals (of DDDs/1000/day)					
	48.03	53.35	56.19	59.29	62.60
No of DDDs	17,530,399	19,473,712	20,509,023	21,641,909	22,847,904
Frequency:	621,412	683,051	683,608	727,739	771,440
Quantity per Form	28.21	28.51	30.00	29.74	29.62

Appendix 4**Benzodiazepine Hypnotics**

International Non-Proprietary Name	DDD per day per 1000 for the adult GMS population	DDD per day per 1000 for the adult GMS population	DDD per day per 1000 for the adult GMS population	DDD per day per 1000 for the adult GMS population	DDD per day per 1000 for the adult GMS population
	1995	1996	1998	1999	2000
Flunitrazepam	6.92	6.69	5.33	4.59	4.32
Flurazepam	10.22	10.38	11.04	10.75	10.76
Loprazolam	0.16	0.19	0.09	0.00	0.00
Lormetazepam	4.10	4.81	5.98	6.36	6.49
Nitrazepam	4.94	10.39	9.87	9.42	9.13
Temazepam	16.70	15.27	15.13	15.40	15.21
Totals (of DDDs/1000/day)					
	43.03	47.73	47.44	46.54	45.91
No of DDDs	15,705,159	17,421,398	17,315,892	16,986,345	16,757,120
Prescribing Frequency	562318	617467	583826	572267	567531
Quantity per Form	27.93	28.21	29.66	29.68	29.53

Appendix 5**Non-benzodiazepine Hypnotics**

International Non-Proprietary Name	DDD per day per 1000 for the adult GMS population	DDD per day per 1000 for the adult GMS population	DDD per day per 1000 for the adult GMS population	DDD per day per 1000 for the adult GMS population	DDD per day per 1000 for the adult GMS population
	1995	1996	1998	1999	2000
Zaleplon	0.00	0.00	0.00	0.04	0.34
Zolpidem	0.00	0.00	0.00	2.41	3.66
Zopiclone	5.00	5.62	8.75	10.31	12.69
Totals (of DDDs/1000/day)	5.00	5.62	8.75	12.75	16.69
No of DDDs	1,825,239	2,052,314	3,193,130	4,655,565	6,090,783
Prescribing Frequency	59,094	65,584	99,782	155,472	203,909
Quantity per Form	30.89	31.29	32.00	29.94	29.87

Appendix 6

Resolution 44/13. Contribution to the appropriate use of benzodiazepines

The Commission on Narcotic Drugs,

Having regard to the need to give full effect to the Convention on Psychotropic Substances of 1971¹ and bearing in mind, in particular, the preamble to that Convention,

Also having regard to paragraphs 170, 171, and 172 of the Report of the International Narcotics Control Board for 1999,²

Further having regard to paragraphs 12, 15, 175 and 176 of the Report of the International Narcotics Control Board for 2000,³

Noting with satisfaction that on 29 and 30 January 2001, the Pompidou Group of the Council of Europe met with a group of experts to examine the issues related to the appropriate use of benzodiazepines,

I Therapeutic usefulness and appropriate use of benzodiazepines

1. Recognizes the usefulness and importance of the benzodiazepines in therapy and believes that, notwithstanding the abuse and excesses resulting from inappropriate use of benzodiazepines, the risk-benefit ratio remains favourable, justifying their retention in the therapeutic armoury;
2. Welcomes Council of Europe resolution AP (90) 3 of 18 October 1990 regarding the prescription of benzodiazepines;
3. Recommends that health care professionals consider the following when prescribing benzodiazepines;
 - (a) The need for a medical investigation to justify their prescription;
 - (b) The setting of precise indications and prescriptions for the shortest possible period of time;
 - (c) The discontinuation of unnecessary treatments;
 - (d) The use of the lowest possible doses;
 - (e) The risk of accidents for drivers and machine operators;
 - (f) The recommendation that alcohol or psychotropic medicaments that might interact with benzodiazepines should not be taken at the same time as benzodiazepines;

¹ United Nations, Treaty Series, vol. 1019, no.14956

² United Nations, publication, sales no. E.00.XI.1.

³ United Nations, publication, sales no. E.01.XI.1.



II Training for health professionals

Emphasizes the importance of initial and in-service training for relevant health professionals concerning the appropriate use of benzodiazepines. Such training should include diagnostic tools, methods for stopping treatment and information about alternative therapies or medicines;

III Information for patients

Recommends that patients be closely involved in the conduct of their treatment. The relevant health professionals should impress upon their patients the importance of strictly complying with the prescribed dosage. Patients should be informed about the problems that can arise from the use and abuse of benzodiazepines;

IV Role of the pharmaceutical industry

Wishes to involve the pharmaceutical industry in efforts to ensure appropriate use of benzodiazepines, urging it, inter alia, to:

- (a) Provide studies on the potential for substance misuse and dependence when registering any medicines that might be put on the market;
- (b) Make available to the public smaller package sizes (for one- to two-week treatment) and appropriate pharmaceutical formulations with suitable doses for individual therapeutic use;
- (c) Comply with a code of ethics on the marketing of benzodiazepines for health professionals;
- (d) Provide health professionals with proper information on the dependence liability of benzodiazepines, including how to implement and follow up therapeutic procedures, in particular with regard to therapeutic discontinuation protocols;

V Industry cooperation with analysis laboratories

Urges the pharmaceutical industry to cooperate with analysis laboratories in the analytical study of benzodiazepines by supplying reference substances and suitable analytical methods;



VI Research

Emphasizes the importance of increased research, in particular, medical and sociological research in order to obtain a better knowledge of the epidemiology, identify the problems and find solutions related to the use, abuse and supply of, as well as dependence on, benzodiazepines;

VII Withdrawal

1. Attaches particular importance to the problem of withdrawal, a priority issue associated with the use of benzodiazepines. The following points should be considered:
 - (a) Any prescription should be part of a pre-established therapeutic programme, with a beginning and an end, for the prescription of the medication;
 - (b) Established protocols for organizing withdrawal should be used;
2. Stresses that the information concerning withdrawal should be practical, so as to encourage relevant health professionals and patients to complete the therapy or the treatment;

VIII Statistics

Draws the attention of the authorities to the benefits of statistics and their analysis. A knowledge of changing trends and national and international comparisons are useful in drawing up strategies;

IX Monitoring

Requests the competent authorities to develop tools with comparable methodology for monitoring any abuse or pharmacodependence liable to result from the use of medicines and, in particular, benzodiazepines;

X Inappropriate benzodiazepine prescription and dispensing

Observes that inappropriate benzodiazepine prescription and dispensing by health professionals can be a major factor in the misuse of those substances. Corrective measures or proceedings should be initiated, if necessary, by supervisory authorities, in cases of serious or repeated breaches;



XI

Crime involving the use of benzodiazepines

Expresses its concern about the use of benzodiazepines for criminal purposes without the victim's knowledge to facilitate sexual assault, robbery and other criminal offences. The use of safety features (colourings, flavourings or others) by the pharmaceutical industry in the manufacture of benzodiazepines is to be encouraged. If necessary, health professionals and the general public should be informed about such matters;

XII

Control measures

Considers that monitoring and control are important tools in the elimination of benzodiazepine misuse. Those substances the abuse of which leads to serious public health problem should be subject to more stringent measures (involving prescription, dispensing, measures to combat illegal trafficking, withdrawal of medicines etc.) at the local and international level in order to prevent misuse and illegal trafficking;

XIII

National health authorities

Emphasizes the decisive role played by competent national authorities, which can involve medical prescriptions, dispensing, pharmaceutical presentation, control methods, statistical systems, monitoring, training and research on benzodiazepines. Such aspects will allow relevant national authorities to be fully informed about the abuse of benzodiazepines and to act accordingly, thus allowing countries to provide the International Narcotics Control Board with information that would enhance its knowledge of the situation.



Appendix 7

Benzodiazepines:

Good Practice Guidelines for Clinicians

The advice on benzodiazepine prescribing given in this document is based on the personal opinions of the benzodiazepine committee. The opinions expressed do not relieve clinicians of the responsibility of exercising their own medical judgement.

Contents

Introduction
Prescribing recommendations
Indications
Unwanted effects
Interactions
Precautions and contra-indications
Special Patient Groups
Appendices

Introduction

Benzodiazepines are one of the most widely used prescription medicinal products in the world. Benzodiazepines may be prescribed safely in the short-term and are a highly effective treatment for anxiety, insomnia and some forms of epilepsy and spasticity. Benzodiazepines are only indicated when the disorder is severe, disabling or subjecting the individual to extreme distress. Dependence is now recognised as a significant risk in patients receiving treatment for longer than one month and the practitioner has to be conscious of this when evaluating the relative benefits and risks of continued prescription. It is recommended that every clinician examines the benefit:risk ratio in each individual case early in treatment, so that if dependence occurs, it is anticipated by therapist and patient alike. The decision to allow dependence to develop is sometimes defensible, but it must be appreciated that, once dependence has become established, it is often extremely difficult to treat and may become a long-term or even permanent state.

While this document deals with benzodiazepines, the information and recommendations made can also refer to other mood modifying medications, such as Zopiclone, Zolpidem and Zaleplon which have similar effects to benzodiazepines.

Prescribing recommendations

Before looking at the use of benzodiazepines some general rules about the use of tranquillisers, and the benzodiazepines in particular are listed below

General rules for treatment with tranquillisers/benzodiazepines

<i>1. Benzodiazepine prescribing should never be purely symptom-orientated. A careful analysis of the causes of the symptoms must be undertaken before benzodiazepines or other tranquillisers are prescribed.</i>
<i>2. Over and above the prescribing of the medication, some sort of psychotherapeutic guidance is required. It is important to spend time with the patient, and pay attention to what he/she is saying.</i>
<i>3. It is vital always to check carefully whether the patient might have a tendency to misuse drugs or, alcohol.</i>
<i>4. It is important to individualise the dose for each patient, to ensure that there is neither under-dosage nor over-dosage.</i>
<i>5. Benzodiazepines should be prescribed only for as long as is necessary, aiming for the shortest possible time but no longer than 4 weeks.</i>
<i>6. If the medication is withdrawn abruptly, rebound anxiety or insomnia can occur. This should not be confused with recurrence of the original symptoms. The patient may require a tapering-off of medication, with ongoing support.</i>
<i>7. Reduction of the dose and discontinuation of benzodiazepine therapy should take place under careful medical observation and with appropriate psychological interventions.</i>

So, before prescribing:

- Take a full history including an alcohol and licit and illicit drug history.
- Inform the patient of the side-effect profile of benzodiazepines and offer an information leaflet.
- Consider and treat, if possible, any underlying causes.
- Consider referral to other services.
- Consider alternative therapies.
- Consider delaying prescribing until a subsequent visit.

When prescribing for the first time:

- Initiate with the lowest recommended dose, but this may need to be adjusted depending on patient's response.
- Do not prescribe for longer than 4 weeks.
- Use phased dispensing where possible.
- Ensure that agreements between doctor and patient are documented.
- Record all details of medication prescribed and duration of treatment.
- Clear, effective and speedy communication concerning benzodiazepine usage should always take place between the prescribing professionals both within and between services.

For patients dependent upon benzodiazepines or patients in receipt of continuing prescribing

Issue small quantities at a time (usually not more than one week).

Review regularly (usually monthly).

Use a long acting benzodiazepine in dosages no higher than diazepam 5 mg three times daily or equivalent.

Ensure that all patients are made aware of the risks of long term benzodiazepine use and document this communication.

Signed consent forms should be used where appropriate.

Encourage all patients with dependency to withdraw and offer them a detoxification programme at regular intervals (at least annually) and document all communication.

A significant number of requests for repeat benzodiazepine prescribing are associated with addiction problems, primarily alcohol, or in urban areas, opiate misuse. A doctor who suspects this is the case should seek specialist advice.

Indications

Anxiety

Benzodiazepine anxiolytics should be prescribed primarily for the short-term relief of anxiety and related symptoms when it is disabling and severe resulting in significant distress or problems in social functioning. Other forms of anxiety may be treated by psychological means or pharmacological treatments suitable for long-term use. The underlying cause should be determined and addressed.

Benzodiazepines should not usually be prescribed for longer than one month.

There are circumstances in which longer-term prescription of benzodiazepines may be considered desirable because the alternative is considered less beneficial. This may be in conditions such as chronic treatment-resistant anxiety or in patients who have established dependency and are unable to withdraw successfully. There are other situations where anxiety is complicated by other illnesses and where the risk of dependence may be considered acceptable because of the severity of the other disorders.

Sleep

Benzodiazepines are effective, safe and approved hypnotics for the short-term treatment of insomnia. The following guidelines should be noted:

Prescription should be:

- limited to between 2 and 4 weeks;
- at the lowest effective dose; and
- prescribed intermittently.

Care should be taken to exclude any other primary condition such as depression or substance misuse as a cause for insomnia.

It may be useful to inform the patient when treatment is started that it will be of limited duration, and explain precisely how the dosage will be progressively decreased. Moreover, it is important that the patient be made aware of the possibility of rebound insomnia, thereby minimising anxiety over such symptoms should they occur while the medication is being discontinued.

Before starting any pharmacological treatment it is important to discuss sleep problems with patients and present them with information which may help them to overcome their sleep difficulties:

- the normal amount of sleep varies widely and usually decreases with age
- temporary sleep problems are common at times of stress or physical illness
- worry about not being able to sleep can worsen insomnia
- alcohol may help in falling asleep, but can lead to restless sleep
- stimulants (including tea and coffee) can cause or worsen insomnia

Because sleep disorders are often caused by inappropriate sleep habits, it is important to give careful advice about a healthy sleep routine (sleep hygiene). For sleep hygiene recommendations and adjunctive /alternative strategies, see Appendix 1. The choice of benzodiazepine (and dose) depends on the type of sleep disorder:

- Patients who have difficulty in falling asleep can be treated effectively with short or intermediate-acting benzodiazepines.
- Patients experiencing situational insomnia or periods of wakefulness during the night, or early awakening, need a benzodiazepine with an intermediate half-life. Long-acting benzodiazepines, in general, should not be prescribed, to ensure there is no sedative hangover during the day.

Unwanted Effects

Withdrawal Symptoms

Withdrawal symptoms may occur on cessation or reduction of benzodiazepine and are characterised by anxiety/nervousness, irritability, depressed mood, insomnia, fatigue or lethargy, lack of energy, restlessness and agitation, tremors, dizziness, headaches, muscle aches or stiffness, weakness and difficulty concentrating and remembering. These symptoms may be difficult to distinguish from the original presenting symptoms. Occasionally, withdrawal phenomenon is so severe that the patient may experience seizures.

The incidence and severity of withdrawal symptoms are dependent on speed of tapering-off, the elimination half-life of the drug, the duration of benzodiazepine therapy and the daily dose. Although the general principles of pharmacology suggest that withdrawal symptoms are linked to a rapid fall in blood concentrations, the clinical emergence of withdrawal symptoms is complex, and is modulated by a number of important factors, including, personality, concurrent diagnoses, patient expectation, social situation, lifestyle and peer influences.

The withdrawal syndrome is more likely if: (a) the benzodiazepine has been taken in regular dosage for more than several months; (b) higher dosages have been used; (c) the drug is stopped suddenly; and (d) a benzodiazepine with a short elimination half-life has been taken (systemic kinetics determine the intensity and time-course of discontinuation phenomena, with these being more florid and more intense in those who were abruptly switched off short elimination half-life drugs such as lorazepam and alprazolam). The true pharmacological withdrawal syndrome is most likely to occur when there is a rapid fall in blood benzodiazepine concentrations.

The syndrome can best be avoided by the prescription of a benzodiazepine for less than 4 weeks with an intermediate or long elimination half-life and by gradual reduction of dosage when a decision is made to discontinue treatment.

Recommendations on the management of benzodiazepine withdrawal are given at Appendix 2.

Dependence

Dependence on benzodiazepines is mainly manifest by withdrawal symptoms on cessation, which may sometimes be prolonged and result in symptoms which may be hard to distinguish from other anxiety-related disorders such as panic disorder. In general, withdrawal reactions are short-lived, lasting for up to a month, but there is controversy about whether symptoms persisting longer are really withdrawal reactions or the manifestations of a chronic underlying neurosis or an exacerbation of the underlying condition triggered by tranquilliser withdrawal.

During therapeutic use, the risk of developing benzodiazepine dependence increases with the dose and duration of treatment, the nature of the illness, the severity of symptoms, the expectation of beneficial effect and the intensity of stress factors.

Patients especially at risk are those with:

- a history of addiction
- chronic physical illness, especially if associated with pain
- dysthymic and personality disorders
- chronic sleep disorders.

Long-term dependence should be treated by gradual withdrawal. Psychological support with the addition of cognitive-behavioural therapy should be offered where appropriate and where services are available in order to attenuate any symptoms which may occur. Contact should be made with local health board psychiatric services for assistance in assessing treatment options for difficult cases.

Pharmacological and psychological aids may only have limited benefit and many patients are unable to stop their drugs, or show persistent symptoms after withdrawal. In patients with persistent symptoms, a decision needs to be taken about whether they are generally better off with or without the medication. This decision needs to be taken in conjunction with the patient.

The long-term risks of using benzodiazepines need to be balanced against the benefits. If a decision to prescribe maintenance benzodiazepines is made then the following recommendations are suggested;

- Use a long acting benzodiazepine
- Do not exceed the equivalent of diazepam 5 mg tds
- Issue small quantities at a time (usually not more than one week)
- Review regularly (usually monthly)
- Ensure that all patients are made aware of the risks of long-term benzodiazepine use and document this communication
- Signed consent forms should be used where appropriate
- Encourage all patients with dependency to withdraw and offer them a withdrawal programme at regular intervals (at least annually) and document all communication

Seek specialist advice before prescribing to patients who have become dependent as a result of substance abuse.

Anterograde amnesia

All benzodiazepines may induce anterograde amnesia. This means that someone given a benzodiazepine may remember information before benzodiazepine administration, but there may be difficulties in later recall of information received after the benzodiazepine was given, until the effects of the drug have worn off.

Anterograde amnesia usually occurs several hours after the drug is taken: to reduce the risk, patients given benzodiazepines as hypnotics should ensure that they will be able to have 7-8 hours uninterrupted sleep.

Paradoxical reactions

Paradoxical reactions such as restlessness, agitation, irritability, aggressiveness, delusion, rages, nightmares, hallucinations, psychoses, inappropriate behaviour and other adverse behavioural effects are known to occur when using benzodiazepines. Should any of these occur, the drug should be stopped. They are more likely to occur in children and the elderly. Another group to pay particular attention to in relation to paradoxical reactions are drug misusers who may take high and fluctuating amounts of benzodiazepines.

Drowsiness and other effects

Drowsiness during the day, 'flat' emotions, reduced alertness, confusion, fatigue, headache, dizziness, muscle weakness, ataxia or double vision are all possible unwanted effects of benzodiazepine treatment. Such phenomena occur predominantly at the start of therapy but usually disappear with repeated administration. Other side-effects, such as gastrointestinal disturbances, changes in libido or skin reactions have been reported occasionally.

Overdosage

Symptoms

Benzodiazepine overdose usually results in central nervous system depression, ranging from drowsiness to coma. In mild cases, symptoms include drowsiness, mental confusion and lethargy. In more serious cases, symptoms may include ataxia, hypotonia, hypotension, respiratory depression, coma (rarely) and death (very rarely). However, overdose does not usually present a threat to life unless combined with other CNS depressants (e.g. alcohol).

Treatment

In the management of overdose with any medicinal product, it should be borne in mind that multiple agents may have been taken. Following overdose with oral benzodiazepines, vomiting should be induced (within 1 hour) if the patient is conscious or gastric lavage undertaken with the airway protected if the patient is unconscious. If there is no advantage in emptying the stomach, activated charcoal should be given to reduce absorption. Special attention should be paid to respiratory and cardiac function in intensive care. Flumazenil may be useful as an antagonist. Caution should be observed in the use of flumazenil in epileptics treated with benzodiazepines.

Interactions

If benzodiazepines are taken in combination with other CNS depressants (including alcohol), the central depressant effect may be enhanced. This can occur with antipsychotics (neuroleptics), hypnotics, anxiolytics/sedatives, antidepressant agents, opioid compounds, antiepileptic drugs, anaesthetics and sedative antihistamines. In the case of opioid compounds, enhancement of euphoric effects may also occur.

Compounds which affect certain hepatic enzymes may alter the effect of benzodiazepines. Such reactions are known to occur with a wide variety of medications.

Precautions and contraindications

Precautions

Effects on ability to drive or use machines

Sedation, amnesia, impaired concentration and impaired muscle function may adversely affect the ability to drive or use machines. This effect may be greatly enhanced if other drugs such as opioid compounds are being taken by the patient. Patients should be advised not to drive or operate machinery if they experience drowsiness or are on opioid compounds.

Depression

Benzodiazepines should not be used alone to treat depression or anxiety associated with depression, as they may mask the symptoms of depression. This can have serious consequences, denying the patient the opportunity of effective antidepressant medication, or resulting in disinhibition which may lead to suicide attempts. Withdrawal from benzodiazepines may, in other cases, precipitate a depression. The need for an anti-depressant is best judged when benzodiazepine issues have been settled either by withdrawal or maintenance therapy.

Benzodiazepines should be used with extreme caution in patients with a history of alcohol or drug abuse. Except where they are expressly indicated, they should not be used as hypnotics in children; when they are used as anxiolytics for children, there should be a careful assessment of the indication, and treatment duration should be kept to a minimum. Elderly patients should be given a reduced dose and checked regularly to minimise the dosage and/or frequency of administration.

A lower dose is recommended in patients with chronic respiratory insufficiency, due to the risk of respiratory depression. Patients with impaired liver function should also receive a reduced dose.

Street Diversion

Doctors should be aware that medication they prescribe may be diverted from the intended patient and fall into the wrong hands and be abused. It is not always possible to know which of our patients will divert some or indeed all of their medication to unintended sources. For instance it is known that patients, even in the older age group, may sell on their prescribed medication. For this reason supplies of benzodiazepines should be dispensed in limited quantities, ideally weekly aliquots. By writing "phased dispensing weekly/daily" as appropriate the pharmacist will dispense as requested for both GMS and non GMS prescriptions. There is a provision for phased dispensing which is budget neutral under the Indicative Drug Budget Scheme for GPs. It is recognised, however, that this recommendation may be more appropriate in younger rather than older people.

Contraindications

Benzodiazepines are generally contraindicated in patients with:

- myasthenia gravis
- hypersensitivity to benzodiazepines
- severe respiratory insufficiency
- sleep apnoea syndrome
- severe hepatic insufficiency

Benzodiazepines are not recommended for the primary treatment of psychotic illness. They are contraindicated for use as hypnotics in children.

Special Patient Groups

1) *Elderly Patients*

Benzodiazepines are the most commonly used psychotropic drug in older people and can be very effective anti anxiety agents. However, adverse effects in this group include impaired cognition and gait and the development of tolerance dependence and withdrawal. Reduced drug clearance with consequent higher plasma levels may be responsible for increased adverse effects in older people. Benzodiazepines with a long duration of action are particularly likely to accumulate and therefore have an even greater potential for sedative effects and psychomotor impairment. Long acting benzodiazepines, therefore, with active metabolites should usually be avoided in the elderly e.g. diazepam, chlordiazepoxide, flurazepam, nitrazepam. When benzodiazepines are prescribed in older people, short acting benzodiazepines with few active metabolites are preferable e.g. lorazepam 0.5mg bd/tid, temazepam 10-20mg nocte, alprazolam 0.25mg bd/tid.

Older people should be checked regularly at the start of treatment in order to minimize the dosage and/or the frequency of administration to prevent undesirable effects due to accumulation.

Older people who are taking benzodiazepines with a long elimination half-life have been shown to have an increased risk of falls and involvement in road traffic accidents compared to users of short-acting benzodiazepines.

Late life depression can present with anxiety symptoms and should primarily be treated with antidepressant medication rather than benzodiazepines. Benzodiazepines may also be used on a time limited period for the short term treatment of severe insomnia.

Many elderly patients have been taking benzodiazepines on a long term basis and are physiologically and psychologically dependent. It is appropriate to try and taper and discontinue benzodiazepines in these cases; however it may be very difficult to discontinue benzodiazepine use completely. Best practice would be to discuss the issue with the patient and see if the patient will agree to a slow taper and possible discontinuation.

It is important for physicians to read the prescribing information for a particular benzodiazepine very carefully and to observe the relevant warnings.

2) *Use During Pregnancy and Lactation*

If a product is prescribed to a woman of child bearing potential, she should be warned to contact the prescriber regarding discontinuance of the product if she intends to become, or suspects she is pregnant.

If, for compelling medical reasons, the product is administered during the late stage of pregnancy, or during labour at high doses, effects on the neonate, such as hypothermia, hypotonia and moderate respiratory depression, can be expected, due the pharmacological action of the compound.

Infants born to mothers who took benzodiazepines chronically during the later stages of pregnancy may have developed physical dependence and may be at risk of developing withdrawal symptoms in the postnatal period.

Since benzodiazepines are found in breast milk, they should not be prescribed to breastfeeding mothers.

3) Hospitals and Institutions

Many patients find admission to hospital a traumatic experience which causes understandable anxiety. The unfamiliar surrounding and noise of a busy hospital ward may also cause loss of sleep. In some hospitals, the prescription of benzodiazepines to overcome anxiety and loss of sleep has become a routine practice and can lead to patients who have not previously received these drugs being prescribed them during the admission and stay and then subsequently discharged on them. Therefore, where patients are prescribed benzodiazepines during a hospital admission this should be for a short period only (say, up to five days).

The short-term nature of the treatment should be explained to the patient and the continued need for benzodiazepines reviewed at discharge. Patients should be advised of the risk of dependency if drug treatment is continued following discharge from the hospital. Where drug treatment is continued following discharge the general practitioner should be fully informed of the indication for the new prescription and the proposed duration.

The creation of new chronic benzodiazepine users by a hospital admission must be considered unacceptable.

The opposite problem can also occur whereby chronic benzodiazepine users may not be prescribed their usual medicines on admission and their illness may be then complicated unnecessarily by withdrawal symptoms.

In order to avoid this problem, at each hospital admission, it should be determined whether the patient is a non-user, occasional user or routine user of benzodiazepines. Regular users should not have their treatment suddenly stopped but it should be recognised that the hospital admission presents an opportunity to encourage withdrawal or dose reduction in all users of benzodiazepines.

Special problems can arise during long-term care where routine prescribing and administration of benzodiazepines (especially as hypnotics on long stay hospital wards such as elderly care units) may cause problems of dependence. In such cases, patients receiving benzodiazepines should be regularly reviewed, as the only clinical justification for continuing use is dependence. Planned withdrawal of patients dependent on benzodiazepines should be considered. Attempts should be made to improve levels of mental stimulation and physical activity on long stay wards.

Alternative strategies for reducing anxiety and insomnia during an admission other than by the prescription of benzodiazepines should be considered. Suggestions include the reduction

of unnecessary noise on wards during normal sleeping hours and the availability of counselling for patients suffering from anxiety. The prescription of alternative hypnotics and sedatives with similar dependence potential to benzodiazepines (e.g. chloral products) and the inappropriate use of antidepressants and anti-psychotics should be discouraged.

4) Alcohol Withdrawal and Benzodiazepines

In an individual with an established alcohol dependence syndrome, the sudden cessation of alcohol can precipitate the onset of an alcohol withdrawal syndrome. The withdrawal syndrome can vary in intensity from mild symptoms of anxiety and sweating to a severe delirium state with associated seizures and mortality. Effectively controlling the symptoms of withdrawal is an important intervention carried out to reduce morbidity. Traditionally benzodiazepines have been used to alleviate the symptoms of withdrawal. These compounds act on specific receptors in the brain called GABA receptors. These are the principal inhibitory receptors in the brain and action on these results in decreasing noradrenaline release which is thought to be responsible for at least some of the symptoms of withdrawals experienced by alcohol dependent individuals. Benzodiazepines may affect, at least in part, the alcohol related mental confusion, depression and fatigue.

Thus benzodiazepines are safe and effective drugs to use in alcohol withdrawals, however the side effects of memory impairment, drowsiness and lethargy as well as the potential for dependence means that they may interfere with other therapeutic approaches dealing with stress management, coping behaviour or drinking behaviour modification. Therefore benzodiazepines used for this purpose should be in reducing dosages over a relatively short period of time, usually for no more than two weeks. Cross dependence between benzodiazepines and alcohol is also a recognised complication presenting to those dealing with both groups of patients.

5) Substance Misusers

Benzodiazepine prescribing would normally not be initiated in this group. It is recommended that before maintenance benzodiazepine is prescribed specialist advice be sought. (See list of health board contacts at Appendix 3). Benzodiazepine misuse is a great problem amongst the drug misusing community. It is often taken in large quantities in order to achieve an altered state of consciousness and euphoric effect. This is often associated with disinhibition which may lead to aggressive and irresponsible behaviour. It is also taken to help the addict tolerate heroin or cocaine withdrawal. Very often benzodiazepine dependency develops and compounds the problem, leading to a continuous pattern of benzodiazepine misuse. It should be remembered however that there is a high incidence of mental illness, sexual abuse and social deprivation amongst this group that often contributed to their drug problem.

The use of maintenance benzodiazepines amongst this group, however, remains controversial as they are often used to supplement benzodiazepines acquired illegally.

It is recommended that before maintenance benzodiazepine is prescribed specialist advice be sought. See Appendix 4 for Guidelines for drug misuse treatment services.

(These guidelines are based on the Report of the Royal College of Psychiatrists- Benzodiazepines: Risks, Benefits or Dependence, January 1997 and also use a number of reference sources, most notably the submissions received by the Benzodiazepine Committee. The Committee would, however, like to particularly acknowledge the submission by the Irish Medicines Board).

Appendices

- 1) Alternative therapies
- 2) Guidelines on withdrawal from benzodiazepines (Roche Pharmaceuticals)
- 3) Health board contacts
- 4) Guidelines for drug misuse treatment services

Appendix 1

Alternative Strategies to the Prescribing of Benzodiazepines

(This is taken from the document produced by the Sandwell Health Authority in the U.K.)

Insomnia

- a) Discussion - frequently talking about what is keeping a person from sleeping is sufficient to address the problem.
- b) Relaxation therapy.
- c) Avoidance of stimulant drugs and beverages during the evening e.g. coffee, tea, alcohol.
- d) Increased physical activity.
- e) Increased mental stimulation during the day.
- f) Explanation that some people (particularly the elderly) require less than a 'full' night's sleep and that five hours is often sufficient.
- g) Avoidance of 'catnapping' during the day.
- h) A relaxing bath or a good book can facilitate sleep.
- i) It is important to rule out the presence of a depressive illness, the treatment of which is commonly with anti-depressant medication.
- j) Yoga -transcendental meditation- exercise.
- k) Consider alternative medication ref: British National Formulary. Caution should be used particularly in the prescribing of Chlormethiazole (Heminevrin).
- l) If an hypnotic must be prescribed it should be used intermittently, e.g. on only 2 - 3 nights per week.

Anxiety

- a) Discussion.
- b) Relaxation.
- c) Exposure.
- d) Increased physical activity.
- e) Yoga - transcendental meditation- exercise.
- f) Self help books - local library, book shops.

Appendix 2

Methods for benzodiazepine withdrawal

Any benzodiazepine withdrawal programme should be carefully planned and structured, the aim being to gradually reduce to zero the amount of drug being taken.

There is no single best technique for withdrawal, but simple dose reduction is successful for most patients. Equally there are no specific data relating to the rate of withdrawal or the total time involved. Nevertheless, whichever technique is used, the regimen must be discussed with the patient, and the goals must be simple and attainable.

Withdrawal can be achieved by many methods. Each involves regular supervision by the general practitioner. For example, the general practitioner can simply gradually reduce the daily dose of the patient's current benzodiazepine over a period of several weeks; or the general practitioner can switch the patient's short-acting benzodiazepine for a long-acting one before attempting withdrawal; alternatively, the withdrawal programme can be supplemented with concomitant therapy.

Listed below are four methods which follow the general structure discussed above. They should be regarded purely as guidelines; the exact withdrawal programme should be tailored to the individual's response due to the wide variation in subjective response.

Method 1

Gradual reduction in dosage

This is the simplest and most common method for withdrawing a benzodiazepine. For example, it is recommended that temazepam be gradually withdrawn, taking 10mg for 2 weeks, 5mg for 2 weeks and then 2.5mg for 2 weeks. Some authorities feel, however, the method is more appropriate for long-acting benzodiazepines, and for short-acting compounds they would recommend method 2.

Method 2

Substitution

1. Substitute the short-acting benzodiazepine with an approximately equivalent dose of a long-acting drug such as diazepam. Because of diazepam's long elimination half-life, the withdrawal symptoms appear to be less severe with little associated 'craving'. However, there may be a problem with daytime sedation if the short-acting benzodiazepine was for night sedation.
2. Substitution should be gradual and the benzodiazepines replaced in increments of one dose per day. This can usually be accomplished within one week but should be tailored to the individual patient. Some patients require a slightly higher dose than the approximate equivalent.
3. Once substitution is achieved, a gradual reduction of the diazepam dosage should follow. Diazepam is available in 2mg, 5mg, and 10mg tablets, all of which can be halved, and in an elixir 2mg in 5ml, which can be diluted.

4. Stepwise reductions in dosage should be made every week or fortnight, or even monthly, depending upon the patient's response. Suggested reductions are:

- Reduce by 2mg if daily dose 15mg to 20mg
- Reduce by 1mg if daily dose 10mg to 15mg
- Reduce by 0.5mg if daily dose 5mg

Tailor the dose reduction to patient response, i.e. weekly, fortnightly or monthly.

Once patient is at a dosage of 0.5mg daily the dose interval can be increased to every two to three days.

Example

Replace the drug being used by equivalent doses of diazepam at the rate of one dose per day.

Patient's dosage: lorazepam 1mg three times daily

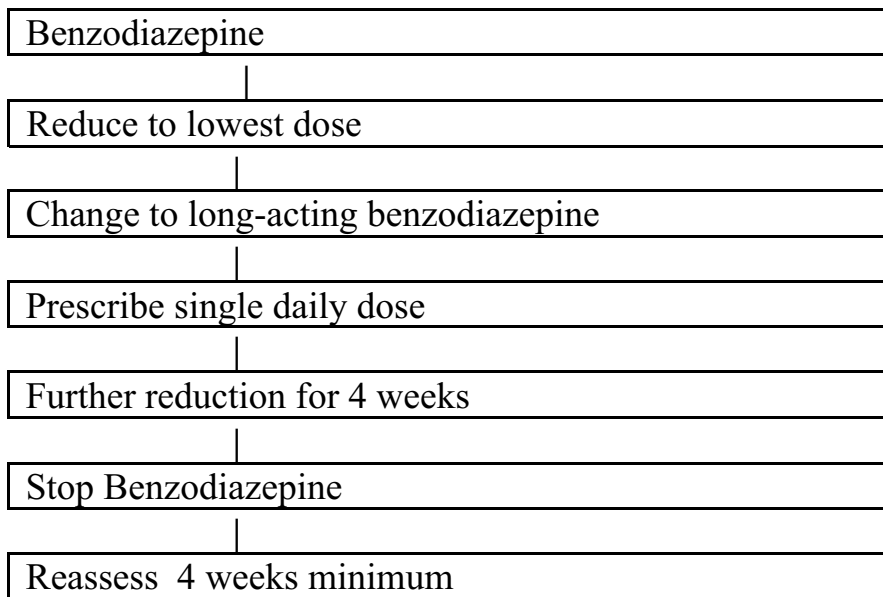
Day 1	Morning	Afternoon	Night
1	Lorazepam	Lorazepam	Lorazepam
2	Lorazepam	Lorazepam	Diazepam 10mg
3	Lorazepam	Diazepam 10mg	Diazepam 10mg
4	Lorazepam	Diazepam 10mg	Diazepam 10mg
5	Diazepam 10mg	Diazepam 10mg	Diazepam 10mg
6	Diazepam 10mg	Diazepam 10mg	Diazepam 10mg

A few patients have difficulties in changeover and may need to achieve this over a longer period of time.

Method 3

Dose reduction then immediate substitution to long-acting benzodiazepine followed by reduction

This approach combines Methods 1 and 2 and will make use of the greater flexibility in dosing of the longer acting preparations such as diazepam.



Whichever method is chosen, if the patient experiences troublesome abstinence effects after a reduction of dosage, the dose should be held at that level for a longer period before continuing the reduction at a slower rate. Try to avoid, if possible, increasing the dose at any stage.

Method 4*Adjuvant pharmacotherapy*

Pharmacotherapy does not help with the psychological problems associated with benzodiazepine withdrawal, although it may help to reduce tension and anxiety with low doses of a sedative type antipsychotic drug.

However, it is possible to reduce some of the physical symptoms of withdrawal. The Table below shows the pharmacotherapy which is accepted by many general practitioners as valuable.

Manifestation	Proposed drug or drug group
Sympathetic overactivity, e.g. tremor, sweating	Propranolol for up to 3 weeks
Insomnia	A short course (about 2 weeks) of an effective hypnotic, e.g. antihistamines, sedative antidepressants, the dose of which is gradually reduced.
To avoid the risk of convulsions	Carbamazepine, or other anticonvulsants for up to 2 weeks may be necessary in rare cases

Adjuvant pharmacotherapy which helps to reduce the physical symptoms of benzodiazepine withdrawal.

Appendix 3

Eastern Regional Health Authority Region

Northern Area Health Board

Dr Des Crowley

Address

The Thompson Centre,
53 Mountjoy St,
Dublin 7.
Ph. 01 8820300

Dr Ide Delargy

c/o 37 Seapoint Avenue,
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Ph. 01 8820300

South Western Area Health Board

Dr Margaret Bourke

37 Castle Street,
Castle Street, Clinic,
Dublin 8.
Ph. 01 4785574

Dr John O'Grady

Aisling Clinic
Cherry Orchard Hospital,
Ballyfermot,
Dublin 10.
Ph. 01 6232200

East Coast Area Health Board

Dr Cathal O'Sullivan

35 York Road,
Dunlaoghaire,
Co Dublin.
Ph. 01 2803335

Liaison Persons in other Health Boards

North Western Health Board

Drugs Co-ordinator's Office
Ms Bernie Hyland
North Western Health Board
Main Street
Ballyshannon
Co Donegal
Ph. 072 7719072

North Eastern Health Board

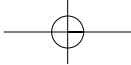
Ms Kate Mulvena
GP Unit
North Eastern Health Board
Railway Street
Navan
Co Meath
Ph. 046 21595

Western Health Board

Drugs Co-ordinator's Office
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Drug Co-ordinator
Western Health Board
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Mid-Western Health Board

Drugs Co-ordinator's Office
Ms Maria McCully
Mid-Western Health Board
57 O'Connell Street
Limerick
Ph. 061 310899



Midland Health Board

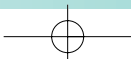
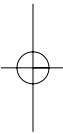
Dr Siobhan Rooney
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Southern Health Board

Dr Catherine Murphy
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South Eastern Health Board

Dr Neville de Souza
South Eastern Health Board
Lacken
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Kilkenny
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Appendix 4

Guidelines for Drug Misuse Treatment Services

It is recommended that;

- Each health board should draw up guidelines for the management of benzodiazepine misuse within its own area. Ideally these guidelines should be drawn up via a consultative process of all relevant staff
- Ongoing evaluation of the implementation of these guidelines should take place
- Due to the complexity of the problems, a multidisciplinary approach should be used to create an individual care plan
- The objective of treatment shall normally be abstinence
- All patients who are considered to be dependent upon benzodiazepine be offered a detoxification programme by a multidisciplinary team
- Education and support including group support/therapy should form the mainstay of treatment
- Prescribed benzodiazepine should be dispensed daily when possible
- Urine metabolites should be monitored to evaluate compliance
- It is recognised that a small group of patients may require benzodiazepine maintenance prescribing. It is recommended that the general guidelines of the main document inform the decision as to which patients fall into this category. Cognisance should be taken of the duration and extent of benzodiazepine use, psychological status and other psycho-social stressors.



**DEPARTMENT
OF HEALTH AND
CHILDREN**
AN ROINN
SLAINTE AGUS LEANAÍ