



BNF

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September 2016

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 2867
Ipswich:	(01473) 704 431
Leeds:	(0113) 206 5377
Leicester:	(0116) 255 5779/258 6491
Liverpool:	(0151) 794 8113/4/5/7, or (0151) 795 8206
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) 9063 2032, or (028) 9063 3847
Republic of Ireland	
Dublin:	(Dublin) 473 0589, or (Dublin) 453 7941 Extn 2348

United Kingdom Medicines Information Pharmacists Group (UKMIPG) website

www.ukmi.nhs.uk

Telephone numbers and email addresses of manufacturers listed in BNF Publications are shown in Index of Proprietary Manufacturers

UK Teratology Information Service

Information on drug and chemical exposures in pregnancy.

Tel: 0344 892 0909

UK Drugs in Lactation Advisory Service (UKDILAS)

Information on the compatibility of drugs with breastfeeding.

Tel: (0116) 258 6491, or (0121) 424 7298

www.ukmi.nhs.uk/ukdilas

Information on drug therapy relating to dental treatment can be obtained by telephoning

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

Patient Information Lines

NHS Urgent Care Services 111

Poisons Information Services

UK National Poisons Information Service 0844 892 0111

Sport

- ▶ Information on substances currently permitted or prohibited is provided in a card supplied by UK Anti-doping.
- ▶ Further information regarding medicines in sport is available from: www.ukad.org.uk
Tel: (020) 7766 7350
information@ukad.org.uk

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 (09.00–12.00 and 14.00–16.30 hours weekdays)
- ▶ Travel Medicine Team, Health Protection Scotland (0141) 300 1130 (14.00–16.00 hours weekdays) www.travax.nhs.uk (for registered users of the NHS website Travax only)
- ▶ Welsh Government Switchboard English language 0300 0603300 (09.00–17.30 hours weekdays only)
- ▶ Welsh Government Switchboard Yr Iaith Gymraeg 0300 0604400 (09.00–17.30 hours 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

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 prescribing advice.

You can be alerted to all the latest updates by signing up to the BNF eNewsletter at www.bnf.org/newsletter.

ONLINE



BNF on MedicinesComplete

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



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MOBILE



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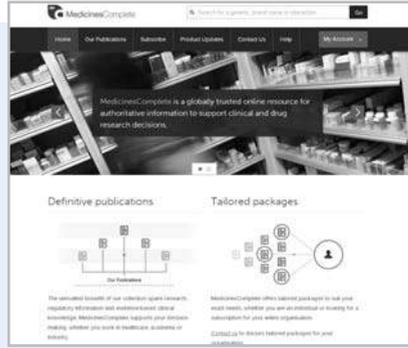
BNF eBook – Available as an ePDF via a range of suppliers. See www.pharmpress.com/bnf.

BNF on MedicinesComplete – Now mobile responsive.

PRINT



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Eligible health 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@binleys.com.

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for Children

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direct@macmillan.co.uk

For all bulk orders of more than 20 copies:

Tel: +44 (0) 207 572 2266

pharmpress@rpharms.com

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

The BNF is also available on www.evidence.nhs.uk and eligible users can download smartphone apps from the relevant app stores.

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/mpc/BritishNationalFormulary.jsp. If you are entitled to an NHS copy of BNF, please call (0) 1268 495 609 or email: bnf@binleys.com

In **Scotland**, email:

nss.psd-bnf@nhs.net

In **Wales**, contact NHS Wales Shared Services Partnership—Contractor Services:

Tel: 01792 607420

In **Northern Ireland**, email:

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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

We receive numerous requests from developing countries for copies of the BNF. The Pharmaid scheme of the Commonwealth Pharmacists Association will dispatch old BNFs to certain Commonwealth countries. For more information on this scheme see

www.commonwealthpharmacy.org/about/projects/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. *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).

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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.

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

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

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How BNF publications are constructed

The BNF is unique in bringing together authoritative, independent guidance on best practice with clinically validated drug information, enabling healthcare professionals to select safe and effective medicines for individual patients.

Information in the BNF has been validated against emerging evidence, best-practice guidelines, and advice from a network of clinical experts.

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

Joint Formulary Committee

The Joint Formulary Committee (JFC) is responsible for the content of the BNF. The JFC includes doctors appointed by the BMJ Group, pharmacists appointed by the Royal Pharmaceutical Society, 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.

Editorial Team

BNF clinical writers have all worked as pharmacists and have a sound understanding of how drugs are used in clinical practice. Each clinical writer is responsible for editing, maintaining, and updating BNF content. During the publication cycle the clinical writers review information in the BNF against a variety of sources.

Amendments to the text are drafted when the clinical writers are satisfied that any new information is reliable and relevant. The draft amendments are passed to expert advisers for comment and then presented to the Joint Formulary Committee for consideration. Additionally, sections are regularly chosen for thorough review. These planned reviews aim to verify all the information in the selected sections and to draft any amendments to reflect the current best practice.

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

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;
- advising on areas where the BNF diverges from summaries of product characteristics;

- 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 routinely received for comment and for assimilation into the BNF.

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 receives 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, despite the ever-increasing volume of information being issued by the pharmaceutical industry. 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;
- seek 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 an extra check;
- identifying potential clinical problems or omissions and seeking further information from manufacturers or from expert advisers;
- careful validation of any areas of divergence of the BNF from the SPC before discussion by the Committee (in the light of supporting evidence);
- 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.

Expert advisers

The role of expert clinical advisers in providing the appropriate clinical context for all BNF information is discussed above.

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 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.

Systematic reviews

The BNF has access to various databases of systematic reviews (including the Cochrane Library and various web-based resources). These are used for answering specific queries, for reviewing existing text, and for constructing new

text. Clinical writers receive training in critical appraisal, literature evaluation, and search strategies. Reviews published in Clinical Evidence are used to validate BNF advice.

Consensus guidelines

The advice in the BNF is checked against consensus guidelines produced by expert bodies. 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 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.

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.

The BNF reflects information from the Drug Tariff, the Scottish Drug Tariff, and the Northern Ireland Drug Tariff.

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, such as drug interactions or changes to the way information is presented in digital formats.

Overview

The BNF is an independent professional publication that is kept up-to-date and 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.

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 the previous edition of the BNF. 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.

The most notable changes to the structure of the content include:

- Drug monographs – where possible, all information that relates to a single drug is now 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. 476), 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. 14.

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 introducing, and 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 follow 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; 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 monograph 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, Beta₂-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 manufacturer's 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, 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. 1026)
- a comparison between a group or groups of drugs (e.g. beta-adrenoceptor blockers (systemic) p. 141)
- an overview of the drug management or prophylaxis of common conditions intended to facilitate rapid appraisal of options (e.g. Hypertension p. 122, or Malaria, prophylaxis p. 536).

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, 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. 396 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.

In this BNF edition, all of the information for the systemic use of a drug is contained within one monograph, so codeine phosphate p. 396 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. 459, 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 will still be 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. 55) or for drugs that are related to a class monograph (see 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.

Clinically relevant *Side-effects* for drugs are included in the monographs or class monographs. Side-effects are listed in order of frequency, where known, and arranged alphabetically. The frequency of side-effects follows the regulatory standard:

- Very common — occurs more frequently than 1 in 10 administrations of a drug
- Common — occurs between 1 in 10 and 1 in 100 administrations of a drug
- Uncommon — between 1 in 100 and 1 in 1,000 administrations of a drug
- Rare — between 1 in 1,000 and 1 in 10,000 administrations of a drug
- Very rare — occurs less than 1 in 10,000 administrations of a drug
- Frequency not known

An exhaustive list of side-effects is not included, particularly for drugs that are used by specialists (e.g. cytotoxic drugs and drugs used in anaesthesia). The BNF also omits effects that are likely to have little clinical consequence (e.g. transient increase in liver enzymes).

Recognising that hypersensitivity reactions can occur with virtually all medicines, this effect is generally not listed, unless the drug carries an increased risk of such reactions, when the information is included under *Allergy and cross sensitivity*.

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. 17, and Prescribing in renal impairment p. 17. Information about drugs that should be avoided or used with caution in hepatic disease or renal impairment can be found in drug monographs under *Hepatic impairment* and *Renal impairment* (e.g. fluconazole p. 525).

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. 19 and Prescribing in breast-feeding p. 19. The Treatment Summaries provide guidance on the drug treatment of common conditions that can occur during pregnancy and breast-feeding (e.g. Asthma p. 211). 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. 525).

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. 1076) 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. 569). 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. 399).

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. 240). Monitoring may, in certain cases, be affected by the impact of a drug on laboratory tests (e.g. hydroxocobalamin p. 854), 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. 138); 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. 506); 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. 150), assess the suitability of a drug for prescribing, understand the NHS funding status for a drug (e.g. sildenafil p. 713), or assess when a patient may be able to purchase a drug without prescription (e.g. loperamide hydrochloride p. 57).

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. 40).

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. 1321. 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.dmd.nhs.uk). The weekly updated dm+d data (including prices) can be accessed using the dm+d browser of the NHS Business Services Authority (www.ppa.org.uk/systems/pcddbrowserv2_3new/browser.jsp). 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.hsbusines.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. 505), was contained within the prescribing notes. In the updated structure, drug-class monographs have been created to contain the common informations; this ensures such information is easier to find, and has a more regularised structure.

For consistency and ease of use, the class monograph follow the same structure as a drug monograph. Class monographs are indicated by the presence of a flag  (e.g. beta-adrenoceptor blockers (systemic) p. 141). 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  (e.g. metoprolol tartrate p. 147). Where the drug monographs run on from a class monograph, no

further cross referencing is given. However, occasionally, due to differences in therapeutic use, the drug monograph may not directly follow the class monograph. In this situation the need to consider a class monograph is still indicated by a flag, but a cross reference is also provided to help navigate the user to the class monograph (e.g. sotalol hydrochloride p. 94).

Other content

Nutrition

Appendix 2, Borderline substances p. 1290, 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. 1324, 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 Practitioners' 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 MedicinesComplete and the NHS Evidence portal. The changes listed below are cumulative (from one print edition to the next).

Significant changes

Significant changes that will appear in the print edition of BNF 71 (March–September 2016):

Welsh translations are now available for each cautionary and advisory label in Appendix 3.

Proton pump inhibitors: very low risk of subacute cutaneous lupus erythematosus [MHRA advice].

Vedolizumab p. 38 for treating moderately to severely active Crohn's disease after prior therapy [NICE guidance].

Sofosbuvir with daclatasvir, sofosbuvir with ledipasvir, and simeprevir with sofosbuvir: risk of severe bradycardia and heart block when taken with amiodarone hydrochloride p. 91 [MHRA advice].

SGLT2 inhibitors (canagliflozin p. 618, dapagliflozin p. 620, empagliflozin p. 621): risk of diabetic ketoacidosis [MHRA/CHM advice].

Denosumab p. 639: osteonecrosis of the jaw—further measures to minimise risk [MHRA advice].

Intravenous bisphosphonates: osteonecrosis of the jaw—further measures to minimise risk [MHRA advice].

Intra-uterine contraception (intra-uterine contraceptive devices (copper) p. 704 and levonorgestrel p. 706): uterine perforation—updated information on risk factors [MHRA/CHM advice].

Everolimus p. 827 (*Certican*[®]) for preventing organ rejection in liver transplantation [NICE guidance].

Crizotinib p. 823: Risk of cardiac failure—updated monitoring recommendations [MHRA/CHM advice].

Vemurafenib p. 839: Risk of potentiation of radiation toxicity [MHRA/CHM advice].

Dexamethasone p. 591 (*Ozurdex*[®]) intravitreal implant for treating diabetic macular oedema [NICE guidance].

Latanoprost p. 995 (*Xalatan*[®])—increased reporting of eye irritation since reformulation [MHRA advice].

Aflibercept p. 818 for treating diabetic macular oedema [NICE guidance].

Meningococcal group B vaccine, meningococcal groups A, C, W135 and Y vaccine, and influenza vaccine added to the childhood Immunisation Schedule (Summer 2015), see Vaccines p. 1090.

Adalimumab p. 925: new indication [hidradenitis suppurativa].

Dose changes

Changes in dose statements that will appear in the print edition of BNF 71 (March–September 2016):

Avanafil p. 712

Colistimethate sodium p. 494 [*Promixin*[®]]

Insulin degludec p. 616 [licensed in children over 1 year]

Oseltamivir p. 580

Oxycodone with naloxone p. 408 [*Targinact*[®]]

Testosterone enantate p. 674

Classification changes

Classification changes made for the print edition of BNF 71 (March–September 2016):

New names

Name changes introduced in the print edition of BNF 71 (March–September 2016):

Deleted preparations

Preparations discontinued for the print edition of BNF 71 (March–September 2016):

Phenoxybenzamine injection

Piportil Depot[®]

Rythmodan[®] injection

New preparations

New preparations included in the print edition of BNF 71 (March–September 2016)

Bemfola[®] pre-filled pen [follitropin alfa p. 651]

Certican[®] [everolimus p. 827]

Duaklir Genuair[®] powder for inhalation [aclidinium bromide with formoterol p. 218]

Kengrexal[®] [cangrelor p. 184]

Levosert[®] [levonorgestrel p. 706]

Magnaspartate[®] [magnesium aspartate p. 879]

Nuwiq[®] [simoctocog alfa (factor VIII fraction, dried) p. 98]

Otezla[®] [apremilast p. 923]

Toujeo[®] [insulin glargine p. 617]

Velphoro[®] [sucroferic oxyhydroxide p. 883]