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Health Service Executive

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Circular 046/16

16th September 2016

Dear Doctor,

The Medicines Management Programme (MMP) will be announcing two further preferred drugs this week in relation to beta blockers and calcium channel blockers. This follows a comprehensive review of the literature and a consultation period which provided valuable submissions from a variety of stakeholders.

- Beta Blocker preferred drug is **Bisoprolol**
- Calcium Channel Blocker preferred drug is **Amlodipine**

A detailed document outlining the reasons for the selection of these preferred drugs along with "Prescribing Tips" will be published on the MMP website www.hse.ie/yourmedicines. Further information on the Preferred Drugs Initiative and the MMP can also be found here.

Please find enclosed a copy of communication from Professor Michael Barry, National Clinical Lead, Medicines Management Programme.

I am also using this opportunity to enclose another document which may be of interest:

- A copy of a Clinical Advisory Note from the Early Warning Emerging Trends Subcommittee of the National Advisory Committee on Drugs and Alcohol.

Thank you for your cooperation on this initiative.

Yours faithfully,

Anne Marie Hoey
Primary Care Reimbursement & Eligibility

16/09/2016

Re: Preferred Drugs Initiative

Dear Colleagues,

The HSE Medicines Management Programme's (MMP) 'preferred drug initiative' aims to promote safe, effective and cost-effective prescribing. We will be announcing two further preferred drugs later this week in relation to beta blockers and calcium channel blockers.

This follows a comprehensive review of the literature and a consultation period during which we received valuable submissions from a variety of stakeholders. Factors which impacted on our choice of agent included the licensed therapeutic indication(s), clinical outcome data, international clinical guidelines, cost, patient-related factors and prescribing trends in Ireland.

Beta Blockers: when initiating therapy with a beta blocker or if a change in therapy is being considered for patients with heart failure/angina or as add on therapy for hypertension:

- Preferred Beta Blocker is **BISOPROLOL**

Calcium Channel Blockers (CCB): when initiating therapy with a calcium channel blocker or if a change in therapy is being considered for the treatment of hypertension/stable angina:

- Preferred CCB is **AMLODIPINE**

A detailed document outlining the reasons for the selection of these preferred drugs along with "Prescribing Tips" will be published on the MMP website www.hse.ie/yourmedicines shortly. We hope that this document will be a useful reference source for prescribers. Choosing to prescribe the preferred drug will enhance quality prescribing while also delivering real savings for the healthcare system and for patients who pay for their medicines.

We welcome your on-going feedback and support which will help to shape the development of the MMP with the aim of creating a prescribing resource for all prescribers. We have now named Preferred Drugs in 10 therapeutic areas.

Statins	SIMVASTATIN	Proton Pump Inhibitor	LANSOPRAZOLE
ACE inhibitor	RAMIPRIL	ARB	CANDESARTAN
SSRI	CITALOPRAM	SNRI	VENLAFAXINE
Oral anticoagulant	WARFARIN (NOAC: APIXABAN)	Antimuscarinics	TOLTERODINE SR
Beta Blocker	BISOPROLOL	Calcium Channel Blocker	AMLODIPINE

I wish to thank you for your continued support of the Preferred Drug Initiative and for more information on the Medicines Management Programme please visit: www.hse.ie/yourmedicines

With best wishes,



Prof Michael Barry,
National Clinical Lead, Medicines Management Programme

Clinical Advisory

To: **Prescribing Doctors, Pharmacists, Emergency Department Doctors and
Emergency Department Nurses**

From: The Early Warning Emerging Trends Subcommittee of the National Advisory
Committee on Drugs and Alcohol

Date: June 2016

Subject: Medicines containing **PREGABALIN** and GABAPENTIN: being used abused and
misused recreationally

Dear Healthcare Professional,

Call for vigilance and reporting

The Early Warning and Emerging Trends (EWET) subcommittee¹, in agreement with the Department of Health wishes to highlight the need for vigilance when prescribing and dispensing pregabalin and gabapentin as both of these drugs present a risk of addiction and a potential for illegal diversion and medicinal misuse. Prescribers should always undertake a risk benefit assessment prior to prescribing either of these medicines for patients under their care.

Summary

The EWET subcommittee wishes to inform you of the serious concern regarding the misuse of prescription-only medicines containing PREGABALIN (Pregabalin, Lyrica, Brieka) and to a lesser extent, GABAPENTIN (Gabapentin, Gabin, Neurontin, Neurostil) and the exponential rise in prescribing rates of these medicines.

Over the past 2 years the EWET has received a number of anecdotal reports on the misuse of pregabalin and to a lesser extent the misuse of gabapentin. Recently this information has been bolstered with evidenced based reports about the misuse of these medicines for recreational use and through their appearance in post mortem toxicology screening tests. Furthermore, dispensing data from the PCRS over the past 5 years shows a dramatic and continued increase in the volume of dispensed pregabalin, suggesting that those who are misusing these drugs may be sourcing them through legal as well as illegal channels.

While this dispensing increase may be partly attributable to the greater number of authorised indications for pregabalin, it appears from the emerging evidence that the misuse of this drug may also be a significant factor in the escalating numbers of pregabalin items being dispensed in Ireland.

Background

Pregabalin and gabapentin were originally developed and authorised as treatments for epilepsy. However, further research has shown that it can also be beneficial in treating other conditions, e.g. generalised anxiety disorder and neuropathic pain.

Initially it was considered that pregabalin and gabapentin had a low potential for misuse, however the EWET Subcommittee is aware of concerns and reports that suggest that abuse of these medicines is on the increase. In 2013 there were 33 drug-related deaths in England and Wales where pregabalin was mentioned on the death certificate. Of 10 patients attending a Belfast hospital following recreational pregabalin abuse, six presented with seizures.

Information as to the numbers of deaths related to pregabalin in Ireland is not available at this time.

Evidence on the misuse of Pregabalin and harm potential

A study into the potential for *misuse of pregabalin* was conducted by researchers at the HSE National Drug Treatment Centre Laboratory in Dublin between June and August 2014. The study found that of 440 people tested, 39 tested positive for pregabalin, representing 9.2% of the total sample, indicating that the misuse of pregabalin is a “serious emerging issue”. Only 10 patients from this group had been prescribed the drug. These findings have been published in the Irish Medical Journal – “Pregabalin Abuse amongst Opioid Substitution Treatment Patients”².

A report published in the UK Emergency Medical Journal in 2013 entitled “Lyrica Nights-Recreational Pregabalin Abuse in an Urban Emergency Department” J Millar, S Sadasivan, N Weatherup, S Lutton, which was based on the outcomes from a one year review of all patients presenting to the Emergency Department of the Royal Victoria Hospital, Belfast after recreational drug abuse. Those who admitted to pregabalin usage were identified and case notes were reviewed. The study found that in Belfast, emergency departments (ED) have witnessed a recent increase in the number of patients presenting after recreational abuse of pregabalin. “Patients, state that the medication induces a state similar to drunkenness, hence the street name ‘Budweiser’s’... Patients are either taking tablets whole or cutting [, crushing] and snorting them. 60% of patients in this case series presented to the ED with seizures and 20% required ICU admission.”

Harm potential related to the recreational use of pregabalin and gabapentin include: physical dependencies; central nervous system depression, resulting in drowsiness, sedation, and respiratory depression; pregabalin and gabapentin related mortalities.

The Therapeutics Today newsletter dated May 2013, No. 5, produced by the National Medicines Information Centre at St. James’s Hospital (SJH) Dublin 8 and Dept of Therapeutics Trinity College, included a “Focus on Pregabalin” to highlight that patients may experience withdrawal symptoms after both short and long-term pregabalin therapy³.

Known issues in other jurisdictions

United Kingdom: In 2013, there were 19 deaths implicated with pregabalin and 17 deaths implicated with gabapentin in the UK. In September 2015, the UK Office for National Statistics (ONS) released registrations information on deaths related to drug related poisoning, which highlighted a significant increase in deaths from 2012 onwards. In 2014, there were 38 deaths where pregabalin was mentioned on the deceased's death certificate; and, 26 deaths where gabapentin was mentioned on the deceased's death certificate⁴.

Germany: Since 2008 pregabalin abuse and dependence has been reported with increasing frequency to a German medical regulatory body (BfArM)⁵.

Finland: The University of Helsinki has undertaken an assessment of pregabalin and gabapentin in opioid overdose deaths, noting that pregabalin abuse with high doses is increasingly common and can be fatal when combined with opioids.

USA: In 2005 the Drug Enforcement Administration placed pregabalin under Schedule V of the Controlled Substances Act; citing that the abuse of pregabalin may lead to limited physical dependence or psychological dependence relative to the drugs or other substances in Schedule IV⁶.

Please remember that any suspected adverse events should be reported to the Health Products Regulatory Authority (formerly the Irish Medicines Board), via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

References

1. Early Warning Emerging Trends Subcommittee (EWET) are a subcommittee of the National Advisory Committee on Drugs and Alcohol and comprises representation from the following organisations:
 - An Garda Síochána,
 - HSE Addiction Services,
 - Health Research Board,
 - Forensic Science Ireland,
 - Department of Justice and Equality,
 - Department of Health,
 - Medical Bureau of Road Safety,
 - State Laboratory,
 - HSE,
 - National Poisons Information Centre,
 - Revenue Customs Service,
 - Health Products Regulatory Authority,
 - Frontline Services Provider,
 - Academic Expert.

2. "Pregabalin Abuse amongst Opioid Substitution Treatment Patients" S McNamara, S Stokes, R Kilduff, A Shine, HSE National Drug Treatment Centre, McCarthy Centre, 30-31 Pearse Street, Dublin 2; The Irish Medical Journal, November December 2015 Vol. 108 No. 10.
<http://www.imj.ie/ViewArticleDetails.aspx?ArticleID=15406>

3. <http://www.stjames.ie/GPsHealthcareProfessionals/Newsletters/TherapeuticsToday/TherapeuticsToday2013/Therapeutics%20Today%20May%20%202013.pdf>

4. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/491854/ACMDAdvice-Pregabalin_and_gabapentin.pdf

5. <http://www.ncbi.nlm.nih.gov/pubmed/23292158>

6. http://www.deadiversion.usdoj.gov/fed_regs/rules/2005/fr0728.htm