

ST. JAMES'S HOSPITAL • DUBLIN 8

TEL 01-4730589 or 1850-727-727 • www.nmic.ie 🕥 @NationalNmic

USEFUL MEDICINES INFORMATION RESOURCES FOR HEALTHCARE PROFESSIONALS

- Healthcare professionals require access to evidence-based, up-to-date sources of information on the benefits and risks associated with medicines
- Image Use of more than one source of information may be required as every resource has limitations
- The Summary of Product Characteristics (SmPC) should be referred to as the primary reference source for information relating to use of a medicinal product
- INF Dosing errors are amongst the most common prescribing errors

INTRODUCTION

The prescribing of medicines is one of the most common interventions made by doctors.¹ The last 20 years has seen an increase in the number of prescribed medicines.² Adverse reactions to medicines are a significant cause of patient morbidity and mortality.³⁻⁵ Prescribing errors frequently occur of which dosing errors are the most common; studies report 4.9% prescribing errors in general practice and 10% in hospital prescriptions.⁶⁻⁹ Healthcare professionals (HCPs) require access to current, evidence-based sources of information on the benefits and risks associated with medicines before prescribing.^{1,10,11} Reliable resources are important due to the increasing prevalence of polypharmacy, the diversity of patients being treated often with multiple co-morbidities and the increasing complexity of medicines.^{2,11} In addition to the licensed indications and dose of a medicine, HCPs require information on contraindications, precautions, drug interactions, adverse effects and monitoring requirements to ensure that the medicine is used safely and effectively for the individual patient.¹ **HCPs may need to use more than one source of information as there is no one perfect source.^{1,12-14}** There are many sources of information on medicines; it can be difficult to identify accurate, current, unbiased and evidence-based information.¹⁵ Pharmacists are medicine experts and are a valuable resource for medicine-related information. General internet search engines should not be used as the primary resource when making decisions on the use of medicines in clinical practice.^{1,15} This bulletin identifies useful prescribing information resources, including specialist resources on pregnancy, lactation and paediatrics.

STANDARD INFORMATION RESOURCES

Summary of Product Characteristics The Summary of Product Characteristics (SmPC) is a legal document that provides information for all HCPs on how to use a medicine safely and effectively in the treatment of a specific disease.^{1,16,17} The SmPC forms an integral part of the marketing authorisation (MA), or product licence of a medicine; **MA approval for a medicine is given on the basis of a positive benefit/risk ratio for a specific therapeutic indication for that medicine.**¹⁷ The content of the SmPC is based on the assessment of data submitted by the marketing authorisation holder (MAH) and is approved by the national medicines regulatory authority (e.g. the Health Products Regulatory Authority [HPRA] in Ireland) or the European Medicine and should be referred to as the primary reference source for information relating to use of a medicine; it is updated when there are any changes (e.g. new licensed therapeutic uses, updated safety information, pharmaceutical changes). The SmPC has an agreed format throughout the EU.¹⁶ The SmPC is the document on which the package leaflet (PL) is based, and is used by other information providers to inform the content of their resources.¹⁶ The SmPC and PL for medicines authorised in Ireland are accessible on <u>www.hpra.ie</u> and <u>www.medicines.ie</u>.

The HPRA website also includes **educational materials for HCPs and patients that focus on important safety concerns related to use of medicines,** for which routine risk minimisation measures, such as information contained in the SmPC and PL, are not considered sufficient to adequately address key safety concerns associated with use of that medicine.¹⁸ Examples of educational materials for HCPs include healthcare professional guides, dosing and administration guides, prescriber checklists and monitoring charts. Educational materials are produced and distributed by the MAH only when it is a requirement of the risk management plan for that specific medicine.

Any use of a medicine outside of the approved therapeutic use is often referred to as "off-label/unlicensed" use as it is outside the terms of the MA of the medicine.¹⁶ Prescribers should be aware that their own responsibility is greater when prescribing unlicensed medicines than when prescribing a licensed medicine.¹⁹

The British National Formulary (BNF) is a prescribing resource that is regarded as the main independent source of medicines information in the UK (subscription required; available via MedicinesComplete).¹³ The BNF includes information from the SmPC and other resources; it includes monographs on individual medicines and has treatment summaries of various conditions. Note that some brand names and some therapeutic indications in the BNF may vary from those in Ireland.

Martindale is a complete drug reference (subscription required; available on MedicinesComplete) that has thousands of monographs for drugs used worldwide and treatment summaries for various conditions.

Many useful evidence-based online clinical resources are available. Table 1 includes some of the freely available online resources in Ireland and other jurisdictions.

Table 1: Standard information resources freely available online

Title	Content	Website
	Useful Irish resources for prescribing of medicines	
HPRA	In addition to hosting the SmPC*, this website also includes educational materials for medicines (includes risk minimisation measures), Drug Safety Newsletters, medicine shortages information, public assessment reports (reflecting the scientific conclusion reached by the HPRA following evaluation of a MA application)	www.hpra.ie
HSE Antibiotic Prescribing	This website contains evidence-based antimicrobial guidelines for primary care in Ireland. The guidelines include 1) treatment of community infections, 2) drug interactions, 3) paediatric prescribing, 4) dental prescribing, 5) prescribing guidance for COVID-19 acute respiratory infection, 6) prescribing in renal impairment, 7) antimicrobial stewardship audit tools, 8) tips on penicillin allergy, 9) AMRIC key messages, 10) safe prescribing, 11) prescribing in pregnancy and 12) prescribing in long-term care facilities	www.antibioticprescribing.ie
National Clinical Guidelines	As of July 2020 there are 23 evidence-based guidelines published by the National Clinical Effectiveness Committee. Guidelines that support evidence-based prescribing include: management of an acute asthma attack in adults; adult type 1 diabetes mellitus; appropriate prescribing of psychotropic medication for non-cognitive symptoms in people with dementia; pharmacological management of cancer pain in adults and management of constipation in adults receiving palliative care	https://www.gov.ie/en/collection/c9fa9a- national-clinical-guidelines/
Medicines Management Programme (MMP)	 The MMP is a multi-disciplinary team which aims to enhance evidence-based and cost-effective prescribing. The MMP has published useful documents on topics including: Preferred drugs including prescribing tips and tools Prescribing and cost guidance for inhaled treatments for asthma and COPD Prescribing information for individual clinical areas including Versatis® medicated plaster, Entresto®, oral anticoagulation, best-value biological medicines, oral nutritional supplements and PCSK9 inhibitors 	www.hse.ie/yourmedicines
Immunisation Guidelines	Published by the National Immunisation Office, which has also published other useful documents including Guidelines for Vaccinations in General Practice (2018)	https://www.hse.ie/eng/health/ immunisation/infomaterials/
STOPP, START criteria	Explicit criteria developed by a consensus method that facilitate medication review in multi-morbid older people in most clinical settings	https://pubmed.ncbi.nlm.nih. gov/25324330/
Palliative Meds Info	This website which is for HCPs only has useful guidance documents on use of medicines in palliative care, and is published by the Palliative Meds Info Service, Our Lady's Hospice	https://olh.ie/our-services/palliative-care/ palliative-meds-info/
COVID-19 HSE Clinical Guidance and Evidence	The HSE library contains a repository of COVID-19 clinical guidance and latest research evidence.	https://hse.drsteevenslibrary. ie/Covid19V2/pharmacy/ medicinesmanagement
Primary Care Eligibility and Reimbursement Service (PCERS)	Information includes an up-to-date list of items that are reimbursed by the HSE (list of reimbursable items), annual and monthly reports on medication use in Ireland (PCRS annual report: statistical analysis of claims and payments) and monthly reports for GPs and pharmacists. Circulars to GPs and to pharmacists are also available here	www.pcrs.ie
	Useful information sources from other jurisdictions	
NICE	UK NICE guidelines which provide evidence-based recommendations for topics including preventing and managing various conditions	www.nice.org.uk
NICE Evidence Search	Provides links to UK and other international guidelines	www.evidence.nhs.uk
SIGN	Evidence-based clinical practice guidelines published by NHS Scotland	www.sign.ac.uk
NHS Specialist Pharmacy Service (SPS)	Resources produced by the UK Medicines Information (UKMi) centres. It includes Medicines Q&As that relate to use of drugs and drug classes	www.sps.nhs.uk
EMA	The EMA is a decentralised agency of the European Union (EU) responsible for the scientific evaluation, supervision and safety monitoring of medicines in the EU.	www.ema.europa.eu
Cochrane library	The Cochrane Database of Systematic Reviews (CDSR) is the leading journal and database for systematic reviews in health care	https://www.cochranelibrary.com/cdsr/ reviews

HPRA- Health Products Regulatory Authority; SmPC-summary of product characteristics; PAR-public assessment reports; MA-marketing authorisation; HSE-Health Service Executive; AMRIC-Antimicrobial Resistance and Infection Control; COPD-chronic obstructive pulmonary disease; ONS-oral nutritional supplements; STOPP-Screening Tool of Older Persons' potentially inappropriate Prescriptions; START-Screening Tool to Alert doctors to the Right Treatment; NICE-National Institute for Health and Care Excellence; SIGN- Scottish Intercollegiate Guidelines Network; EMA-European Medicines Agency; *also available on www.medicines.ie

In Ireland, professional organisations including the Irish College of General Practitioners (ICGP) (<u>www.icgp.ie</u>) and Royal College of Physicians of Ireland (RCPI) (<u>www.rcpi.ie</u>) publish clinical guidelines that include practical advice on medicine use. Other sources include the HSE National Clinical Programmes which provide models of care and best practice recommendations for individual therapeutic areas (e.g. diabetes, asthma, COPD, heart failure, rheumatology, dermatology) and the HSE Integrated Care Programme for chronic disease management (<u>www.hse.ie</u>).

Many international professional organisations publish online clinical guidelines including the European Society of Cardiology, British Association of Dermatologists, British Thoracic Society, British Society for Haematology, American College of Chest Physicians and American Academy of Dermatology.

There are also evidence-based online clinical resources which provide rapid access to information on treatment of specific conditions including BMJ Best Practice, UpToDate® and Clinical Knowledge Summaries (through Prodigy; subscription required). The professional area of patient.co.uk is another useful resource (https://patient.info/patientplus). The medical information department of an MAH can also offer advice in special circumstances. Note that the HSE Library (hselibrary.ie) hosts a large number of online journals and resources; all HSE sites have access to MedicinesComplete; UpToDate® is available to HSE employees and BMJ Best Practice is freely available to all HCPs.

PRESCRIBING RESOURCES FOR SPECIFIC POPULATIONS

There are many clinical situations where HCPs need more detailed information for specific populations of patients. These resources should be used in association with specialist input when appropriate and with available clinical guidelines. **Resources for prescribing contraceptives**

Contraceptives are used by the majority of sexually active women (63%) aged 15 to 49 years.¹⁷ It is estimated that use of modern contraceptives in 2017 prevented approximately 308 million unplanned pregnancies.²⁰ However, **unplanned pregnancies can occur due to contraceptive failure (which can be often due to incorrect [e.g. due to drug interaction] and/or inconsistent use).²¹ Conversely, some contraceptives can lower essential medication to sub-therapeutic levels (e.g. combined hormonal contraception moderately reduces lamotrigine exposure).²² Table 2 includes some of the freely accessible online resources that may be useful.**

Table 2: Freely available resources for prescribing contraceptives

Title	Content	Website
HPRA	SmPCs* of the individual hormonal contraceptives	www.hpra.ie
FSRH	The UK FSRH website has evidence-based useful guidance documents on the choice of a contraceptive in various scenarios including: 1) different ages, 2) breast feeding, 3) drug interactions, 4) missed pills, 5) emergency hormonal contraception, 6) using pills outside their product licence and 6) comprehensive information on contraceptive choices for women with certain medical conditions. (Note that some of the contraceptives in the guidance documents may not be available in Ireland)	Ŭ
NMIC bulletins	Updated bulletin on contraception 2015	www.nmic.ie

HPRA- Health Products Regulatory Authority; SmPC-summary of product characteristics; FSRH-Faculty of Sexual and Reproductive Healthcare;

*also available on www.medicines.ie

The BNF includes information on hormonal contraception, including treatment summaries. Useful textbooks on prescribing contraceptives include current editions of "Contraception: Your Questions Answered" (John Guillebaud and Anne MacGregor) and "Contraception Today" (John Guillebaud).^{23,24}

Resources for prescribing in pregnancy

The use of medicines in pregnancy has increased over the last 40 years;²⁵⁻³⁰ almost half of all women use four or more medicines during their pregnancy.²⁵⁻²⁹ A frequent problem facing HCPs is the lack of information on the risks and benefits of using medicines in pregnancy,³⁰ as the majority of medicines are not licensed for use in pregnancy.³¹ Table 3 includes some freely accessible online resources that may be useful.

Table 3: Freely available resources for prescribing in pregnancy

Title	Content	Website
HPRA	Section 4.6 of the SmPC* contains recommendations on the use of the product during pregnancy based on the available scientific evidence, and in cases of a known teratogen this may include contraindications, special warnings and a pregnancy prevention programme. Additional educational materials for HCPs and patients, as well as other risk minimisation tools, for medicines with a pregnancy prevention programme are also available on the HPRA website	www.hpra.ie
HSE Antibiotic Prescribing	Includes guidelines for prescribing antimicrobials in pregnancy	www.antibioticprescribing.ie
NCP for Obstetrics & Gynaecology	Several clinical guidelines available on the management of common and serious conditions in pregnancy including infections, hyperemesis and nausea/vomiting and chickenpox	https://www.hse.ie/eng/about/who/cspd/ ncps/obstetrics-gynaecology/resources/ national-clinical-guidelines/ and www. rcpi.ie
Royal College of Obstetrics and Gynaecology	There is a range of guidelines on women's health available including clinical Green- top guidelines	https://www.rcog.org.uk
UKTIS	Summary monographs for HCPs (prescribers can contact the NMIC for more detailed monographs)	www.uktis.org
UKTIS BUMPS	Fact sheets produced by UKTIS for pregnant women and their partners	www.medicinesinpregnancy.org
Mother to Baby	A US teratology information website which provides information for patients and healthcare professionals	https://mothertobaby.org/
European Association of Dermatology & Venereology	This website includes patient leaflets on skin conditions in pregnancy and on the various drug treatments	www.eadv.org/patient-corner/leaflets/
NMIC bulletins	Published 3 bulletins on prescribing in pregnancy (2018)	www.nmic.ie

HPRA- Health Products Regulatory Authority; SmPC-summary of product characteristics; HSE-Health Service Executive; NCP-National Clinical Programme; BNF-British National Formulary; UKTIS-UK Teratology Information Service; BUMPS-Best Use of Medicines in Pregnancy; *also available on www.medicines.ie

The BNF has information and guidance on prescribing in pregnancy. The UK Teratology Information Service (UKTIS) publishes detailed monographs on the use of medicines and the management of various conditions in pregnancy (prescribers can contact the NMIC for such monographs). Drugs in Pregnancy and Lactation (Briggs) is an online source that has detailed monographs of medicines used in pregnancy (subscription required; available on MedicinesComplete).

Resources for prescribing in lactation

During the post-partum period, breastfeeding women may require medicines for conditions including infection, depression and pain, or may need to continue medicines for chronic medical conditions.³²⁻³⁴ It can be challenging to determine which medicines are suitable for breastfeeding women. Table 4 includes some of the freely accessible online resources that may be useful.

Table 4: Freely available resources for prescribing in lactation

Title	Content	Website
HPRA	The SmPC* has prescribing information on lactation; it is generally regarded as being conservative in terms of its advice	www.hpra.ie
HSE Antibiotic Prescribing	Includes guidelines for prescribing antimicrobials in lactation	www.antibioticprescribing.ie
NCP for Obstetrics & Gynaecology	Clinical guideline available on antimicrobial safety in pregnancy and lactation	https://www.hse.ie/eng/about/who/cspd/ncps/ obstetrics-gynaecology/resources/national-clinical- guidelines/ and www.rcpi.ie
UKDILAS	Monographs on use of drugs in lactation which are available on the SPS website	www.sps.nhs.uk
LactMed	US database which includes monographs on the safety of drugs in breastfeeding	https://www.ncbi.nlm.nih.gov/books/NBK501922/
The Breastfeeding Network	This is a website that provides evidence-based and practical information for mothers who breastfeed; it has information leaflets on use of drugs in lactation	https://www.breastfeedingnetwork.org.uk/drugs- factsheets/
Academy of Breastfeeding Medicine	This website includes protocols (guidelines) aimed to facilitate best practices in breastfeeding medicine	https://www.bfmed.org/
Association of anaesthetics	The Association of anaesthetics published a guideline on anaesthesia and sedation in breastfeeding women in 2020	https://anaesthetists.org/Home/Resources- publications/Guidelines/Anaesthesia-and-sedation- in-breastfeeding-women-2020

HPRA- Health Products Regulatory Authority; SmPC-summary of product characteristics; HSE-Health Service Executive; NCP-National Clinical Programme; BNF-British National Formulary; UKDILAS-UK Drugs In Lactation Advisory Service; SPS-Specialist Pharmacy Service; *also available on www.medicines.ie

A useful textbook on prescribing in lactation is the current edition of "Hale's Medications & Mothers' Milk" (Thomas Hale).³⁵ Resources for prescribing for paediatrics

The unlicensed or off-label use of medicines in children is common (frequently >50%),^{19,36,37} as many medicines do not have a product licence for use in children.^{16,36,37} Children in particular are at increased risk of adverse drug reactions and dosing errors. **The British National Formulary for Children (BNFC; subscription required) and the BNF are useful resources**; the online content is updated monthly. Some paediatric hospitals have produced paediatric formularies, including the CHI at Crumlin & CHI at Connolly Paediatric Formulary (available as an app to download on some mobile devices).³⁸ Table 5 includes some freely accessible online sources that may be useful.

Table 5: Freely available resources for prescribing for paediatrics

Title	Content	Website	
General Resource			
HPRA	The SmPC* may provide information on dosing in children for some medicines	www.hpra.ie	
HSE Antibiotic Prescribing	Includes general prescribing principles for children and information on prescribing of antimicrobials for children	www.antibioticprescribing.ie	
Evelina London Paediatric Formulary	This formulary uses a colour coded system to provide guidance on prescribing responsibilities; e.g. red (hospital specialist only), amber (combined hospital specialist/non-specialist) and green (specialist and non-specialist)	http://cms.ubqo.com/public/d2595446-ce3c-47ff-9dcc-63167d9f4b80	
Medicines for Children	This UK website has advice for HCPs and parents, including leaflets on specific medicines and general medicines advice. The website is maintained by the Royal College of Paediatric and Child Health (RCPCH), the Neonatal and Paediatric Pharmacists Group (NPPC) and the charity "WellChild"	https://www.medicinesforchildren.org.uk/	
Association of Paediatric Palliative Medicine Master Formulary	This formulary gives valuable information on the (frequently unlicensed/off-label) use of medicines in paediatric palliative care.	https://www.appm.org.uk/_webedit/uploaded-files/All%20Files/Event%20 Resources/2020%20APPM%20Master%20Formulary%202020%20 protected.pdf **	
Neonatal and Paediatric Pharmacists Group	Paediatric news from NICE Medicines Awareness. This is useful for keeping abreast of developments in the use of medicines in children.	http://nppg.org.uk/news/	
Merck Manual	US website with general information on treating various conditions. See chapter 'Pediatrics'.	https://www.merckmanuals.com/professional/pediatrics	

HPRA- Health Products Regulatory Authority; SmPC-summary of product characteristics; HSE-Health Service Executive; HCP-healthcare professionals; *also available on www.medicines.ie; **this is a pdf from 2020, check website for updates

dicines.ie, this is a partition 2020, check website for updates

Resources on drug interactions

Drug interactions are one of the causes of medication safety incidents;¹³ prescribers should be aware of the main serious drug interactions for regularly prescribed medicines. In addition to the SmPC, the BNF provides information on drug interactions. Another well-known UK reference resource is Stockley's Drug Interactions (subscription required; available on MedicinesComplete). Table 6 includes some freely accessible online sources that may be useful.

Table 6: Freely available resources for information on drug interactions

Title	Content and notes	Website
HPRA	SmPCs* of the individual medicines contains information on pharmacodynamic and pharmacokinetic drug interactions	www.hpra.ie
HIV drug interactions checker	This website is maintained by the University of Liverpool; it provides useful information on interactions with HIV medicines	http://www.hiv-druginteractions.org
Hepatitis drug interactions	This website is maintained by the University of Liverpool; it provides useful information on drug interactions with hepatitis C medicines	https://www.hep-druginteractions.org/
Cancer Drug Interactions	Published by Radboud University Medical Centre, Netherlands and University of Liverpool; provides a clinically useful, reliable, comprehensive, up-to-date, evidence-based drug-drug interaction resource, freely available	http://cancer-druginteractions.org/checker
CredibleMeds	This is a US database of medicines that prolong the QT interval and/or induce torsades de Pointes. The drugs are categorised according to risk. This resource comments on CYP3A4 drug interaction issues	www.crediblemeds.org
Drugs.com interactions checker	To be used only after other approved sources have been used. Useful for information not readily available in UK sources	http://www.drugs.com/drug_interactions.html
Medscape Drug Interaction checker	Caution must be exercised with the Medscape Drug Interaction Checker, which is widely used; to be used only after other approved sources have been used. It is based primarily on drugs used in the USA and there may be some inconsistencies	www.medscape.com/druginfo/druginterchecker

HPRA- Health Products Regulatory Authority; SmPC-summary of product characteristics; *also available on www.medicines.ie

SUMMARY

There are many information resources that are available to HCPs on the use of medicines. It is important that the resources used for an individual patient are evidence-based, up-to-date and relevant for the patient.

The NMIC has a clinical enquiry answering service available for prescribers on all aspects of the use of medicines including indications, contraindications and dosage for specific drugs, drug interactions, adverse effects, drug use in pregnancy, breastfeeding, liver and renal impairment. You can contact us by emailing us at nmic@stjames.ie.

FOR PERSONAL USE ONLY. NOT TO BE REPRODUCED WITHOUT PERMISSION OF THE EDITOR

List of references available on NMIC website. Date of preparation: August 2020 Every effort has been made to ensure that this information is correct and is prepared from the best available resources at our disposal at the time of issue. Prescribers are recommended to refer to the individual Summary of Product Characteristics (SmPC) for specific information on a drug. The NMIC is not responsible for the content of external internet sites.