BNF

79

March –
September 2020

bnf.org

Medicines Information Services

Information on drug therapy
Information on any aspect of drug therapy can be obtained from Regional and District Medicines Information Services. Details regarding the *local* services provided within your region can be obtained by telephoning the following numbers.

England	
Birmingham:	(0121) 424 7298
Bristol:	(0117) 342 6655
Ipswich:	(01473) 704 431
Leeds:	(0113) 206 5377
Leicester:	(0116) 258 6491
Liverpool:	(0151) 794 8113/7, or (0151) 794 8118
London:	
• Guy's Hospital	(020) 7188 8750, or (020) 7188 3849, or (020) 7188 3855
• Northwick Park Hospital	(020) 8869 2761, or (020) 8869 3973
Newcastle:	(0191) 282 4631
Southampton:	(023) 8120 6908/9
Wales	
Cardiff:	(029) 2074 2979, or (029) 2074 2251
Scotland	
Aberdeen:	(01224) 552 316
Dundee:	(01382) 632 351, or (01382) 660 111 Extn 32351
Edinburgh:	(0131) 242 2920
Glasgow:	(0141) 211 4407
Northern Ireland	
Belfast:	(028) 9504 0558
Republic of Ireland	
Dublin:	(01) 473 0589, or (01) 453 7941 Extn 2348

United Kingdom Medicines Information (UKMI) website
www.sps.nhs.uk/

Manufacturers
Telephone numbers and email addresses of manufacturers listed in BNF Publications are shown in the Index of manufacturers p. 1670

UK Teratology Information Service
Information on drug and chemical exposures in pregnancy.
Tel: 0344 892 0909
www.uktis.org

UK Drugs in Lactation Advisory Service (UKDILAS)
Information on the compatibility of drugs with breastfeeding.
Tel: (0116) 258 6491, or (0121) 424 7298
Email: ukdilas.enquiries@nhs.net
www.sps.nhs.uk/ukdilas

Medicines in Dentistry Specialist Advisory Service
Information on drug therapy relating to dental treatment.
Liverpool: (0151) 794 8206

Driver and Vehicle Licensing Agency (DVLA)
Information on the national medical guidelines of fitness to drive is available from:
www.gov.uk/government/publications/at-a-glance

Medicines for Children Information Leaflets
Medicines information for parents and carers.
www.medicinesforchildren.org.uk

Patient Information Lines
NHS Urgent Care Services 111

Poisons Information Services
UK National Poisons Information Service (for healthcare professionals only)
Tel: 0344 892 0111
www.toxbase.org

Sport
- Information regarding the use of medicines in sport is available from UK Anti-Doping:
  www.ukad.org.uk
  Tel: (020) 7842 3450
  ukad@ukad.org.uk
  UK Anti-Doping
  Fleetbank House
  2-6 Salisbury Square
  London
  EC4Y 8AE
- Information about the prohibited status of specific medicines based on the current World Anti-Doping Agency Prohibited List is available from Global Drug Reference Online: www.globaldro.com/UK/search

Travel Immunisation
Up-to-date information on travel immunisation requirements may be obtained from:
- National Travel Health Network and Centre (for healthcare professionals only) 0845 602 6712 Monday and Friday: 9–11 a.m. and 1–2 p.m, Tuesday to Thursday: 9–11 a.m. and 1–3:30 p.m.
- travelhealthpro.org.uk/
  Travel Medicine Team, Health Protection Scotland (0141) 300 1100 (2–4 p.m. weekdays)
- www.travax.nhs.uk(for registered users of the NHS website Travax only)
- Welsh Government Switchboard English language 0300 0603300 (9 a.m.–5:30 p.m. weekdays only)
- Welsh Government Switchboard Yr laith Gymraeg 0300 0604400 (9 a.m.–5:30 p.m. weekdays only)
- Department of Health and Social Services (Belfast) (028) 9052 2118 (weekdays)

List of Registered Medical Practitioners
Details on whether doctors are registered and hold a licence to practise medicine in the UK can be obtained from the General Medical Council.
Tel: (0161) 923 6602
www.gmc-uk.org/register

MedicinesComplete

Reduced rate subscription for independent pharmacy owners

Essential information to help you make the right decision

As a community pharmacist, we know you strive to provide safe and effective patient care.

That's why community pharmacists working in independent pharmacies can now benefit from a reduced rate subscription of our trusted and respected drugs information platform MedicinesComplete. A community pharmacy subscription includes: **Stockley's Drug Interactions** and **Stockley's Interactions Checker** plus **Martindale: The Complete Drug Reference** and **Martindale's Adverse Reactions Checker**.

MedicinesComplete gives you easy-to-access, comprehensive medicines information and tools, supporting you make confident decisions at the point of care.

Find out more at

about.medicinescomplete.com/communitypharmacyoffer

Access the BNF *your* way

The *British National Formulary* (BNF) and BNF *for Children* are updated monthly online via MedicinesComplete, ensuring healthcare professionals always have the latest medicines information.

ONLINE

BNF on MedicinesComplete
Access BNF and BNF *for Children* on MedicinesComplete and receive the very latest drug information through monthly online updates.

FormularyComplete
Create, edit and manage your own local formulary content built upon the trusted prescribing advice of the BNF and BNF *for Children.*

BNF on Evidence Search
Search the BNF and BNF *for Children* alongside other authoritative clinical and non-clinical evidence and best practice at www.evidence.nhs.uk from NICE.

PRINT

Eligible healthcare professionals will now receive one print copy a year – the September issue – to supplement online access. If you are entitled to an NHS copy please refer to page ii for full details on distribution, call 01268 495 609 or email BNF@wilmingtonhealthcare.com.

PRINT SUBSCRIPTION

BNF subscription – Take advantage of our print subscription option. We will send you the new BNF as soon as the book is published. One or two year packages (including or excluding BNF *for Children*) are available. Discounted pricing is also available on bulk sales.

MOBILE

BNF app – Stay up to date anywhere with the BNF app available for iOS and Android.
BNF eBook – Available as an ePDF. See www.pharmpress.com/bnf.
BNF on MedicinesComplete – Now mobile responsive.

How to purchase

Buy direct from Pharmaceutical Press by visiting **www.pharmpress.com/bnf**

For enquiries about the BNF or BNF *for Children* in print, contact
direct@macmillan.co.uk
Tel: **+44 (0) 1256 302 699**

For enquiries concerning MedicinesComplete, FormularyComplete, or bulk orders of the print edition, contact
pharmpress-support@rpharms.com
Tel: **+44 (0) 20 7572 2266**

Download mobile apps by visiting your appropriate app store. Available for iOS and Android

For pricing information please visit the website at **www.pharmpress.com/bnf**

For international sales contact your local sales agent. Contact details at **www.pharmpress.com/Information-Help/Bookseller-contacts/agents**

Stay up to date - sign up to the BNF eNewsletter at **www.bnf.org/newsletter**

BNF

79

March –
September 2020

BMA

ROYAL
PHARMACEUTICAL
SOCIETY

Published jointly by
BMJ Group
Tavistock Square, London, WC1H 9JP, UK

and

Pharmaceutical Press
Pharmaceutical Press is the publishing division of the Royal Pharmaceutical Society.
66-68 East Smithfield, London E1W 1AW, UK

ISBN: 978 0 85711 365 8

ISBN: 978 0 85711 366 5 (ePDF)

Printed by GGP Media GmbH, Pößneck, Germany

Typeset by Data Standards Ltd, UK

Text design by Peter Burgess

A catalogue record for this book is available from the British Library.

Requesting copies of BNF publications

Paper copies may be obtained through any bookseller or direct from:

Pharmaceutical Press
c/o Macmillan Distribution (MDL)
Hampshire International Business Park
Lime Tree Way
Basingstoke
Hampshire
RG24 8YJ
Tel: +44 (0) 1256 302 699
Fax: +44 (0) 1256 812 521
direct@macmillan.co.uk

or via our website www.pharmpress.com/

For all bulk orders of more than 20 copies:
Tel: +44 (0) 207 572 2266
pharmpress-support@rpharms.com

The *BNF* is available as a mobile app, online (bnf.nice.org.uk/) and also through MedicinesComplete; a PDA version is also available. In addition, *BNF* content can be integrated into a local formulary by using *BNF* on FormularyComplete; see www.bnf.org for details.

Distribution of printed BNFs
In **England**, NICE purchases print editions of the *BNF* (September editions only) for distribution within the NHS. For details of who is eligible to receive a copy and further contact details, please refer to the NICE website: www.nice.org.uk/about/what-we-do/evidence-services/british-national-formulary. If you are entitled to a shared copy of the *BNF*, please call (0)1268 495 609 or email: *BNF*@wilmingtonhealthcare.com.

In **Scotland**, email:
nss.psd-bnf@nhs.net

In **Wales**, email:
nwssp-primarycareservices@wales.nhs.uk

In **Northern Ireland**, email:
ni.bnf@hscni.net

About BNF content
The *BNF* is designed as a digest for rapid reference and it may not always include all the information necessary for prescribing and dispensing. Also, less detail is given on areas such as obstetrics, malignant disease, and anaesthesia since it is expected that those undertaking treatment will have specialist knowledge and access to specialist literature. *BNF for Children* should be consulted for detailed information on the use of medicines in children. The *BNF* should be interpreted in the light of professional knowledge and supplemented as necessary by specialised publications and by reference to the product literature. Information is also available from Medicines Information Services.

Please refer to digital versions of *BNF* for the most up-to-date content. *BNF* is published in print but interim updates are issued and published in the digital versions of *BNF*. The publishers work to ensure that the information is as accurate and up-to-date as possible at the date of publication, but knowledge and best practice in this field change regularly. *BNF's* accuracy and currency cannot be guaranteed and neither the publishers nor the authors accept any responsibility for errors or omissions. While considerable efforts have been made to check the material in this publication, it should be treated as a guide only. Prescribers, pharmacists and other healthcare professionals are advised to check www.bnf.org/ for information about key updates and corrections.

Pharmaid
Numerous requests have been received from developing countries for *BNFs*. The Pharmaid scheme of the Commonwealth Pharmacists Association will dispatch old *BNFs* to certain Commonwealth countries. For more information on this scheme see commonwealthpharmacy.org/what-we-do/pharmaid/.
If you would like to donate your copy email:
admin@commonwealthpharmacy.org

Preface

The BNF is a joint publication of the British Medical Association and the Royal Pharmaceutical Society. It is published under the authority of a Joint Formulary Committee which comprises representatives of the two professional bodies, the UK Health Departments, the Medicines and Healthcare products Regulatory Agency, and a national guideline producer. The Dental Advisory Group oversees the preparation of advice on the drug management of dental and oral conditions; the Group includes representatives of the British Dental Association and a representative from the UK Health Departments. The Nurse Prescribers' Advisory Group advises on the content relevant to nurses and includes representatives from different parts of the nursing community and from the UK Health Departments.

The BNF aims to provide prescribers, pharmacists, and other healthcare professionals with sound up-to-date information about the use of medicines.

The BNF includes key information on the selection, prescribing, dispensing and administration of medicines. Medicines generally prescribed in the UK are covered and those considered less suitable for prescribing are clearly identified. Little or no information is included on medicines promoted for purchase by the public.

Information on drugs is drawn from the manufacturers' product literature, medical and pharmaceutical literature, UK health departments, regulatory authorities, and professional bodies. Advice is constructed from clinical literature and reflects, as far as possible, an evaluation of the evidence from diverse sources. The BNF also takes account of authoritative national guidelines and emerging safety concerns. In addition, the editorial team receives advice on all therapeutic areas from expert clinicians; this ensures that the BNF's recommendations are relevant to practice.

The BNF is designed as a digest for rapid reference and it may not always include all the information necessary for prescribing and dispensing. Also, less detail is given on areas such as obstetrics, malignant disease, and anaesthesia since it is expected that those undertaking treatment will have specialist knowledge and access to specialist literature. Similarly, little or no information is included on medicines for very rare conditions. *BNF for Children* should be consulted for detailed information on the use of medicines in children. The BNF should be interpreted in the light of professional knowledge and supplemented as necessary by specialised publications and by reference to the product literature. Information is also available from medicines information services, see Medicines Information Services (see inside front cover).

It is **important** to use the most recent BNF information for making clinical decisions. The print edition of the BNF is updated in March and September each year. Monthly updates are provided online via Medicines Complete and the NHS Evidence portal. The more important changes are listed under Changes; changes listed online are cumulative (from one print edition to the next), and can be printed off each month to show the main changes since the last print edition as an aide memoire for those using print copies.

The BNF Publications website (www.bnf.org) includes additional information of relevance to healthcare professionals. Other digital formats of the BNF—including versions for mobile devices and integration into local formularies—are also available.

BNF Publications welcomes comments from healthcare professionals. Comments and constructive criticism should be sent to:

British National Formulary,
Royal Pharmaceutical Society,
66–68 East Smithfield
London
E1W 1AW
editor@bnf.org

The contact email for manufacturers or pharmaceutical companies wishing to contact BNF Publications is manufacturerinfo@bnf.org

Contents

Acknowledgements

The Joint Formulary Committee is grateful to individuals and organisations that have provided advice and information to the *BNF*.

Contributors for this update were:

K.W. Ah-See, M.N. Badminton, A.K. Bahl, P.R.J. Barnes, D. Bilton, S.L. Bloom, M.F. Bultitude, I.F. Burgess, D.J. Burn, C.E. Dearden, D.W. Denning, P.N. Durrington, D.A.C. Elliman, P. Emery, M.D. Feher, A. Freyer, B.G. Gazzard, A.M. Geretti, N.J.L. Gittoes, P.J. Goadsby, M. Gupta, T.L. Hawkins, B.G. Higgins, S.P. Higgins, S.H.D. Jackson, A. Jones, D.M. Keeling, J.R. Kirwan, P.G. Kopelman, T.H. Lee, A. Lekkas, D.N.J. Lockwood, A.M. Lovering, M.G. Lucas, L. Luzzatto, P.D. Mason, D.A. McArthur, K.E.L. McColl, L.M. Melvin, E. Miller, R.M. Mirakian, P. Morrison, S.M.S. Nasser, C. Nelson-Piercy, J.M. Neuberger, D.J. Nutt, R. Patel, W.J. Penny, A.B. Provan, A.S.C. Rice, D.J. Rowbotham, J.W. Sander, J.A.T. Sandoe, M. Schacter, S.E. Slater, J. Soar, S.C.E. Sporton, M.D. Stewart, S. Thomas, J.P. Thompson, A.D. Weeks, A. Wilcock, A.P.R. Wilson.

Expert advice on the management of oral and dental conditions was kindly provided by M. Addy, P. Coulthard, A. Crighton, M.A.O. Lewis, J.G. Meechan, N.D. Robb, C. Scully, R.A. Seymour, R. Welbury, and J.M. Zakrzewska. S. Kaur provided valuable advice on dental prescribing policy.

Valuable advice has been provided by the following expert groups: Advisory Committee on Malaria Prevention, Association of British Neurologists, British Association of Dermatologists' Therapy & Guidelines Sub-committee, British Geriatrics Society, British Society of Gastroenterology, British Society of Paediatric Gastroenterology, Hepatology and Nutrition, Faculty of Sexual and Reproductive Healthcare, Neonatal and Paediatric Pharmacists Group, Royal College of Anaesthetists, Royal College of Obstetricians and Gynaecologists, Royal College of Psychiatrists, Vascular Society.

The MHRA have provided valuable assistance.

Correspondents in the pharmaceutical industry have provided information on new products and commented on products in the BNF.

Numerous doctors, pharmacists, nurses, and others have sent comments and suggestions.

The BNF team are grateful for the support and access to in-house expertise at Pharmaceutical Press and acknowledge the assistance of A. Lourie, J. Macdonald, N. Potter and their teams.

BNF Staff

BNF DIRECTOR

Karen Baxter *BSc, MSc, FRPharmS*

SENIOR EDITORIAL STAFF

Kiri Aikman *BPharm (NZ), PGDipClinPharm (NZ), ARPharmS*

Alison Brayfield *BPharm, MRPharmS*

Robert Buckingham *BSc, SRPharmS*

Catherine Cadart *BPharm (AU), BA(Hons), GradDipHospPharm (AU), MRPharmS*

Mahinaz Harrison *BPharm, DipPharmPract, IP, MRPharmS*

Holly Hayne *BSc (Pharmacology) (NZ), BPharm (NZ)*

Rebecca Luckhurst *BSc, MSc*

Alexander McPhail *MPharm, PGDipClinPharm*

Claire McSherry *BPharm (NZ), PGCertClinPharm (NZ)*

Claire Preston *BPharm, PGDipMedMan, MRPharmS*

Kate Towers *BPharm (AU), GCClinPharm (AU)*

EDITORIAL STAFF

Mohammed Abou Daya *MPharm, PGDipGPP, MRPharmS*

Hannah Arnold *BPharm (NZ)*

Natasha Bell-Asher *BPharm (NZ), PGDipClinPharm (NZ)*

Lucía Camañas Sáez *MPharm (ESP), PGDipClinPharm, PGCertPsychTherap, MRPharmS*

Rochelle Chin *BPharm (AU)*

Kathleen Eager *BPharm*

Emily Henderson *BPharm (NZ), PGCertClinPharm (NZ)*

Sue Ho *BPharm (AU), MRPharmS*

Elizabeth King *MAPharmT*

Sonal Ladani *MPharm, PGDipGPP, MRPharmS*

David Lipanovic *BPharm (NZ), PGCertClinPharm (NZ)*

Jean MacKershan *BSc, PgDip*

John Martin *BPharm, PhD, MRPharmS*

Angela McFarlane *BSc, DipClinPharm*

Deirdre McGuirk *BComm, MPharm, MRPharmS*

Anna McLachlan *BPharm (NZ), PGCertClinPharm (NZ)*

Liliana Moreira Vilas Boas *MPharm(PT), PGDipHPS(PT), PGCertHSDM(PT), PGCertGPP, MRPharmS*

Merusha Naidoo *BPharm (NZ), PGCertClinPharm (NZ)*

Hana Numan *BPharm (NZ), PGDipClinPharm (NZ)*

Barbara Okpala *MPharm, PGDipHospPharm*

Catherine Pitt *MPharm, PGDipClinPharm, MRPharmS*

Stephanie Powell *MBioSci*

Rebekah Raymond *BSc, DipPharmPrac, MRPharmS*

Caraliese Rebello *BPharm (NZ), PGDipClinPharm (NZ)*

Sharyl Rodrigues *BPharm (NZ), PGDipClinPharm (NZ)*

Jannah Ryan *BSc(Hons)*

Harpreet Sandhu *MPharm, MRPharmS*

Beejal Shah *MPharm, PGDipClinPharm, IP, MRPharmS*

Lucy Sheed *BPharm (NZ)*

Tadeh Tahmasi *MPharm, MRPharmS*

Hannah Tan *BPharm (AU)*

SUPPORT STAFF

Matt Bradbury *BSc(Hons)*

Darren Chan *BSc, MSc*

Lauren Cheetham *BA(Hons)*

Filsane Haji *BSc, MSc*

Philip Lee *BSc, PhD*

Olivia Maskill *BSc(Hons)*

Vicky Pollington *BSc(Hons)*

Carina Redig de Campos

Louise Symmons *BSc(Hons), MSc*

Nikolaos Tsimplis *BSc, MRes*

Joint Formulary Committee

CHAIR

Derek G. Waller
BSc, MB BS, DM, FRCP

COMMITTEE MEMBERS

Andy Burman (lay member)
CMgr, FCMI, FRSA, FIAM

Jo Lyn Chooi
BMedSc, BM BS, FRCA

Carmel M. Darcy
BSc, MSc, IP, MPSNI, MRPharmS

Andrew Evans
BPharm, MPH, DipClinPharm, MRPharmS

Sue Faulding
BPharm, MSc, FRPharmS

Tracy Hall
BSc, MSc, Cert N, Dip N, RGN, DN, NIP, QN

Brian Hawkins
BSc, PhD, MRPharmS, FFRPS, IP

Lynn Haygarth
BPharm, MEd, FFRPS, FRPharmS, FCMHP

Simon Hurding
MB, ChB, MRCGP

Sandeep Kapur
BSc(Hons), MB BS, MRCGP(Dist)

W. Moira Kinnear
BSc, MSc, FRPharmS

Mark P. Lythgoe
MB BS, MRPharmS

Louise Picton
BSc, DipCommPharm, MSc, MRPharmS

Bernadette Rae
Pg Cert Ed, Fellow HEA, MSc Nursing, Pg CertANP, BSc(Hons), Grad Cert NMP, RGN

Muhammad Magdi Yaqoob
MD, FRCP

Dental Advisory Group

CHAIR

Sarah Manton
BDS, FDSRCS Ed, FHEA, PhD, FDFTEd

COMMITTEE MEMBERS

Andrew K. Brewer
BSc, BchD, MFDS (Glas)

Alexander Crighton
BDS, MB, ChB, FDS, OM

Hannah Giles
BPharm (NZ)

Michelle Moffat
BDS MFDS RCS Ed, M Paed Dent RCPS, FDS (Paed Dent) RCS Ed

Barbara Okpala
MPharm, PGDipHospPharm

Wendy Thompson
BSc(Hons), BDS(Hons), MJDF

Kate Towers
BPharm (AU), GCClinPharm (AU)

SECRETARY

Arianne J. Matlin
MA, MSci, PhD

ADVICE ON DENTAL PRACTICE

The **British Dental Association** has contributed to the advice on medicines for dental practice through its representatives on the Dental Advisory Group.

Nurse Prescribers' Advisory Group

CHAIR

Molly Courtenay
PhD, MSc, Cert Ed, BSc, RGN

COMMITTEE MEMBERS

Penny M. Franklin
RN, RCN, RSCPHN(HV), MA, PGCE

Matt Griffiths
BA(Hons), FAETC, RGN, Cert A&E, NISP, PHECC

Tracy Hall
BSc, MSc, RGN, DN, Dip N, Cert N

Penny Harrison
BSc(Hons)

Julie MacAngus
BSc(Hons), RGN, RM, PGCE

Joan Myers
MSc, BSc, RGN, RSCN, Dip DN

Fiona Peniston-Bird
BSc(Hons), NIP, RHV, RGN

Kathy Radley
BSc, RGN

Kate Towers
BPharm (AU), GCClinPharm (AU)

How BNF Publications are constructed

Overview

The BNF is an independent professional publication that addresses the day-to-day prescribing information needs of healthcare professionals. Use of this resource throughout the health service helps to ensure that medicines are used safely, effectively, and appropriately.

Hundreds of changes are made between print editions, and are published monthly in a number of digital formats. The most clinically significant updates are listed under Changes p. xvi.

The BNF is unique in bringing together authoritative, independent guidance on best practice with clinically validated drug information. Validation of information follows a standardised process, reviewing emerging evidence, best-practice guidelines, and advice from a network of clinical experts. Where the evidence base is weak, further validation is undertaken through a process of peer review. The process and its governance are outlined in greater detail in the sections that follow.

Joint Formulary Committee

The Joint Formulary Committee (JFC) is responsible for the content of the BNF. The JFC includes pharmacy, medical, nursing and lay representatives; there are also representatives from the Medicines and Healthcare products Regulatory Agency (MHRA), the UK Health Departments, and a national guideline producer. The JFC decides on matters of policy and reviews amendments to the BNF in the light of new evidence and expert advice.

Dental Advisory Group

The Dental Advisory Group oversees the preparation of advice on the drug management of dental and oral conditions; the group includes representatives from the British Dental Association and a representative from the UK Health Departments.

Nurse Prescribers' Advisory Group

The Nurse Prescribers' Advisory Group oversees the list of drugs approved for inclusion in the Nurse Prescribers' Formulary; the group includes representatives from a range of nursing disciplines and stakeholder organisations.

Expert advisers

The BNF uses about 60 expert clinical advisers (including doctors, pharmacists, nurses, and dentists) throughout the UK to help with clinical content. The role of these expert advisers is to review existing text and to comment on amendments drafted by the clinical writers. These clinical experts help to ensure that the BNF remains reliable by:

- commenting on the relevance of the text in the context of best clinical practice in the UK;
- checking draft amendments for appropriate interpretation of any new evidence;
- providing expert opinion in areas of controversy or when reliable evidence is lacking;
- providing independent advice on drug interactions, prescribing in hepatic impairment, renal impairment, pregnancy, breast-feeding, children, the elderly, palliative care, and the emergency treatment of poisoning.

In addition to consulting with regular advisers, the BNF calls on other clinical specialists for specific developments when particular expertise is required.

The BNF works closely with a number of expert bodies that produce clinical guidelines. Drafts or pre-publication copies of guidelines are often received for comment and assimilation into the BNF.

Editorial team

BNF clinical writers have all worked as pharmacists or possess a pharmacy degree and a further, relevant post-graduate qualification, and have a sound understanding of how drugs are used in clinical practice. As a team, the clinical writers are responsible for editing, maintaining, and updating BNF content. They follow a systematic prioritisation process in response to updates to the evidence base in order to ensure the most clinically important topics are reviewed as quickly as possible. In parallel the team of clinical writers undertakes a process of rolling revalidation, aiming to review all of the content in the BNF over a 3- to 4-year period.

Amendments to the text are drafted when the clinical writers are satisfied that any new information is reliable and relevant. A set of standard criteria define when content is referred to expert advisers, the Joint Formulary Committee or other advisory groups, or submitted for peer review.

Clinical writers prepare the text for publication and undertake a number of validation checks on the knowledge at various stages of the production process.

Sources of BNF information

The BNF uses a variety of sources for its information; the main ones are shown below.

Summaries of product characteristics

The BNF reviews summaries of product characteristics (SPCs) of all new products as well as revised SPCs for existing products. The SPCs are the principal source of product information and are carefully processed. Such processing involves:

- verifying the approved names of all relevant ingredients including 'non-active' ingredients (the BNF is committed to using approved names and descriptions as laid down by the Human Medicine Regulations 2012);
- comparing the indications, cautions, contra-indications, and side-effects with similar existing drugs. Where these are different from the expected pattern, justification is sought for their inclusion or exclusion;
- seeking independent data on the use of drugs in pregnancy and breast-feeding;
- incorporating the information into the BNF using established criteria for the presentation and inclusion of the data;
- checking interpretation of the information by a second clinical writer before submitting to a content manager; changes relating to doses receive a further check;
- identifying potential clinical problems or omissions and seeking further information from manufacturers or from expert advisers;
- constructing, with the help of expert advisers, a comment on the role of the drug in the context of similar drugs.

Much of this processing is applicable to the following sources as well.

Literature

Clinical writers monitor core medical and pharmaceutical journals. Research papers and reviews relating to drug therapy are carefully processed. When a difference between the advice in the BNF and the paper is noted, the new information is assessed for reliability (using tools based on SIGN methodology) and relevance to UK clinical practice. If necessary, new text is drafted and discussed with expert advisers and the Joint Formulary Committee. The BNF enjoys a close working relationship with a number of national information providers.

In addition to the routine process, which is used to identify 'triggers' for changing the content, systematic literature searches are used to identify the best quality evidence available to inform an update. Clinical writers receive training in critical appraisal, literature evaluation, and search strategies.

Consensus guidelines

The advice in the BNF is checked against consensus guidelines produced by expert bodies. The quality of the guidelines is assessed using adapted versions of the AGREE II tool. A number of bodies make drafts or pre-publication copies of the guidelines available to the BNF; it is therefore possible to ensure that a consistent message is disseminated. The BNF routinely processes guidelines from the National Institute for Health and Care Excellence (NICE), the All Wales Medicines Strategy Group (AWMSG), the Scottish Medicines Consortium (SMC), and the Scottish Intercollegiate Guidelines Network (SIGN).

Reference sources

Textbooks and reference sources are used to provide background information for the review of existing text or for the construction of new text. The BNF team works closely with the editorial team that produces *Martindale: The Complete Drug Reference*. The BNF has access to *Martindale* information resources and each team

keeps the other informed of significant developments and shifts in the trends of drug usage.

Peer review

Although every effort is made to identify the most robust data available, inevitably there are areas where the evidence base is weak or contradictory. While the BNF has the valuable support of expert advisers and the Joint Formulary Committee, the recommendations made may be subject to a further level of scrutiny through peer review to ensure they reflect best practice.

Content for peer review is posted on bnf.org and interested parties are notified via a number of channels, including the BNF e-newsletter.

Statutory information

The BNF routinely processes relevant information from various Government bodies including Statutory Instruments and regulations affecting the Prescriptions only Medicines Order. Official compendia such as the British Pharmacopoeia and its addenda are processed routinely to ensure that the BNF complies with the relevant sections of the Human Medicines Regulations 2012.

The BNF maintains close links with the Home Office (in relation to controlled drug regulations) and the Medicines and Healthcare products Regulatory Agency (including the British Pharmacopoeia Commission). Safety warnings issued by the Commission on Human Medicines (CHM) and guidelines on drug are issued by the UK health departments are processed as a matter of routine.

Relevant professional statements issued by the Royal Pharmaceutical Society are included in the BNF as are guidelines from bodies such as the Royal College of General Practitioners.

Medicines and devices

NHS Prescription Services (from the NHS Business Services Authority) provides non-clinical, categorical information (including prices) on the medicines and devices included in the BNF.

Comments from readers

Readers of the BNF are invited to send in comments. Numerous letters and emails are received by the BNF team. Such feedback helps to ensure that the BNF provides practical and clinically relevant information. Many changes in the presentation and scope of the BNF have resulted from comments sent in by users.

Comments from industry

Close scrutiny of BNF by the manufacturers provides an additional check and allows them an opportunity to raise issues about BNF's presentation of the role of various drugs; this is yet another check on the balance of BNF's advice. All comments are looked at with care and, where necessary, additional information and expert advice are sought.

Market research

Market research is conducted at regular intervals to gather feedback on specific areas of development.

Assessing the evidence

From January 2016, recommendations made in BNF publications have been evidence graded to reflect the strength of the recommendation. The addition of evidence grading is to support clinical decision making based on the best available evidence.

The BNF aims to revalidate all content over a rolling 3- to 4-year period and evidence grading will be applied to recommendations as content goes through the revalidation process. Therefore, initially, only a small number of recommendations will have been graded.

Grading system

The BNF has adopted a five level grading system from A to E, based on the former SIGN grading system. This grade is displayed next to the recommendation within the text.

Evidence used to make a recommendation is assessed for validity using standardised methodology tools based on AGREE II and assigned a level of evidence. The recommendation is then given a grade that is extrapolated from the level of evidence, and an assessment of the body of evidence and its applicability.

Evidence assigned a level 1- or 2- score has an unacceptable level of bias or confounding and is not used to form recommendations.

Levels of evidence

- **Level 1++**
  High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias.
- **Level 1+**
  Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias.
- **Level 1–**
  Meta-analyses, systematic reviews, or RCTs with a high risk of bias.
- **Level 2++**
  High quality systematic reviews of case control or cohort studies; or high quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal.
- **Level 2+**
  Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal.
- **Level 2–**
  Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal.
- **Level 3**
  Non-analytic studies, e.g. case reports, case series.
- **Level 4**
  Expert advice or clinical experience from respected authorities.

Grades of recommendation

- **Grade A: High strength**
  NICE-accredited guidelines; or guidelines that pass AGREE II assessment; or at least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results.
- **Grade B: Moderate strength**
  A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 1++ or 1+.
- **Grade C: Low strength**
  A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or extrapolated evidence from studies rated as 2++.
- **Grade D: Very low strength**
  Evidence level 3; or extrapolated evidence from studies rated as 2+; or tertiary reference source created by a transparent, defined methodology, where the basis for recommendation is clear.
- **Grade E: Practice point**
  Evidence level 4.

How to use BNF Publications in print

How to use the BNF

This edition of the BNF continues to display the fundamental change to the structure of the content that was first shown in BNF 70. The changes were made to bring consistency and clarity to BNF content, and to the way that the content is arranged within print and digital products, increasing the ease with which information can be found.

For reference, the most notable changes to the structure of the content include:

- Drug monographs – where possible, all information that relates to a single drug is contained within its drug monograph, moving information previously contained in the prescribing notes. Drug monographs have also changed structurally: additional sections have been added, ensuring greater regularity around where information is located within the publication.
- Drug class monographs – where substantial amounts of information are common to all drugs within a drug class (e.g. macrolides p. 553), a drug class monograph has been created to contain the common information.
- Medicinal forms – categorical information about marketed medicines, such as price and pack size, continues to be sourced directly from the Dictionary of Medicines and Devices provided by the NHS Business Services Authority. However, clinical information curated by the BNF team has been clearly separated from the categorical pricing and pack size information and is included in the relevant section of the drug monograph.
- Section numbering – the BNF section numbering has been removed. This section numbering tied the content to a rigid structure and enforced the retention of defunct classifications, such as mercurial diuretics, and hindered the relocation of drugs where therapeutic use had altered. It also caused constraints between the BNF and BNF *for Children*, where drugs had different therapeutic uses in children.
- Appendix 4 – the content has been moved to individual drug monographs. The introductory notes have been replaced with a new guidance section, Guidance on intravenous infusions p. 17.

Introduction

In order to achieve the safe, effective, and appropriate use of medicines, healthcare professionals must be able to use the BNF effectively, and keep up to date with significant changes in the BNF that are relevant to their clinical practice. This *How to Use the BNF* is key in reinforcing the details of the new structure of the BNF to all healthcare professionals involved with prescribing, monitoring, supplying, and administering medicines, as well as supporting the learning of students training to join these professions.

Structure of the BNF

This BNF edition continues to broadly follows the high-level structure of earlier editions of the BNF (i.e. those published before BNF 70):

Front matter, comprising information on how to use the BNF, the significant content changes in each edition, and guidance on various prescribing matters (e.g. prescription writing, the use of intravenous drugs, particular considerations for special patient populations).

Chapters, containing drug monographs describing the uses, doses, safety issues and other considerations involved in the use of drugs; drug class monographs; and treatment summaries, covering guidance on the selection of drugs. Monographs and treatment summaries are divided into chapters based on specific aspects of medical care, such as Chapter 5, Infections, or Chapter 16, Emergency treatment of poisoning; or drug use related to a particular system of the body, such as Chapter 2, Cardiovascular.

Within each chapter, content is organised alphabetically by therapeutic use (e.g. Airways disease, obstructive), with the treatment summaries first, (e.g. asthma), followed by the monographs of the drugs used to manage the conditions discussed in the treatment summary. Within each therapeutic use, the drugs are organised alphabetically by classification (e.g. Antimuscarinics, Beta $_2$-agonist bronchodilators) and then alphabetically within each classification (e.g. Aclidinium bromide, Glycopyrronium bromide, Ipratropium bromide).

Appendices, covering interactions, borderline substances, cautionary and advisory labels, and woundcare.

Back matter, covering the lists of medicines approved by the NHS for Dental and Nurse Practitioner prescribing, proprietary and specials manufacturers' contact details, and the index. Yellow cards are also included, to facilitate the reporting of adverse events, as well as quick reference guides for life support and key drug doses in medical emergencies, for ease of access.

Navigating the BNF

The contents page provides the high-level layout of information within the BNF; and in addition, each chapter begins with a small contents section, describing the therapeutic uses covered within that chapter. Once in a chapter, location is guided by the side of the page showing the chapter number (the *thumbnail*), alongside the chapter title. The top of the page includes the therapeutic use (the *running head*) alongside the page number.

Once on a page, visual cues aid navigation: treatment summary information is in black type, with therapeutic use titles similarly styled in black, whereas the use of colour indicates drug-related information, including drug classification titles, drug class monographs, and drug monographs.

Although navigation is possible by browsing, primarily access to the information is via the index, which covers the titles of drug class monographs, drug monographs, and treatment summaries. The index also includes the names of branded medicines and other topics of relevance, such as abbreviations, guidance sections, tables, and images.

Content types

Treatment summaries

Treatment summaries are of three main types;

- an overview of delivering a drug to a particular body system (e.g. Skin conditions, management p. 1257)
- a comparison between a group or groups of drugs (e.g. beta-adrenoceptor blockers (systemic) p. 153)
- an overview of the drug management or prophylaxis of common conditions intended to facilitate rapid appraisal of options (e.g. Hypertension p. 146, or Malaria, prophylaxis p. 627).

In order to select safe and effective medicines for individual patients, information in the treatment summaries must be used in conjunction with other prescribing details about the drugs and knowledge of the patient's medical and drug history.

Monographs

Overview

In earlier editions (i.e. before BNF 70), a systemically administered drug with indications for use in different body systems was split across the chapters relating to those body systems. So, for example, codeine phosphate p. 466 was found in chapter 1, for its antimotility effects and chapter 4 for its analgesic effects. However, the monograph in chapter

1 contained only the dose and some selected safety precautions.

Now, all of the information for the systemic use of a drug is contained within one monograph, so codeine phosphate p. 466 is now included in chapter 4. This carries the advantage of providing all of the information in one place, so the user does not need to flick back and forth across several pages to find all of the relevant information for that drug. Cross references are included in chapter 1, where the management of diarrhoea is discussed, to the drug monograph to assist navigation.

Where drugs have systemic and local uses, for example, chloramphenicol p. 585, p. 1209, p. 1233, and the considerations around drug use are markedly different according to the route of administration, the monograph is split, as with earlier editions, into the relevant chapters.

This means that the majority of drugs are still placed in the same chapters and sections as earlier editions, and although there may be some variation in order, all of the relevant information will be easier to locate.

One of the most significant changes to the monograph structure is the increased granularity, with a move from around 9 sections to over 20 sections; sections are only included when relevant information has been identified. The following information describes these sections and their uses in more detail.

Nomenclature

Monograph titles follow the convention of recommended international non-proprietary names (rINNs), or, in the absence of a rINN, British Approved Names. Relevant synonyms are included below the title and, in some instances a brief description of the drug action is included. Over future editions these drug action statements will be rolled out for all drugs.

In some monographs, immediately below the nomenclature or drug action, there are a number of cross references or flags used to signpost the user to any additional information they need to consider about a drug. This is most common for drugs formulated in combinations, where users will be signposted to the monographs for the individual ingredients (e.g. senna with ispaghula husk p. 63) or for drugs that are related to a drug class monograph (see Drug class monographs, below).

Indication and dose

User feedback has highlighted that one of the main uses of the BNF is identifying indications and doses of drugs. Therefore, indication and dose information has been promoted to the top of the monograph and highlighted by a coloured panel to aid quick reference.

The indication and dose section is more highly structured than in earlier editions, giving greater clarity around which doses should be used for which indications and by which route. In addition, if the dose varies with a specific preparation or formulation, that dosing information has been moved out of the preparations section and in to the indication and dose panel, under a heading of the preparation name.

Doses are either expressed in terms of a definite frequency (e.g. 1 g 4 times daily) or in the total daily dose format (e.g. 6 g daily in 3 divided doses); the total daily dose should be divided into individual doses (in the second example, the patient should receive 2 g 3 times daily).

Doses for specific patient groups (e.g. the elderly) may be included if they are different to the standard dose. Doses for children can be identified by the relevant age range and may vary according to their age or body-weight.

In earlier editions of the BNF, age ranges and weight ranges overlapped. For clarity and to aid selection of the correct dose, wherever possible these age and weight ranges now do not overlap. When interpreting age ranges it is important to understand that a patient is considered to be 64 up until the point of their 65th birthday, meaning that an age range of adult 18 to 64 is applicable to a patient from the day of their 18th birthday until the day before their 65th birthday. All age ranges should be interpreted in this way. Similarly, when interpreting weight ranges, it should be understood that a weight of up to 30 kg is applicable to a patient up to, but not including, the point that they tip the scales at 30 kg and a weight range of 35 to 59 kg is applicable to a patient as soon as they tip the scales at 35 kg right up until, but not including, the point that they tip the scales at 60 kg. All weight ranges should be interpreted in this way.

In all circumstances, it is important to consider the patient in question and their physical condition, and select the dose most appropriate for the individual.

Other information relevant to Indication and dose

The dose panel also contains, where known, an indication of **pharmacokinetic considerations** that may affect the choice of dose, and **dose equivalence** information, which may aid the selection of dose when switching between drugs or preparations.

The BNF includes **unlicensed use** of medicines when the clinical need cannot be met by licensed medicines; such use should be supported by appropriate evidence and experience. When the BNF recommends an unlicensed medicine or the 'off-label' use of a licensed medicine, this is shown below the indication and dose panel in the unlicensed use section.

Minimising harm and drug safety

The drug chosen to treat a particular condition should minimise the patient's susceptibility to adverse effects and, where co-morbidities exist, have minimal detrimental effects on the patient's other diseases. To achieve this, the *Contra-indications*, *Cautions* and *Side-effects* of the relevant drug should be reviewed.

The information under Cautions can be used to assess the risks of using a drug in a patient who has co-morbidities that are also included in the Cautions for that drug—if a safer alternative cannot be found, the drug may be prescribed while monitoring the patient for adverse-effects or deterioration in the co-morbidity. Contra-indications are far more restrictive than Cautions and mean that the drug should be avoided in a patient with a condition that is contra-indicated.

The impact that potential side-effects may have on a patient's quality of life should also be assessed. For instance, in a patient who has difficulty sleeping, it may be preferable to avoid a drug that frequently causes insomnia.

The *Important safety advice* section in the BNF, delineated by a coloured outline box, highlights important safety concerns, often those raised by regulatory authorities or guideline producers. Safety warnings issued by the Commission on Human Medicines (CHM) or Medicines and Healthcare products Regulatory Agency (MHRA) are found here.

Drug selection should aim to minimise drug interactions. If it is necessary to prescribe a potentially serious combination of drugs, patients should be monitored appropriately. The mechanisms underlying drug interactions are explained in Appendix 1, followed by details of drug interactions.

Use of drugs in specific patient populations

Drug selection should aim to minimise the potential for drug accumulation, adverse drug reactions, and exacerbation of pre-existing hepatic or renal disease. If it is necessary to prescribe drugs whose effect is altered by hepatic or renal disease, appropriate drug dose adjustments should be made, and patients should be monitored adequately. The general principles for prescribing are outlined under Prescribing in hepatic impairment p. 20, and Prescribing in renal impairment p. 20. Information about drugs that should be avoided or used with caution in hepatic disease or renal

Typical layout of a monograph and associated medicinal forms

❶ Class Monographs and drug monographs

In most cases, all information that relates to an individual drug is contained in its drug monograph and there is no symbol. Class monographs have been created where substantial amounts of information are common to all drugs within a drug class, these are indicated by a flag symbol in a circle:

Drug monographs with a corresponding class monograph are indicated by a tab with a flag symbol: 1234

The page number of the corresponding class monograph is indicated within the tab. For further information, see How to use BNF Publications

❷ Drug classifications

Used to inform users of the class of a drug and to assist in finding other drugs of the same class. May be based on pharmacological class (e.g. opioids) but can also be associated with the use of the drug (e.g. cough suppressants)

❸ Review date

The date of last review of the content

❹ Specific preparation name

If the dose varies with a specific preparation or formulation it appears under a heading of the preparation name

Class monograph ❶

CLASSIFICATION ❷

1234

Drug monograph ❶ ❸ 01-Jun-2016

(Synonym) another name by which a drug may be known

- DRUG ACTION how a drug exerts its effect in the body

- INDICATIONS AND DOSE

Indications are the clinical reasons a drug is used. The dose of a drug will often depend on the indications

Indication

- ROUTE
- Age groups: [Child/Adult/Elderly]
  Dose and frequency of administration (max. dose)

SPECIFIC PREPARATION NAME ❹

Indication

- ROUTE
- Age groups: [Child/Adult/Elderly]
  Dose and frequency of administration (max. dose)

DOSE ADJUSTMENTS DUE TO INTERACTIONS dosing information when used concurrently with other drugs

DOSES AT EXTREMES OF BODY-WEIGHT dosing information for patients who are overweight or underweight

DOSE EQUIVALENCE AND CONVERSION information around the bioequivalence between formulations of the same drug, or equivalent doses of drugs that are members of the same class

PHARMACOKINETICS how the body affects a drug (absorption, distribution, metabolism, and excretion)

POTENCY a measure of drug activity expressed in terms of the concentration required to produce an effect of given intensity

- UNLICENSED USE describes the use of medicines outside the terms of their UK licence (off-label use), or use of medicines that have no licence for use in the UK

IMPORTANT SAFETY INFORMATION
Information produced and disseminated by drug regulators often highlights serious risks associated with the use of a drug, and may include advice that is mandatory

- CONTRA-INDICATIONS circumstances when a drug should be avoided
- CAUTIONS details of precautions required
- INTERACTIONS when one drug changes the effects of another drug; the mechanisms underlying drug interactions are explained in Appendix 1
- SIDE-EFFECTS listed in order of frequency, where known, and arranged alphabetically
- ALLERGY AND CROSS-SENSITIVITY for drugs that carry an increased risk of hypersensitivity reactions
- CONCEPTION AND CONTRACEPTION potential for a drug to have harmful effects on an unborn child when prescribing for a woman of childbearing age or for a man trying to father a child; information on the effect of drugs on the efficacy of latex condoms or diaphragms

- **PREGNANCY** advice on the use of a drug during pregnancy
- **BREAST FEEDING** EvGr advice on the use of a drug during breast feeding Ⓐ ❺
- **HEPATIC IMPAIRMENT** advice on the use of a drug in hepatic impairment
- **RENAL IMPAIRMENT** advice on the use of a drug in renal impairment
- **PRE-TREATMENT SCREENING** covers one off tests required to assess the suitability of a patient for a particular drug
- **MONITORING REQUIREMENTS** specifies any special monitoring requirements, including information on monitoring the plasma concentration of drugs with a narrow therapeutic index
- **EFFECTS ON LABORATORY TESTS** for drugs that can interfere with the accuracy of seemingly unrelated laboratory tests
- **TREATMENT CESSATION** specifies whether further monitoring or precautions are advised when the drug is withdrawn
- **DIRECTIONS FOR ADMINISTRATION** practical information on the preparation of intravenous drug infusions; general advice relevant to other routes of administration
- **PRESCRIBING AND DISPENSING INFORMATION** practical information around how a drug can be prescribed and dispensed including details of when brand prescribing is necessary
- **HANDLING AND STORAGE** includes information on drugs that can cause adverse effects to those who handle them before they are taken by, or administered to, a patient; advice on storage conditions
- **PATIENT AND CARER ADVICE** for drugs with a special need for counselling
- **PROFESSION SPECIFIC INFORMATION** provides details of the restrictions certain professions such as dental practitioners or nurse prescribers need to be aware of when prescribing on the NHS
- **NATIONAL FUNDING/ACCESS DECISIONS** details of NICE Technology Appraisals, SMC advice and AWMSG advice
- **LESS SUITABLE FOR PRESCRIBING** preparations that are considered by the Joint Formulary Committee to be less suitable for prescribing
- **EXCEPTION TO LEGAL CATEGORY** advice and information on drugs which may be sold without a prescription under specific conditions

- **MEDICINAL FORMS**

Form

CAUTIONARY AND ADVISORY LABELS if applicable
EXCIPIENTS clinically important but not comprehensive [consult manufacturer information for full details]
ELECTROLYTES if clinically significant quantities occur

▸ **Preparation name** (Manufacturer/Non-proprietary)
Drug name and strength pack sizes PoM ❻ Prices

Combinations available this indicates a combination preparation is available and a cross reference page number is provided to locate this preparation

❺ Evidence grading

Evidence grading to reflect the strengths of recommendations will be applied as content goes through the revalidation process. A five level evidence grading system based on the former SIGN grading system has been adopted. The grades Ⓐ Ⓑ Ⓒ Ⓓ Ⓔ are displayed next to the recommendations within the text, and are preceded by the symbol: EvGr

For further information, see How BNF Publications are constructed

❻ Legal categories

PoM This symbol has been placed against those preparations that are available only on a prescription issued by an appropriate practitioner. For more detailed information see *Medicines, Ethics and Practice*, London, Pharmaceutical Press (always consult latest edition)

CD1 CD2 CD3 CD4–1 CD4–2 CD5 These symbols indicate that the preparations are subject to the prescription requirements of the Misuse of Drugs Act

For regulations governing prescriptions for such preparations, see Controlled Drugs and Drug Dependence

Not all monographs include all possible sections; sections are only included when relevant information has been identified

impairment can be found in drug monographs under *Hepatic impairment* and *Renal impairment* (e.g. fluconazole p. 614).

Similarly, drug selection should aim to minimise harm to the fetus, nursing infant, and mother. The infant should be monitored for potential side-effects of drugs used by the *mother during pregnancy or breast-feeding*. The general principles for prescribing are outlined under Prescribing in pregnancy p. 24 and Prescribing in breast-feeding p. 24. The Treatment Summaries provide guidance on the drug treatment of common conditions that can occur during pregnancy and breast-feeding (e.g. Asthma, acute p. 247). Information about the use of specific drugs during pregnancy and breast-feeding can be found in their drug monographs under *Pregnancy*, and *Breast-feeding* (e.g. fluconazole p. 614).

A section, *Conception and contraception*, containing information around considerations for females of childbearing potential or men who might father a child (e.g. isotretinoin p. 1308) has been included.

Administration and monitoring

When selecting the most appropriate drug, it may be necessary to screen the patient for certain genetic markers or metabolic states. This information is included within a section called *Pre-treatment screening* (e.g. abacavir p. 666). This section covers one-off tests required to assess the suitability of a patient for a particular drug.

Once the drug has been selected, it needs to be given in the most appropriate manner. A *Directions for administration* section contains the information about intravenous administration previously located in Appendix 4. This provides practical information on the preparation of intravenous drug infusions, including compatibility of drugs with standard intravenous infusion fluids, method of dilution or reconstitution, and administration rates. In addition, general advice relevant to other routes of administration is provided within this section (e.g. fentanyl p. 470).

After selecting and administering the most appropriate drug by the most appropriate route, patients should be monitored to ensure they are achieving the expected benefits from drug treatment without any unwanted side-effects. The *Monitoring* section specifies any special monitoring requirements, including information on monitoring the plasma concentration of drugs with a narrow therapeutic index (e.g. theophylline p. 281). Monitoring may, in certain cases, be affected by the impact of a drug on laboratory tests (e.g. hydroxocobalamin p. 1061), and this information is included in *Effects on laboratory tests*.

In some cases, when a drug is withdrawn, further monitoring or precautions may be advised (e.g. clonidine hydrochloride p. 150): these are covered under *Treatment cessation*.

Choice and supply

The prescriber and the patient should agree on the health outcomes that the patient desires and on the strategy for achieving them (see *Taking Medicines to Best Effect*). Taking the time to explain to the patient (and carers) the rationale and the potential adverse effects of treatment may improve adherence. For some medicines there is a special need for counselling (e.g. appropriate posture during administration of doxycycline p. 582); this is shown in *Patient and carer advice*.

Other information contained in the latter half of the monograph also helps prescribers and those dispensing medicines choose medicinal forms (by indicating information such as flavour or when branded products may not be interchangeable (e.g. diltiazem hydrochloride p. 163), assess the suitability of a drug for prescribing, understand the NHS funding status for a drug (e.g. sildenafil p. 840), or assess when a patient may be able to purchase a drug without prescription (e.g. loperamide hydrochloride p. 67).

Medicinal forms

In the BNF, preparations follow immediately after the monograph for the drug that is their main ingredient.

In earlier editions, when a particular preparation had safety information, dose advice or other clinical information specific to the product, it was contained within the preparations section. This information has been moved to the relevant section in the main body of the monograph under a heading of the name of the specific medicinal form (e.g. peppermint oil p. 48).

The medicinal forms (formerly preparations) section provides information on the type of formulation (e.g. tablet), the amount of active drug in a solid dosage form, and the concentration of active drug in a liquid dosage form. The legal status is shown for prescription-only medicines and controlled drugs, as well as pharmacy medicines and medicines on the general sales list. Practitioners are reminded, by a statement under the heading of "Medicinal Forms" that not all products containing a specific drug ingredient may be similarly licensed. To be clear on the precise licensing status of specific medicinal forms, practitioners should check the product literature for the particular product being prescribed or dispensed.

Details of all medicinal forms available on the dm+d for each drug in BNF Publications appears online on MedicinesComplete. In print editions, due to space constraints, only certain branded products are included in detail. Where medicinal forms are listed they should not be inferred as equivalent to the other brands listed under the same form heading. For example, all the products listed under a heading of "Modified release capsule" will be available as modified release capsules, however, the brands listed under that form heading may have different release profiles, the available strengths may vary and/or the products may have different licensing information. As with earlier editions of the BNF, practitioners must ensure that the particular product being prescribed or dispensed is appropriate.

As medicinal forms are derived from dm+d data, some drugs may appear under names derived from that data; this may vary slightly from those in previous BNF versions, e.g. sodium acid phosphate, is now sodium dihydrogen phosphate anhydrous.

Patients should be prescribed a preparation that complements their daily routine, and that provides the right dose of drug for the right indication and route of administration. When dispensing liquid preparations, a sugar-free preparation should always be used in preference to one containing sugar. Patients receiving medicines containing cariogenic sugars should be advised of appropriate dental hygiene measures to prevent caries.

In earlier editions, the BNF only included excipients and electrolyte information for proprietary medicines. This information is now covered at the level of the dose form (e.g. tablet). It is not possible to keep abreast of all of the generic products available on the UK market, and so this information serves as a reminder to the healthcare professional that, if the presence of a particular excipient is of concern, they should check the product literature for the particular product being prescribed or dispensed.

Cautionary and advisory labels that pharmacists are recommended to add when dispensing are included in the medicinal forms section. Details of these labels can be found in Appendix 3, Guidance for cautionary and advisory labels p. 1637. As these labels have now been applied at the level of the dose form, a full list of medicinal products with their relevant labels would be extensive. This list has therefore been removed, but the information is retained within the monograph.

In the case of compound preparations, the prescribing information for all constituents should be taken into account.

Prices in the BNF

Basic NHS **net prices** are given in the BNF to provide an indication of relative cost. Where there is a choice of suitable preparations for a particular disease or condition the relative cost may be used in making a selection. Cost-effective prescribing must, however, take into account other factors (such as dose frequency and duration of treatment) that affect the total cost. The use of more expensive drugs is justified if it will result in better treatment of the patient, or a reduction of the length of an illness, or the time spent in hospital.

Prices are regularly updated using the Drug Tariff and proprietary price information published by the NHS dictionary of medicines and devices (dm+d, www.nhsbsa.nhs.uk/pharmacies-gp-practices-and-appliance-contractors/dictionary-medicines-and-devices-dmd). The weekly updated dm+d data (including prices) can be accessed using the dm+d browser of the NHS Business Services Authority (apps.nhsbsa.nhs.uk/DMDBrowser/DMDBrowser.do). Prices have been calculated from the net cost used in pricing NHS prescriptions and generally reflect whole dispensing packs. Prices for extemporaneously prepared preparations are not provided in the BNF as prices vary between different manufacturers. In Appendix 4, prices stated are per dressing or bandage.

BNF prices are not suitable for quoting to patients seeking private prescriptions or contemplating over-the-counter purchases because they do not take into account VAT, professional fees, and other overheads.

A fuller explanation of costs to the NHS may be obtained from the Drug Tariff. Separate drug tariffs are applicable to England and Wales (www.ppa.org.uk/ppa/edt_intro.htm), Scotland (www.isdscotland.org/Health-Topics/Prescribing-and-Medicines/Scottish-Drug-Tariff/), and Northern Ireland (www.hscbusiness.hscni.net/services/2034.htm); prices in the different tariffs may vary.

Drug class monographs

In earlier editions of the BNF, information relating to a class of drugs sharing the same properties (e.g. tetracyclines p. 581), was contained within the prescribing notes. In the updated structure, drug class monographs have been created to contain the common information; this ensures such information is easier to find, and has a more regularised structure.

For consistency and ease of use, the class monograph follows the same structure as a drug monograph. Class monographs are indicated by the presence of a flag (e.g. beta-adrenoceptor blockers (systemic) p. 153). If a drug monograph has a corresponding class monograph, that needs to be considered in tandem, in order to understand the full information about a drug, the monograph is also indicated by a flag 1234 (e.g. metoprolol tartrate p. 160). Within this flag, the page number of the drug class monograph is provided (e.g. 1234), to help navigate the user to this information. This is particularly useful where occasionally, due to differences in therapeutic use, the drug monograph may not directly follow the drug class monograph (e.g. sotalol hydrochloride p. 111).

Evidence grading

The BNF has adopted a five level evidence grading system (see How BNF Publications are constructed p. viii). Recommendations that are evidence graded can be identified by a symbol appearing immediately before the recommendation. The evidence grade is displayed at the end of the recommendation.

Other content

Nutrition

Appendix 2, Borderline substances p. 1606, includes tables of ACBS-approved enteral feeds and nutritional supplements based on their energy and protein content. There are separate tables for specialised formulae for specific clinical conditions. Classified sections on foods for special diets and nutritional supplements for metabolic diseases are also included.

Wound dressings

A table on wound dressings in Appendix 4, Wound management products and elasticated garments p. 1640, allows an appropriate dressing to be selected based on the appearance and condition of the wound. Further information about the dressing can be found by following the cross-reference to the relevant classified section in the Appendix.

Advanced wound contact dressings have been classified in order of increasing absorbency.

Other useful information

Finding significant changes in the BNF

- ***Changes***, provides a list of significant changes, dose changes, classification changes, new names, and new preparations that have been incorporated into the BNF, as well as a list of preparations that have been discontinued and removed from the BNF. Changes listed online are cumulative (from one print edition to the next), and can be printed off each month to show the main changes since the last print edition as an aide memoire for those using print copies. So many changes are made for each update of the BNF, that not all of them can be accommodated in the *Changes* section. We encourage healthcare professionals to regularly review the prescribing information on drugs that they encounter frequently;
- ***Changes to the Dental Practioners' Formulary***, are located at the end of the Dental List;
- ***E-newsletter***, the BNF & BNFC e-newsletter service is available free of charge. It alerts healthcare professionals to details of significant changes in the clinical content of these publications and to the way that this information is delivered. Newsletters also review clinical case studies, provide tips on using these publications effectively, and highlight forthcoming changes to the publications. To sign up for e-newsletters go to www.bnf.org.
- An e-learning programme developed in collaboration with the Centre for Pharmacy Postgraduate Education (CPPE), enables pharmacists to identify and assess how significant changes in the BNF affect their clinical practice. The module can be found at www.cppe.ac.uk.

Using other sources for medicines information

The BNF is designed as a digest for rapid reference. Less detail is given on areas such as obstetrics, malignant disease, and anaesthesia since it is expected that those undertaking treatment will have specialist knowledge and access to specialist literature. *BNF for Children* should be consulted for detailed information on the use of medicines in children. The BNF should be interpreted in the light of professional knowledge and supplemented as necessary by specialised publications and by reference to the product literature. Information is also available from medicines information services.

Changes

Monthly updates are provided online via Medicines Complete and the NHS Evidence portal. The changes listed below are cumulative (from one print edition to the next).

Significant changes

Significant changes that appear in the print edition of BNF 79 (March — September 2020):

- Abemaciclib p. 997 with fulvestrant p. 983 for treating hormone receptor-positive, HER2-negative advanced breast cancer after endocrine therapy [NICE guidance].
- Adrenaline/epinephrine auto-injectors p. 229: recent action taken to support safety [MHRA/CHM advice].
- Alemtuzumab p. 884 (*Lemtrada*®) and serious cardiovascular and immune-mediated adverse reactions: new restrictions to use and strengthened monitoring requirements [MHRA/CHM advice].
- Ambrisentan p. 190 (*Volibris*®): patient alert card available [MHRA/CHM advice].
- Asthma, acute p. 247: updated guidance on management.
- Asthma, chronic p. 244: updated guidance on management.
- Atezolizumab p. 887 in combination for treating metastatic non-squamous non-small-cell lung cancer [NICE guidance].
- Bacillus Calmette-Guérin vaccine p. 1336: updated guidance in-line with Public Health England recommendations.
- Benralizumab p. 273 for treating severe eosinophilic asthma (updated advice) [NICE guidance].
- Blinatumomab p. 891 for treating acute lymphoblastic leukaemia in remission with minimal residual disease activity [NICE guidance].
- Botulinum toxin type A p. 417 for treating chronic sialorrhea [NICE guidance].
- Carfilzomib p. 996 (*Kyprolis*®): reminder of risk of potentially fatal cardiac events [MHRA/CHM advice].
- Carfilzomib p. 996 (*Kyprolis*®): risk of reactivation of hepatitis B virus [MHRA/CHM advice].
- Cemiplimab p. 893 for treating metastatic or locally advanced cutaneous squamous cell carcinoma [NICE guidance].
- Cerebral palsy and spasticity p. 415: inclusion of overview.
- Chronic obstructive pulmonary disease p. 249: updated guidance on management.
- Contraceptives, hormonal p. 816: updated guidance on combined hormonal contraceptives.
- Crohn's disease p. 38: updated guidance on management.
- Dacomitinib p. 1008 for untreated EGFR mutation-positive non-small-cell lung cancer [NICE guidance].
- Dapagliflozin p. 725 with insulin for treating type 1 diabetes [NICE guidance].
- Daratumumab p. 895 (*Darzalex*®): risk of reactivation of hepatitis B virus [MHRA/CHM advice].
- Direct-acting oral anticoagulants (DOACs) (apixaban p. 129, dabigatran etexilate p. 141, edoxaban p. 130, and rivaroxaban p. 132): increased risk of recurrent thrombotic events in patients with antiphospholipid syndrome [MHRA/CHM advice].
- Durvalumab p. 897 for treating locally advanced unresectable non-small-cell lung cancer after platinum-based chemoradiation [NICE guidance].
- Dyspepsia p. 68, Gastro-oesophageal reflux disease p. 84, and Peptic ulcer disease p. 72: updated guidance and dosing regimens.
- Enzalutamide p. 977 for hormone-relapsed non-metastatic prostate cancer [NICE guidance].
- Ertugliflozin p. 729 with metformin and a dipeptidyl peptidase-4 inhibitor for treating type 2 diabetes [NICE guidance].
- Febuxostat p. 1158 (*Adenuric*®): increased risk of cardiovascular death and all-cause mortality in clinical trial in patients with a history of major cardiovascular disease [MHRA/CHM advice].
- Fingolimod p. 881 (*Gilenya*®): increased risk of congenital malformations; new contra-indication during pregnancy and in women of childbearing potential not using effective contraception [MHRA/CHM advice].
- Fluocinolone acetonide p. 1228 intravitreal implant for treating chronic diabetic macular oedema in phakic eyes after an inadequate response to previous therapy [NICE guidance].
- Fluocinolone acetonide p. 1228 intravitreal implant for treating recurrent non-infectious uveitis [NICE guidance].
- GLP-1 receptor agonists (dulaglutide p. 718, exenatide p. 719, liraglutide p. 720 (*Victoza*®), lixisenatide p. 721, and semaglutide p. 721): reports of diabetic ketoacidosis when concomitant insulin was rapidly reduced or discontinued [MHRA/CHM advice].
- Helicobacter pylori infection p. 85: updated guidance and dosing regimens.
- Hormone replacement therapy (HRT) (conjugated oestrogens (equine) p. 778 and estradiol p. 780): further information on the known increased risk of breast cancer with HRT and its persistence after stopping [MHRA/CHM advice].
- Human papillomavirus vaccine p. 1340 updated guidance in-line with Public Health England recommendations.
- Hyperparathyroidism p. 1080: New guidance on management of primary hyperparathyroidism.
- Hypertension p. 146: updated guidance on management of hypertension in pregnancy.
- Idelalisib p. 1017 for treating refractory follicular lymphoma [NICE guidance].
- Ingenol mebutate p. 1321 gel (*Picato*®): increased incidence of skin tumours seen in some clinical studies [MHRA/CHM advice].
- Immunisation schedule p. 1335: updated national human papillomavirus immunisation programme in-line with Public Health England recommendations.
- Inotersen p. 419 for treating hereditary transthyretin amyloidosis [NICE guidance].
- Lanadelumab p. 298 for preventing recurrent attacks of hereditary angioedema [NICE guidance].
- Lenalidomide p. 989 for the treatment of multiple myeloma in people who have received at least 2 prior therapies [NICE guidance].
- Lenalidomide p. 989 for treating myelodysplastic syndromes associated with an isolated deletion 5q cytogenetic abnormality [NICE guidance].
- Lenalidomide p. 989 plus dexamethasone for multiple myeloma after 1 treatment with bortezomib [NICE guidance].
- Lenalidomide p. 989 plus dexamethasone for previously untreated multiple myeloma [NICE guidance].
- Letermovir p. 659 for preventing cytomegalovirus disease after a stem cell transplant [NICE guidance].
- Magnesium sulfate p. 1088: risk of skeletal adverse effects in the neonate following prolonged or repeated use in pregnancy [MHRA/CHM advice].
- Migraine p. 486: updated guidance on management.
- Mitomycin p. 948 (*Mitomycin-C Kyowa*®40 mg): restricted to intravesical administration only for treatment of superficial bladder cancer [MHRA/CHM advice].
- Montelukast p. 276 (*Singulair*®): reminder of the risk of neuropsychiatric reactions [MHRA/CHM advice].
- Naltrexone with bupropion p. 94 (*Mysimba*®): risk of adverse reactions that could affect ability to drive [MHRA/CHM advice].

- Neratinib p. 1024 for extended adjuvant treatment of hormone receptor-positive, HER2-positive early stage breast cancer after adjuvant trastuzumab [NICE guidance].
- Nivolumab p. 902 (*Opdivo*®): reports of cytomegalovirus (CMV) gastrointestinal infection or reactivation [MHRA/CHM advice].
- Nivolumab p. 902 with ipilimumab p. 900 for untreated advanced renal cell carcinoma [NICE guidance].
- Nusinersen p. 1161 for treating spinal muscular atrophy.
- Ocrelizumab p. 886 for treating primary progressive multiple sclerosis [NICE guidance].
- Olaparib p. 1040 for maintenance treatment of BRCA mutation-positive advanced ovarian, fallopian tube or peritoneal cancer after response to first-line platinum-based chemotherapy [NICE guidance].
- Olaratumab (*Lartruvo*®): withdrawal of the EU marketing authorisation due to lack of efficacy [MHRA/CHM advice].
- Oral retinoid medicines (acitretin p. 1299, alitretinoin p. 1300, bexarotene p. 968, isotretinoin p. 1308, and tretinoin p. 969): revised and simplified pregnancy prevention educational materials for healthcare professionals and women [MHRA/CHM advice].
- Patisiran p. 420 for treating hereditary transthyretin amyloidosis [NICE guidance].
- Pembrolizumab p. 907 with carboplatin and paclitaxel for untreated metastatic squamous non-small-cell lung cancer [NICE guidance].
- Pentosan polysulfate sodium p. 814 (*Elmiron*®): rare risk of pigmentary maculopathy [MHRA/CHM advice].
- Pentosan polysulfate sodium p. 814 (*Elmiron*®): risk of pigmentary maculopathy [MHRA/CHM advice].
- Pentosan polysulfate sodium p. 814 for treating bladder pain syndrome [NICE guidance].
- Prescribing in renal impairment p. 20: using the appropriate estimate of renal function to avoid the risk of adverse drug reactions [MHRA/CHM advice].
- Prostate Cancer p. 975: updated guidance on management.
- Respiratory system infections, antibacterial therapy p. 529: updated guidance for community-acquired pneumonia.
- Respiratory system infections, antibacterial therapy p. 529: updated guidance for hospital-acquired pneumonia.
- Ribociclib p. 1032 with fulvestrant for treating hormone receptor-positive, HER2-negative, advanced breast cancer [NICE guidance].
- Risankizumab p. 1297 for treating moderate to severe plaque psoriasis [NICE guidance].
- Rivaroxaban p. 132 for preventing atherothrombotic events in people with coronary or peripheral artery disease [NICE guidance].
- Rivaroxaban p. 132 (*Xarelto*®): reminder that 15 mg and 20 mg tablets should be taken with food [MHRA/CHM advice].
- Rotavirus vaccine p. 1346: updated guidance in-line with Public Health England recommendations.
- Rucaparib p. 1042 for maintenance treatment of relapsed platinum-sensitive ovarian, fallopian tube or peritoneal cancer [NICE guidance].
- Tofacitinib p. 1142 (*Xeljanz*®): restriction of 10 mg twice daily dose in patients at high risk of pulmonary embolism while safety review is ongoing [MHRA/CHM advice].
- Sodium zirconium cyclosilicate p. 1093 for treating hyperkalaemia [NICE guidance].
- Stroke p. 121: updated guidance on management.
- Tocilizumab p. 1137 (*RoActemra*®): rare risk of serious liver injury including cases requiring transplantation [MHRA/CHM advice].
- Typhoid vaccine p. 1347: updated guidance in-line with Public Health England recommendations.
- Ulcerative colitis p. 39: updated guidance on management.
- Urinary incontinence and pelvic organ prolapse in women p. 801: updated guidance on management.
- Urinary-tract infections p. 606: updated guidance on management.
- Vedolizumab p. 46 for treating moderately to severely active ulcerative colitis [NICE guidance].
- Yellow fever vaccine, live p. 1367: stronger precautions in people with weakened immunity and in those aged 60 years or older [MHRA/CHM advice].

Dose changes

Changes in dose statements that appear in the print edition of BNF 79 (March — September 2020):

- Emicizumab p. 114 [alternative dosing for existing indications added].
- *Epipen*®preparations (adrenaline/epinephrine p. 229) [body-weight ranges for children's dosing updated].
- Human papillomavirus vaccines p. 1361 [dosing now includes male patients].
- Magnesium sulfate p. 1088 [change to additional dose for seizure recurrence in pre-eclampsia and eclampsia].
- Pembrolizumab p. 907 [alternative dosing for monotherapy indications added].
- *Syner-KINASE*® (urokinase p. 143) [clarification of the intravenous infusion dosage units for the follow-on treatment of pulmonary embolism].
- Typhoid vaccine p. 1356 [Booster dose added].
- Vitamin B substances with ascorbic acid p. 1117 [duration and route for the treatment of suspected or established Wernicke's encephalopathy, and prophylaxis of Wernicke's encephalopathy updated].

New preparations

New preparations that appear in the print edition of BNF 79 (March — September 2020):

- *Ajovy*® [fremanezumab p. 490].
- *Betesil*® [betamethasone p. 694].
- *Blissel*® [estriol p. 859].
- *Brinavess*® [vernakalant p. 111].
- *Cablivi*® [caplacizumab p. 1068].
- Cannabidiol p. 319.
- *Cuprior*® [trientine dihydrochloride p. 1107].
- *Dovato*® [lamivudine with dolutegravir p. 673].
- *Dupixent*® [dupilumab p. 1294].
- *Emgality*® [galcanezumab p. 491].
- *Gardasil* 9® [human papillomavirus vaccines p. 1361].
- *Glyxambi*® [empagliflozin with linagliptin p. 728].
- *Imvaggis*®pessary [estriol p. 859].
- *Jorveza*® [budesonide p. 45].
- Lamivudine with tenofovir disoproxil p. 673.
- *Ledaga*®gel [chlormethine p. 923].
- *Libtayo*® [cemiplimab p. 893].
- *Lokelma*® [sodium zirconium cyclosilicate p. 1093].
- *Lorviqua*® [lorlatinib p. 1022].
- *Nerlynx*® [neratinib p. 1024].
- *Nyxoid*® [naloxone hydrochloride p. 1409].
- *Ondexxya*® [andexanet alfa p. 124].
- *Onpattro*® [patisiran p. 420].
- *Pepto-Bismol*® [bismuth subsalicylate p. 73].
- *Renapime*® [cefepime p. 547].
- *Renoxitin*® [cefoxitin p. 541].
- *Rizmoic*® [naldemedine p. 65].
- *Softacort*® [hydrocortisone eye drops p. 1199].
- *Skyrizi*® [risankizumab p. 1297].
- *Takhzyro*® [lanadelumab p. 298].
- *Talzenna*® [talazoparib p. 1042].
- *Vaborem*® [meropenem with vaborbactam p. 538].
- *Vitrakvi*® [larotrectinib p. 1020].
- *Vizimpro*® [dacomitinib p. 1008].
- *Waylivra*® [volanesorsen p. 214].
- *Xospata*® [gilteritinib p. 1015].

Guidance on prescribing

General guidance

Medicines should be prescribed only when they are necessary, and in all cases the benefit of administering the medicine should be considered in relation to the risk involved. This is particularly important during pregnancy, when the risk to both mother and fetus must be considered. It is important to discuss treatment options carefully with the patient to ensure that the patient is content to take the medicine as prescribed. In particular, the patient should be helped to distinguish the adverse effects of prescribed drugs from the effects of the medical disorder. When the beneficial effects of the medicine are likely to be delayed, the patient should be advised of this.

Never Events Never events are serious and avoidable medical errors for which there should be preventative measures in place to stop their occurrence.
The NHS Never Events policy and framework can be viewed at: improvement.nhs.uk/documents/2265/Revised_Never_Events_policy_and_framework_FINAL.pdf.
For never events related to single drugs or drug classes, BNF Publications contain information within the monographs, in the important safety information section.

Prescribing competency framework The Royal Pharmaceutical Society has published a Prescribing Competency Framework that includes a common set of competencies that form the basis for prescribing, regardless of professional background. The competencies have been developed to help healthcare professionals to be safe and effective prescribers, with the aim of supporting patients to get the best outcomes from their medicines. It is available at www.rpharms.com/resources/frameworks/prescribers-competency-framework.

Multimorbidity

The presence of two or more long-term health conditions in a patient (multimorbidity) is associated with reduced quality of life, higher mortality, higher rates of adverse drug reactions, greater use of the health service, and a higher treatment burden (due to polypharmacy or multiple appointments). [EvGr] Treatment decisions in these patients should involve consideration of the patient's needs, preferences for treatment, health priorities, and lifestyle with the aim of improving quality of life by reducing treatment burden, adverse events, and unplanned or uncoordinated care.
Prescribers should consider the risks and benefits of treatments recommended for patients with multimorbidity from guidance for single health conditions; evidence for these recommendations is commonly drawn from patients without multimorbidity or who are taking fewer prescribed regular medicines.
Treatments intended to relieve symptoms should be reviewed for effectiveness, including reducing or stopping the treatment and monitoring the effects. Alternatively, non-pharmacological treatments may be offered or treatments of limited benefit can be considered for discontinuation. [A] The management of risk factors for future disease can be a major treatment burden for patients with multimorbidity and is not always appropriate.

Deprescribing

Deprescribing is the process of discontinuing or reducing the dose of medicines, supervised by a healthcare professional, with the aim of managing polypharmacy and improving outcomes. Deprescribing requires careful counselling and shared decision-making with patients, and is considered part of routine clinical care.

Taking medicines to best effect

Difficulties in adherence to drug treatment occur regardless of age. Factors contributing to poor compliance with prescribed medicines include:

- prescription not collected or not dispensed;
- purpose of medicine not clear;
- perceived lack of efficacy;
- real or perceived adverse effects;
- patients' perception of the risk and severity of side-effects may differ from that of the prescriber;
- instructions for administration not clear;
- physical difficulty in taking medicines (e.g. swallowing the medicine, handling small tablets, or opening medicine containers);
- unattractive formulation (e.g. unpleasant taste);
- complicated regimen.

The prescriber and the patient should agree on the health outcomes that the patient desires and on the strategy for achieving them ('concordance'). The prescriber should be sensitive to religious, cultural, and personal beliefs that can affect a patient's acceptance of medicines.
Taking the time to explain to the patient (and relatives) the rationale and the potential adverse effects of treatment may improve adherence. Reinforcement and elaboration of the physician's instructions by the pharmacist and other members of the healthcare team also helps. Advising the patient of the possibility of alternative treatments may encourage the patient to seek advice rather than merely abandon unacceptable treatment.
Simplifying the drug regimen may help; the need for frequent administration may reduce adherence, although there appears to be little difference in adherence between once-daily and twice-daily administration. Combination products reduce the number of drugs taken but at the expense of the ability to titrate individual doses.

Advanced Pharmacy Services

Advanced Services are provided as part of the NHS Community Pharmacy Contractual Framework, and include services such as the New Medicines Service and Medicines Use Review service. These services are provided by accredited community pharmacists, with the aim of targeting specific patients to help manage their medicines more effectively, improve adherence, and reduce medicines wastage.

New Medicines Service The New Medicines Service (NMS) provides education and support to patients who are newly prescribed a medicine to manage a long-term condition. The service is split into three stages; patient engagement, intervention and follow-up. As of 2018, this service is available for patients living in England who have either been prescribed a new medicine for one of the following conditions – asthma, chronic obstructive pulmonary disease (COPD), type 2 diabetes, or hypertension, or have been prescribed a new antiplatelet or anticoagulant. Patients can be offered the service by prescriber referral, or opportunistically by the community pharmacy. For further information, see: psnc.org.uk/services-commissioning/advanced-services/nms/.

Medicines Use Review The Medicines Use Review (MUR) service consists of structured adherence-centred reviews with patients on multiple medicines, particularly those receiving medicines for long-term conditions. The service is

undertaken periodically, or when there is a need to make an adherence-focused intervention due to a problem identified while providing the dispensing service.
The pharmacist providing the service is required to ensure that at least 70% of all MURs undertaken in a year are for patients who fall into one or more of the national target groups. The national target groups for MURs in England are:

- patients taking high-risk medicines (NSAIDs, anticoagulants (including low molecular weight heparin), antiplatelets, or diuretics);
- patients recently discharged from hospital who have had changes made to their medicines;
- patients prescribed certain respiratory medicines;
- patients with, or at risk of cardiovascular disease, and are regularly prescribed at least four medicines.

For further information, see: psnc.org.uk/services-commissioning/advanced-services/murs/.
Wales, Northern Ireland, and Scotland have variations on this service, including different national target groups.
In Wales, see www.cpwales.org.uk/Contract-support-and-IT/Advanced-Services/Medicines-Use-review-MUR.aspx
In Northern Ireland, see www.hscbusiness.hscni.net/services/2427.htm.
In Scotland, see www.communitypharmacyscotland.org.uk/nhs-care-services/services/chronic-medication-service/.

Biological medicines

Biological medicines are medicines that are made by or derived from a biological source using biotechnology processes, such as recombinant DNA technology. The size and complexity of biological medicines, as well as the way they are produced, may result in a degree of natural variability in molecules of the same active substance, particularly in different batches of the medicine. This variation is maintained within strict acceptable limits. Examples of biological medicines include insulins and monoclonal antibodies. EvGr Biological medicines must be prescribed by brand name and the brand name specified on the prescription should be dispensed in order to avoid inadvertent switching. Automatic substitution of brands at the point of dispensing is not appropriate for biological medicines. A

Biosimilar medicines

A **biosimilar medicine** is a biological medicine that is highly similar and clinically equivalent (in terms of quality, safety, and efficacy) to an existing biological medicine that has already been authorised in the European Union (known as the reference biological medicine or originator medicine). The active substance of a biosimilar medicine is similar, but not identical, to the originator biological medicine. Once the patent for a biological medicine has expired, a biosimilar medicine may be authorised by the European Medicines Agency (EMA). A biosimilar medicine is not the same as a generic medicine, which contains a simpler molecular structure that is identical to the originator medicine.

Therapeutic equivalence EvGr Biosimilar medicines should be considered to be therapeutically equivalent to the originator biological medicine within their authorised indications. A Biosimilar medicines are usually licensed for all the indications of the originator biological medicine, but this depends on the evidence submitted to the EMA for authorisation and must be scientifically justified on the basis of demonstrated or extrapolated equivalence.

Prescribing and dispensing The choice of whether to prescribe a biosimilar medicine or the originator biological medicine rests with the clinician in consultation with the patient. EvGr Biological medicines (including biosimilar medicines) must be prescribed by brand name and the brand name specified on the prescription should be dispensed in order to avoid inadvertent switching. Automatic substitution of brands at the point of dispensing is not appropriate for biological medicines. A

Safety monitoring Biosimilar medicines are subject to a black triangle status (▼) at the time of initial authorisation. EvGr It is important to report suspected adverse reactions using the Yellow Card Scheme (see Adverse reactions to drugs p. 13). For all biological medicines, adverse reaction reports should clearly state the brand name and the batch number of the suspected medicine. A
UK Medicines Information centres have developed a validated tool to determine potential safety issues associated with all new medicines. These 'in-use product safety assessment reports' will be published for new biosimilar medicines as they become available, see www.sps.nhs.uk/home/medicines/.

National funding/access decisions The Department of Health has confirmed that, in England, NICE can decide to apply the same remit, and the resulting technology appraisal guidance, to relevant biosimilar medicines which appear on the market subsequent to their originator biological medicine. In other circumstances, where a review of the evidence for a particular biosimilar medicine is necessary, NICE will consider producing an evidence summary (see *Evidence summary: new medicines*, www.nice.org.uk/about/what-we-do/our-programmes/nice-advice/evidence-summaries-new-medicines).

National information In England, see www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/biosimilars-statement.pdf.
In Northern Ireland, see niformulary.hscni.net/ManagedEntry/bios/Pages/default.aspx.
In Scotland, see www.scottishmedicines.org.uk/About_SMC/Policy_statements/Biosimilar_Medicines.
In Wales, see www.wales.nhs.uk/sites3/Documents/814/BIOSIMILARS-ABUHBpositionStatement%5BNov2015%5D.pdf.

Availability The following drugs are available as a biosimilar medicine:

- Adalimumab p. 1144
- Bevacizumab p. 890
- Enoxaparin sodium p. 137
- Epoetin alfa p. 1050
- Epoetin zeta p. 1052
- Etanercept p. 1149
- Filgrastim p. 1065
- Follitropin alfa p. 767
- Infliximab p. 1153
- Insulin glargine p. 739
- Insulin lispro p. 736
- Rituximab p. 911
- Somatropin p. 770
- Teriparatide p. 755
- Trastuzumab p. 914

Complementary and alternative medicine

An increasing amount of information on complementary and alternative medicine is becoming available. The scope of the BNF is restricted to the discussion of conventional medicines but reference is made to complementary treatments if they affect conventional therapy (e.g. interactions with St John's wort). Further information on herbal medicines is available at www.mhra.gov.uk.

Abbreviation of titles

In general, titles of drugs and preparations should be written in full. Unofficial abbreviations should not be used as they may be misinterpreted.

Non-proprietary titles

Where non-proprietary ('generic') titles are given, they should be used in prescribing. This will enable any suitable product to be dispensed, thereby saving delay to the patient

and sometimes expense to the health service. The only exception is where there is a demonstrable difference in clinical effect between each manufacturer's version of the formulation, making it important that the patient should always receive the same brand; in such cases, the brand name or the manufacturer should be stated. Non-proprietary titles should not be invented for the purposes of prescribing generically since this can lead to confusion, particularly in the case of compound and modified-release preparations. Titles used as headings for monographs may be used freely in the United Kingdom but in other countries may be subject to restriction.

Many of the non-proprietary titles used in this book are titles of monographs in the European Pharmacopoeia, British Pharmacopoeia, or British Pharmaceutical Codex 1973. In such cases the preparations must comply with the standard (if any) in the appropriate publication, as required by the Human Medicines Regulations 2012.

Proprietary titles

Names followed by the symbol ® are or have been used as proprietary names in the United Kingdom. These names may in general be applied only to products supplied by the owners of the trade marks.

Marketing authorisation and BNF advice

In general the *doses, indications, cautions, contra-indications,* and *side-effects* in the BNF reflect those in the manufacturers' data sheets or Summaries of Product Characteristics (SPCs) which, in turn, reflect those in the corresponding marketing authorisations (formerly known as Product Licences). The BNF does not generally include proprietary medicines that are not supported by a valid Summary of Product Characteristics or when the marketing authorisation holder has not been able to supply essential information. When a preparation is available from more than one manufacturer, the BNF reflects advice that is the most clinically relevant regardless of any variation in the marketing authorisations. Unlicensed products can be obtained from 'special-order' manufacturers or specialist importing companies.

Where an unlicensed drug is included in the BNF, this is indicated in the unlicensed use section of the drug monograph. When the BNF suggests a use that is outside the terms defined by the licence ('off-label' use), this too is indicated. Unlicensed or off-label use may be necessary if the clinical need cannot be met by licensed medicines; such use should be supported by appropriate evidence and experience.

The doses stated in the BNF are intended for general guidance and represent, unless otherwise stated, the usual range of doses that are generally regarded as being suitable for adults.

Prescribing unlicensed medicines

Prescribing medicines outside the recommendations of their marketing authorisation alters (and probably increases) the prescriber's professional responsibility and potential liability. The prescriber should be able to justify and feel competent in using such medicines, and also inform the patient or the patient's carer that the prescribed medicine is unlicensed.

Oral syringes

An **oral syringe** is supplied when oral liquid medicines are prescribed in doses other than multiples of 5 mL. The oral syringe is marked in 0.5 mL divisions from 1 to 5 mL to measure doses of less than 5 mL (other sizes of oral syringe may also be available). It is provided with an adaptor and an instruction leaflet. The 5–*mL spoon* is used for doses of 5 mL (or multiples thereof).

Important To avoid inadvertent intravenous administration of oral liquid medicines, only an appropriate oral or enteral syringe should be used to measure an oral liquid medicine (if a medicine spoon or graduated measure cannot be used); these syringes should not be compatible with intravenous or other parenteral devices. Oral or enteral syringes should be clearly labelled 'Oral' or 'Enteral' in a large font size; it is the healthcare practitioner's responsibility to label the syringe with this information if the manufacturer has not done so.

Excipients

Branded oral liquid preparations that do not contain *fructose, glucose,* or *sucrose* are described as 'sugar-free' in the BNF. Preparations containing hydrogenated glucose syrup, mannitol, maltitol, sorbitol, or xylitol are also marked 'sugar-free' since there is evidence that they do not cause dental caries. Patients receiving medicines containing cariogenic sugars should be advised of appropriate dental hygiene measures to prevent caries. Sugar-free preparations should be used whenever possible.

Where information on the presence of *aspartame, gluten, sulfites, tartrazine, arachis (peanut) oil* or *sesame oil* is available, this is indicated in the BNF against the relevant preparation.

Information is provided on selected excipients in skin preparations, in vaccines, and on *selected preservatives* and *excipients* in eye drops and injections.

The presence of *benzyl alcohol* and *polyoxyl castor oil* (polyethoxylated castor oil) in injections is indicated in the BNF. Benzyl alcohol has been associated with a fatal toxic syndrome in preterm neonates, and therefore, parenteral preparations containing the preservative should not be used in neonates. Polyoxyl castor oils, used as vehicles in intravenous injections, have been associated with severe anaphylactoid reactions.

The presence of *propylene glycol* in oral or parenteral medicines is indicated in the BNF; it can cause adverse effects if its elimination is impaired, e.g. in renal failure, in neonates and young children, and in slow metabolisers of the substance. It may interact with disulfiram p. 509 and metronidazole p. 559.

The *lactose* content in most medicines is too small to cause problems in most lactose-intolerant patients. However in severe lactose intolerance, the lactose content should be determined before prescribing. The amount of lactose varies according to manufacturer, product, formulation, and strength.

Important In the absence of information on excipients in the BNF and in the product literature (available at www.medicines.org.uk/emc), contact the manufacturer (see Index of Manufacturers) if it is essential to check details.

Extemporaneous preparation

A product should be dispensed extemporaneously only when no product with a marketing authorisation is available.

The BP direction that a preparation must be *freshly prepared* indicates that it must be made not more than 24 hours before it is issued for use. The direction that a preparation should be *recently prepared* indicates that deterioration is likely if the preparation is stored for longer than about 4 weeks at 15–25° C.

The term **water** used without qualification means either potable water freshly drawn direct from the public supply and suitable for drinking or freshly boiled and cooled purified water. The latter should be used if the public supply is from a local storage tank or if the potable water is unsuitable for a particular preparation (Water for injections).

Drugs and driving

Prescribers and other healthcare professionals should advise patients if treatment is likely to affect their ability to perform skilled tasks (e.g. driving). This applies especially to drugs

with sedative effects; patients should be warned that these effects are increased by alcohol. General information about a patient's fitness to drive is available from the Driver and Vehicle Licensing Agency at www.dvla.gov.uk.
A new offence of driving, attempting to drive, or being in charge of a vehicle, with certain specified controlled drugs in excess of specified limits, came into force on 2nd March 2015. This offence is an addition to the existing rules on drug impaired driving and fitness to drive, and applies to two groups of drugs—commonly abused drugs, including amfetamines, cannabis, cocaine, and ketamine p. 1385, and drugs used mainly for medical reasons, such as opioids and benzodiazepines. Anyone found to have any of the drugs (including related drugs, for example, apomorphine hydrochloride p. 430) above specified limits in their blood will be guilty of an offence, whether their driving was impaired or not. This also includes prescribed drugs which metabolise to those included in the offence, for example, selegiline hydrochloride p. 439. However, the legislation provides a statutory "medical defence" for patients taking drugs for medical reasons in accordance with instructions, *if their driving was not impaired*—it continues to be an offence to drive if actually impaired. Patients should therefore be advised to continue taking their medicines as prescribed, and when driving, to carry suitable evidence that the drug was prescribed, or sold, to treat a medical or dental problem, and that it was taken according to the instructions given by the prescriber, or information provided with the medicine (e.g. a repeat prescription form or the medicine's patient information leaflet). Further information is available from the Department for Transport at www.gov.uk/government/collections/drug-driving.

Patents

In the BNF, certain drugs have been included notwithstanding the existence of actual or potential patent rights. In so far as such substances are protected by Letters Patent, their inclusion in this Formulary neither conveys, nor implies, licence to manufacture.

Health and safety

When handling chemical or biological materials particular attention should be given to the possibility of allergy, fire, explosion, radiation, or poisoning. Substances such as corticosteroids, some antimicrobials, phenothiazines, and many cytotoxics, are irritant or very potent and should be handled with caution. Contact with the skin and inhalation of dust should be avoided.

Safety in the home

Patients must be warned to keep all medicines out of the reach of children. All solid dose and all oral and external liquid preparations must be dispensed in a reclosable *child-resistant container* unless:

- the medicine is in an original pack or patient pack such as to make this inadvisable;
- the patient will have difficulty in opening a child-resistant container;
- a specific request is made that the product shall not be dispensed in a child-resistant container;
- no suitable child-resistant container exists for a particular liquid preparation.

All patients should be advised to dispose of *unwanted medicines* by returning them to a supplier for destruction.

Labelling of prescribed medicines

There is a legal requirement for the following to appear on the label of any prescribed medicine:

- name of the patient;
- name and address of the supplying pharmacy;
- date of dispensing;
- name of the medicine;
- directions for use of the medicine;
- precautions relating to the use of the medicine.

The Royal Pharmaceutical Society recommends that the following also appears on the label:

- the words 'Keep out of the sight and reach of children';
- where applicable, the words 'Use this medicine only on your skin'.

A pharmacist can exercise professional skill and judgement to amend or include more appropriate wording for the name of the medicine, the directions for use, or the precautions relating to the use of the medicine.

Non-proprietary names of compound preparations

Non-proprietary names of **compound preparations** which appear in the BNF are those that have been compiled by the British Pharmacopoeia Commission or another recognised body; whenever possible they reflect the names of the active ingredients.
Prescribers should avoid creating their own compound names for the purposes of generic prescribing; such names do not have an approved definition and can be misinterpreted.
Special care should be taken to avoid errors when prescribing compound preparations; in particular the hyphen in the prefix 'co-' should be retained.
Special care should also be taken to avoid creating generic names for **modified-release** preparations where the use of these names could lead to confusion between formulations with different lengths of action.

EEA and Swiss prescriptions

Pharmacists can dispense prescriptions issued by doctors and dentists from the European Economic Area (EEA) or Switzerland (except prescriptions for controlled drugs in Schedules 1, 2, or 3, or for drugs without a UK marketing authorisation). Prescriptions should be written in ink or otherwise so as to be indelible, should be dated, should state the name of the patient, should state the address of the prescriber, should contain particulars indicating whether the prescriber is a doctor or dentist, and should be signed by the prescriber.

Security and validity of prescriptions

The Councils of the British Medical Association and the Royal Pharmaceutical Society have issued a joint statement on the security and validity of prescriptions.
In particular, prescription forms should:

- not be left unattended at reception desks;
- not be left in a car where they may be visible; and
- when not in use, be kept in a locked drawer within the surgery and at home.

Where there is any doubt about the authenticity of a prescription, the pharmacist should contact the prescriber. If this is done by telephone, the number should be obtained from the directory rather than relying on the information on the prescription form, which may be false.

Patient group direction (PGD)

In most cases, the most appropriate clinical care will be provided on an individual basis by a prescriber to a specific individual patient. However, a Patient Group Direction for supply and administration of medicines by other healthcare professionals can be used where it would benefit patient care without compromising safety.
A Patient Group Direction is a written direction relating to the supply and administration (or administration only) of a licensed prescription-only medicine (including some Controlled Drugs in specific circumstances) by certain classes of healthcare professionals; the Direction is signed by a doctor (or dentist) and by a pharmacist. Further

information on Patient Group Directions is available in Health Service Circular HSC 2000/026 (England), HDL (2001) 7 (Scotland), and WHC (2000) 116 (Wales); see also the Human Medicines Regulations 2012.

NICE, Scottish Medicines Consortium and All Wales Medicines Strategy Group

Advice issued by the National Institute for Health and Care Excellence (NICE), the Scottish Medicines Consortium (SMC) and the All Wales Medicines Strategy Group (AWMSG) is included in the BNF when relevant. Details of the advice together with updates can be obtained from: www.nice.org.uk, www.scottishmedicines.org.uk and www.awmsg.org.