Nurse and Midwife Medicinal Product Prescribing Toolkit

Authorised Medicinal Products, Off-label Prescription and Exempt Medicinal Products Toolkit

Changing practice to support service delivery
Introduction and Background

The purpose of this Toolkit is to provide information for registered nurse prescribers (RNPs) on medicinal product authorisation, as well as other situations that might be encountered such as off-label prescribing of authorised medicinal products or the prescribing of Exempt Medicinal Products.

This toolkit should be read in conjunction with the following documents:

- Practice Standards and Guidelines for Nurses and Midwives with Prescriptive Authority (An Bord Altranais, 2010; reissued 2016)
- National Policy for Nurse and Midwife Medicinal Product Prescribing (Office of the Nursing and Midwifery Services Director, 2012).

The Irish Medicines Board (Miscellaneous Provisions) Act 2006 (No. 3 of 2006) was passed in May 2006 to provide for prescriptive authority for nurses and midwives, subject to specific conditions and professional regulation. In May 2007 the relevant sections of the 2006 Act were commenced and the following statutory instruments (SI) were signed:

- Medicinal Products (Prescription and Control of Supply) (Amendment) Regulations 2007, (S.I. No. 201 of 2007)

Each RNP must have a thorough knowledge of the authorisation status of each medicinal product they are proposing to include within their Collaborative Practice Agreement (CPA).

Most prescribing in Ireland will involve authorised medicinal products, used within the terms of their marketing authorisations (MA), (also known as the product authorisation or licence). The terms of the MA are described in the Summary of Product Characteristics (SmPC) for each medicinal product. The SmPCs for all authorised medicinal products are accessible via the Health Products Regulatory Authority (HPRA) website, www.hpra.ie. RNPs may prescribe authorised medicinal products within the terms of the MA and within their scope of practice.

In certain circumstances it may be necessary to prescribe an authorised medicinal product outside the terms of its MA. This is known as off-label prescribing. RNPs may prescribe a medicinal product off-label provided certain criteria are fulfilled (see page 3).

On occasion Exempt Medicinal Products (EMP) (formerly known as unlicensed or unauthorised medicinal products) may be prescribed by a medical practitioner in Ireland in order to fulfil a specific patient’s needs. RNPs cannot prescribe an Exempt Medicinal Product (see page 4).
Authorised Medicinal Product

Definition: A medicinal product which is authorised by the HPRA to be marketed in Ireland, or by the European Commission (following a common EU assessment procedure coordinated by the European Medicines Agency (EMA)) to allow medicinal products to be placed on the markets in EU Member States. Under European and Irish legislation, all medicinal products must be authorised before being placed on the market (Directive 2001/83/EC).

The HPRA/EU Commission grant marketing authorisations (MAs) for medicinal products following clinical and pharmaceutical assessment of data relating to the safety, quality and efficacy of the medicinal product for which an application is received. The decision to grant or vary an authorisation is based on the outcome of this assessment of applications submitted by pharmaceutical companies in relation to their products, for which the benefit/risk profile is considered acceptable.

Following authorisation, the HPRA and EMA continue to monitor the safety, quality and efficacy of medicinal products through national and EU regulatory procedures, including the operation of national adverse reaction and quality defect reporting systems and inspection.

Manufacturing licences are also granted to the companies who make, distribute and market medicinal products in Ireland. This follows onsite inspections to ensure compliance with relevant standards and legislation.

The HPRA monitors national experience and intelligence regarding the importation and/or online sale of falsified (including counterfeit and illegal) medicinal products in Ireland, which may pose a serious health risk for people.

RNPs prescribing Authorised Medicinal Products

- RNPs have authority to prescribe authorised medicinal products within their scope of practice and as listed on their Collaborative Practice Agreement (CPA).
- The list of authorised medicinal products should be agreed with the Collaborating Medical Practitioner/s, reviewed by the Drugs and Therapeutics Committee/Review Group, and approved by the Director of Nursing/Midwifery/Public Health Nursing/Service Manager on behalf of the health service provider.
- Authorised Medicinal Products may become unavailable for various reasons, including shortages of supply due to manufacturing difficulties; safety recalls; or product discontinuation by the marketing authorisation holder.
- It is the responsibility of the RNP to register with the HPRA for relevant updates and alerts and to facilitate awareness of the status of the medicinal products listed on their CPA.
Off-label Use

Definition: Off-label use refers to the use of an authorised medicinal product outside the terms of its MA. It is the prescribing of the medicinal product that is off-label, rather than the medicinal product itself.

Examples of off-label use include:

- Use in a specific patient population or age-group not covered by the SmPC, e.g. SmPC specifies adults only, however, the medicinal product is prescribed for infants or children.
- Use for a specific clinical indication/condition not specified in the SmPC, e.g. SmPC specifies the treatment of post-operative nausea; however, the medicinal product is prescribed for nausea other than in the post-operative setting.

Off-label prescribing of authorised medicinal products is not considered to be within the terms of the SmPC/MA as issued by the HPRA or EU Commission (in the case of a centrally authorised medicinal product), as data relating to the quality, safety and efficacy of medicinal products in such circumstances will not have been subject to regulatory assessment and approval.

It should be noted that such use falls within the professional responsibility of the prescriber. In accordance with current legislative provisions, the HPRA wish to receive reports of suspected adverse reactions associated with off-label use as part of the on-going monitoring of overall safety data for medicinal products (pharmacovigilance). RNPs are encouraged to report suspected adverse reactions or quality issues or defects associated with the use of medicinal products to the HPRA.

RNPs Prescribing Medicinal Products Off-Label

There is no impediment in the relevant legislation or professional regulation to an RNP prescribing a medicinal product for off-label use. The issuing of a prescription for a medicinal product, including off-label prescribing must be in accordance with Regulation 5A of the Medicinal Products (Prescription and Control of Supply) Regulations 2003 (S.I. No. 540 of 2003), as amended.

The Practice Standards and Guidelines for Nurses and Midwives with Prescriptive Authority (An Bord Altranais, 2010; reissued 2016), Practice Standard 7, provides guidance on the off-label prescribing of authorised medicinal products by RNPs.

The HSE developed a template (see Appendix 1) for the statutory and voluntary services of the Health Service Executive (HSE) to assist in the decision making process for authorising off-label prescribing of an authorised medicinal product by an RNP. This template provides a guide for health service providers in reviewing the RNP’s listing of medicinal products on their CPA where the listing refers to the off-label prescribing of an authorised medicinal product. The Nursing and Midwifery Board of Ireland (NMBI) supports the use of this template for all RNPs to ensure the safety and quality of care for patients and service users requiring the off-label prescription of an authorised medicinal product.
Exempt Medicinal Product

Definition: An Exempt Medicinal Product (EMP) is a medicinal product that is **not authorised in Ireland**, either by the HPRA or, in the case of a centrally authorised medicinal product, by the EMA, but which can legally be supplied in response to a **bona fide** unsolicited order, formulated in accordance with the specifications of a registered medical practitioner or registered dentist for use by their individual patients on her/his direct personal responsibility, in order to fulfil the special needs of those patients (Medicinal Products (Control of Placing on the Market) Regulations 2007 (S.I. No. 540 of 2007), as amended).

The term exempt refers to the fact that such products are exempt from the legal requirement to hold a MA, on condition that their supply is in line with the above requirements.

An EMP may not be prescribed or supplied in situations where an authorised equivalent (i.e. same active substance(s), strength and dosage form) is available in Ireland.

It is essential that all healthcare professionals in the supply chain are aware that EMPs have not been assessed by the HPRA against the criteria of safety, quality and efficacy, and that the responsibility for the clinical use of such products lies with the prescriber.

Under the relevant legislation, Irish manufacturers and wholesalers of medicinal products are required to notify the HPRA of their sourcing of EMPs. These EMPs are then distributed in response to orders from pharmacies, hospitals and registered practitioners which confirm that the EMPs have been ordered in response to a bona fide unsolicited order from a registered medical practitioner or registered dentist.

The HPRA maintains a database for the notification, by wholesalers and manufacturers, of EMPs sourced for supply to the Irish market. This is particularly important where a notification of a quality defect (or other type of non-compliance issue) in a medicinal product is received from another market. This allows the HPRA to check if a notification has been received indicating that the product concerned has been imported and supplied to Irish patients. Where this has occurred the HPRA institutes appropriate risk-mitigating measures (such as a product recall) in order to protect those patients in the event of a quality defect or other issue necessitating market action.

For further information please see the HPRA’s Guide to the Notification System for Exempt Medicinal Products, available at www.hpra.ie

RNPs and Exempt Medicinal Products

The prescribing of EMPs by RNPs is **not** provided for in the current medicinal products legislation and regulation. The RNP is legally and professionally accountable and responsible for their prescribing practices as mandated by the medicinal products legislation and the Practice Standards and Guidelines for Nurses and Midwives with Prescriptive Authority (An Bord Altranais, 2010). A patient/service user’s requirement for a prescription for an EMP should be referred by the RNP to the appropriate registered medical practitioner.
Glossary of Terms

Collaborative Practice Agreement (CPA) The CPA is a document that is drawn up by the candidate/registered nurse prescriber, collaborating medical practitioner/s and the employer outlining the parameters of the registered nurse prescriber’s prescriptive authority (i.e. his/her scope of practice). The principles of professional accountability, responsibility, competence and clinical governance underpin the CPA. The CPA is approved by the Director of Nursing/Midwifery/Public health Nursing (Nursing and Midwifery Board of Ireland, 2016).

European Medicines Agency (EMA) An agency of the European Union, located in London. The Agency is responsible for the scientific evaluation of medicinal products developed by pharmaceutical companies for use in the European Union. The Agency is responsible for the co-ordination of the scientific evaluation of applications for European marketing authorisations for both human and veterinary medicinal products (centralised procedure). Under the centralised procedure, companies submit a single marketing authorisation application to the Agency. Once granted by the European Commission, a centralised (or community) marketing authorisation is valid in all European Union and EEA-EFTA states (Iceland, Liechtenstein and Norway).

Health Products Regulatory Authority (HPRA) The role of the Health Products Regulatory Authority (HPRA) is to protect and enhance public and animal health by regulating medicinal products, medical devices and other health products. The HPRA has a role in regulating human and veterinary medicinal products, clinical trials and investigations, medical devices and controlled drugs, blood components, tissues and cells, cosmetic products, protection of animals used for scientific purposes and human organs intended for transplantation.

Medicinal Product The definition of a medicinal product is defined in Article 1 of Directive 2001/83/EC, as amended by Directive 2004/27/EC, as:

- Any substance or combination of substances presented as having properties for treating or preventing disease in human beings.
- Any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action or by making a medical diagnosis.

Summary of Product Characteristics (SmPC) This is a legal document outlining the key quality, safety and efficacy data that were assessed during the authorisation process. It provides specific product information for prescribers and healthcare professionals on how to use that medicinal product safely and effectively, and also provides the basis for the package leaflet and product labelling. The content of the SmPC provides specific details on the use of the medicinal product in its treatment of the conditions for which it is authorised (HPRA, 2015).
Nurse Midwife Medicinal Product Prescribing Form

Governance process for health service providers to authorise Registered Nurse Prescribers (RNPs) to prescribe medicinal products for off-label use

Section 1: To be completed by the Candidate/RNP

<p>| | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>1</td>
<td>Name of Candidate/RNP (as per NMBI) NMBI Personal Identification Number (PIN)</td>
</tr>
<tr>
<td>2</td>
<td>Clinical area(s) of practice</td>
</tr>
<tr>
<td>3</td>
<td>Name of medicinal product</td>
</tr>
<tr>
<td>4</td>
<td>Dose, route, form</td>
</tr>
<tr>
<td>5</td>
<td>Clinical indication for off-label prescribing of this medicinal product</td>
</tr>
<tr>
<td>6</td>
<td>Rationale for inclusion of this off-label medicinal product on my Collaborative Practice Agreement (CPA) (evidence base must be included/attached)</td>
</tr>
<tr>
<td>7</td>
<td>Is this medicinal product regularly used to treat patients/service users in this clinical area(s) of practice?</td>
</tr>
<tr>
<td>8</td>
<td>Is this medicinal product included in the health service providers’ prescribing guidelines (where such guidelines exist)</td>
</tr>
<tr>
<td>9</td>
<td>Is there an alternative authorised medicinal product that could be prescribed? <em>If the answer is “YES” the Candidate/RNP must not submit this form for authorisation</em></td>
</tr>
<tr>
<td>10</td>
<td>Is this an investigational medicinal product, intended for use in the context of a clinical trial? <em>If the answer is “YES” the Candidate/RNP must not submit this form for authorisation</em></td>
</tr>
</tbody>
</table>

Signature of Candidate/RNP _________________________________________________

Date ________________________

*If the answer is “YES” the Candidate/RNP must not submit this form for authorisation*
**Section 2: To be completed by the Collaborating Medical Practitioner/s**

I have discussed this with the candidate/RNP and I support the inclusion of the above medicinal product for off-label use (ordinarily used in the clinical setting) on the CPA.

**Signature of Collaborating Medical Practitioner:** ________________________________
**Date:** ______________________

**Signature of Collaborating Medical Practitioner:** ________________________________
**Date:** ______________________

**Signature of Collaborating Medical Practitioner:** ________________________________
**Date:** ______________________

**Section 3: To be completed by the Drugs and Therapeutics Committee**

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<tbody>
<tr>
<td>1</td>
<td>Name of medicinal product</td>
</tr>
<tr>
<td>2</td>
<td>The medicinal product is regularly used to treat patients/service users in the candidate/RNP's clinical area of practice?</td>
</tr>
<tr>
<td>3</td>
<td>The medicinal product is included in the health service providers' prescribing guidelines (where such guidelines exist)</td>
</tr>
<tr>
<td>4</td>
<td>Is this medicinal product authorised for use in any European country or other international country? (please specify the country and authorising authority)</td>
</tr>
<tr>
<td>5</td>
<td>There is no alternative medicinal product that could be prescribed?</td>
</tr>
<tr>
<td>6</td>
<td>The use of this medicinal product is not in the context of a clinical trial?</td>
</tr>
</tbody>
</table>
7 Is the committee satisfied with the prescribing information, safety profile and appropriateness of the proposed clinical indications for the off-label prescribing of the medicinal product?

8 Is there a clear rationale and evidence base for this medicinal product to be prescribed by this RNP?

The committee has reviewed and considered the information supplied and supports the inclusion of the medicinal product for off-label use on the RNP’s CPA.

Signature of Chair of Drugs and Therapeutics Committee

Signature of Candidate/RNP

Date: __________________________

Section 4: Approval

This candidate/RNP is approved to include this medicinal product for off-label use on their CPA and when registered as a RNP is authorised to prescribe this medicinal product off-label within their scope of practice and the health service provider’s prescribing policy.

Name of Medicinal Product

Name of RNP

Clinical Area of Practice

Signature of Director of Nursing/Midwifery/Public Health Nursing/Services Manager or authorised representative of the Health Service Provider

Name

Title

Date __________________________