Injectable Drugs Guide

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Preface

The *Injectable Drugs Guide* provides a user-friendly, single point of reference for health-care professionals in the prescribing, preparation, administration and monitoring of injectable medicines.

The idea for such a book grew out from some of the entries in our sister book *Clinical Pharmacy Pocket Companion*, which, as well as covering many clinical topics such as electrolyte disturbances and perioperative management of medicines, also deals with a number of medicines requiring therapeutic monitoring. It became apparent that the benefits of such an approach could be rolled out to a greater number of medicines. At around the same time the UK National Patient Safety Agency issued a patient safety alert entitled 'Promoting safer use of injectable medicines' (NPSA/2007/20). This requires organisations to risk assess individual parenteral drugs and put procedures in place to allow them to be handled more safely.

The *Injectable Drugs Guide* is a handbook supporting the risk assessment process (each drug has a risk rating). It also provides a holistic approach to injectable medicines to meet the needs of the many disciplines involved in the clinical use of injectables and also those providing advice about injectable drug use.

The book comprises primarily individual drug monographs. There are a number of appendices giving further guidance on specific aspects of injectable therapy and additional clinical information (the full list of these is found on the Contents page).

In the main, cancer chemotherapy agents are not covered in the monographs. This is because there are tight controls around the use of these agents in clinical practice. Their handling in clinical settings is highly protocol driven and locality specific; use by inexperienced individuals is inappropriate.

Alistair Gray Jane Wright Vince Goodey Lynn Bruce November 2010

How to use the Injectable Drugs Guide monographs

Each monograph is presented in a format that sequences the information as needed by healthcare professionals from *contemplation* of treatment, through preparation and administration, to the monitoring that may be required during and after therapy.

Monographs are generally presented in the following order:

Drug name and form(s) of the preparation(s)

Background information about each medicine including,

- · Type of drug
- What it is used to treat (licensed and unlicensed indications and routes)
- · Additional miscellany of interest to the user
- If appropriate, how doses of the drug are usually expressed

Pre-treatment checks including,

- · Contraindications and cautions to be considered prior to use
- Any measures and/or tests that should be undertaken before commencing therapy. In some cases these tests are mandatory; in others they are dependent on the circumstances in which the drug is being used. These are listed alphabetically.
- Pregnancy and breast-feeding information has not been included except in a few special cases (standard reference sources or the advice of a Medicines Information department should be sought if this information is needed).

Dose including indication-specific information and any adjustments required in renal or hepatic impairment. Unless otherwise stated, doses are for adults (child and neonatal doses have not been included).

Routes of administration

- A series of headings outline the route(s) by which a particular drug may be given; the specifics of preparation and administration are provided for each route. In some cases the individual heading indicates the circumstances in which a particular route is appropriate.
- For drugs given by infusion, most monographs specify the quantity of infusion fluid to use. However, some monographs use the phrase 'dilute in a suitable volume of compatible infusion fluid'. In this case the prescriber should choose a volume and fluid that is appropriate to the patient's needs and clinical condition (compatibility data are given further down the monograph in the Technical Information table).

Technical information includes details of:

- Incompatibilities with fluids, other drugs by Y-site administration and also sometimes with materials
- · Compatibilities with infusion fluids and also drugs where co-administration and concentrations are likely to be used in practice. Drugs for which compatibility is concentration-specific are not included in this list. More detailed sources such as Trissel¹ should be used to clarify these.
- **pH**, particularly for drugs which are given intravenously
- **Sodium content** is stated if it is >1 mmol per likely dose; information about other significant electrolytes is given where appropriate
- · Osmolarity for the most significantly hyperosmolar products
- Excipients where allergy is a possibility or where these could have significant sideeffects in certain individuals
- Storage conditions advised for long-term and in-use storage plus, in some cases details on the significance of any change in appearance
- · Displacement value for dry powder products
- Special handling and management of spillage information if appropriate
- **Stability after preparation information.** This is *not* provided so that infusions can be prepared significantly prior to use in a clinical area, but rather to indicate how long a preparation is stable if it is not possible to administer it immediately. Stability information is also provided for reconstituted multidose vials.

Monitoring includes the measures required to ensure the medicine is used safely throughout therapy, the clinical outcome and other parameters that need consideration, e.g. certain adverse effects. The frequency of monitoring of each parameter is stated and the rationale for monitoring. In some cases the frequency is precise, e.g. 'daily', in others the frequency is not clearly defined in the literature and an individual clinician will need to decide what is reasonable. In these cases the term 'periodically' has been used.

Additional information includes

Common and serious undesirable effects including:

- Immediate adverse reactions or those that may occur shortly after administration
- Injection- or infusion-related adverse events, either due to rapid administration or those which are injection-site related
- Other adverse reactions

Pharmacokinetics in the main provides an indication of the elimination half-life of the drug, which can be useful in determining duration of effect. Some monographs provide information on other pharmacokinetic or pharmacodynamic parameters where these might be helpful.

Significant interactions drugs are grouped together under subheadings to give an indication of likely effect of the interaction. These lists are not comprehensive and more detailed sources such as Stockley's Drug Interactions² should be used if required.

Action in case of overdose gives guidance on managing therapeutic overdose of the drug and in most cases lists general supportive measures required. For the management of significant overdose an on-line source such as Toxbase³ should always be consulted. **Counselling** points are intended to provide a prompt for healthcare professionals as they speak to patients about their therapy.

Risk rating. Each medicine has been risk-assessed, considering the worst case scenario, to provide an overall risk rating based on the NPSA tool for risk assessment of individual injectable medicine products prepared in clinical areas.⁴ The assessment is displayed pictorially with icons and as a risk score. See Appendix 11 for more information on the risk rating used.

References. In general the main reference source used to assemble the information has been the manufacturer's product literature (in the UK this is the Summary of Product Characteristics or SPC) and MedicinesComplete (see below). In the main, SPCs mentioned can be accessed on-line at http://www.medicines.org.uk/EMC/. To save space references have not been included if information has been sourced from MedicinesComplete, although the SPCs used have been stated for clarity. Any other reference source used is stated in the normal way using the Vancouver system of referencing.

References

- 1. Trissel L, ed. Handbook on Injectable Drugs, 14th edn. Bethesda, MD: American Society of Health-System Pharmacists, 2007 (accessible via MedicinesComplete).
- 2. Baxter K, ed. Stockley's Drug Interactions 9 (accessible via MedicinesComplete).
- 3. Toxbase accessible at http://www.toxbase.org.
- 4. National Patient Safety Agency. Promoting safer use of injectable medicines (NPSA/2007/20) (accessible at www.npsa.nhs.uk/health/alerts).

Feedback

Feedback on any aspect of the book would be welcome via the e-mail address pharmpresseditorial@rpharms.com.

About the authors

Lynn Bruce studied pharmacy at Aston University. The first 20 years of her working life were based in secondary care variously as MI pharmacist, clinical pharmacy lead, clinical economist and latterly in various management positions. She migrated across the divide to primary care in 1997 becoming PCG and then PCT prescribing advisor. Hospital clinical pharmacy beckened her back to secondary care in 2002: she is now Pharmacy Team Leader on the Medical Assessment Unit at the Royal Blackburn Hospital.

Lynn is married and, when she's not writing pharmacy books, loves studying wildlife and travelling and is addicted to puzzles of all types.

Vince Goodey graduated in 1985 from the London School of Pharmacy, and has since worked primarily in the hospital sector in clinical and managerial roles. As a postgraduate Vince studied at the University of Manchester to attain an MSc in Pharmacy Practice in 1996.

Although hailing originally from Essex, Vince is currently Deputy Director of Pharmacy at East Lancashire Hospitals NHS Trust.

Alistair Gray is from Sunderland. He studied pharmacy at Sunderland Polytechnic, graduating in 1988 with first-class honours, and then completed his pre-registration year with Boots in Newcastle-upon-Tyne. He continued working for Boots in a variety of pharmacy and store management positions in the North West of England. In 2002 he changed disciplines and became Community Services pharmacist at Queens Park Hospital in Blackburn. He completed a Diploma in Clinical & Health Services Pharmacy at the University of Manchester in 2008 and subsequently became Clinical Services Lead Pharmacist for East Lancashire Hospitals NHS Trust in 2009 based at the now re-named Royal Blackburn Hospital.

Alistair is married with two children and loves spending time with his family. He follows Formula One motor racing closely, enjoys reading, eating out, going to the movies, playing guitar and songwriting.

Jane Wright, after working for 18 years in the Civil Service, attended the University of Manchester to study pharmacy. Jane graduated in 1994 and did her pre-registration year at the Royal Preston Hospital. For the next ten years Jane worked in Blackburn hospitals in a variety of clinical roles, her last being Clinical Services Manager with responsibility for education and training. In 1999 she obtained a Diploma in Clinical & Health Services Pharmacy at the University of Manchester. She moved to Lancashire Care NHS Foundation Trust in April 2005 where she is currently employed as Lead Pharmacist for East Lancashire.

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Abbreviations

 \uparrow increased, raised or hyper- (as in $\uparrow\!K\!=\!$ hyperkalaemia)

↓ decreased or hypo- (as in ↓K = hypokalaemia)

ABGs arterial blood gases
ABW actual bodyweight

ACE angiotensin-converting enzyme
ACS acute coronary syndromes
ACT activated clotting time

ACTH adrenocorticotrophic hormone, corticotrophin

ADH anti-diuretic hormone; vasopressin

ADR adverse drug reaction
AF atrial fibrillation

AIDS acquired immune deficiency syndrome

Alk Phos alkaline phosphatase

ALT alanine transaminase (alanine aminotransferase)

AML acute myeloid leukaemia
ANC absolute neutrophil count
ANTT aseptic non-touch technique
APTT activated partial thromboplastin time
ARDS adult respiratory distress syndrome

AST aspartate transaminase (aspartate aminotransferase)

AUC area under the curve AV atrioventricular

AZT azidothymidine (zidovudine) BAL British anti-Lewisite (dimercaprol)

BCG Bacillus Calmette–Guérin
BMD bone mineral density
BP blood pressure
bpm beats per minute

Ca calcium

CABG coronary artery bypass graft

CAPD continuous ambulatory peritoneal dialysis

L-carnitine levocarnitine

CCPD continuous cyclic peritoneal dialysis CHM Commission on Human Medicines

CHMP Committee for Medicinal Products for Human Use

CIVAS Centralised Intravenous Additive Service
CK creatine kinase, creatine phosphokinase, CPK

CKD chronic kidney disease

xviii | Abbreviations

Cl chloride

CMV cytomegalovirus CNS central nervous system

CO₂ carbon dioxide

COPD chronic obstructive pulmonary disease

CPR cardiopulmonary resuscitation

Cr creatinine

CrCl creatinine clearance
CRP C-reactive protein
CSF cerebrospinal fluid

CSII continuous subcutaneous insulin infusion
CSM Committee on Safety of Medicines

cSSTI complicated skin and soft-tissue infections

CTZ chemoreceptor trigger zone
CVA cerebrovascular accident
CVP central venous pressure

DAFNE dose adjustment for normal eating

DAS disease activity score

DIC disseminated intravascular coagulation

DKA diabetic ketoacidosis

DMARDs disease-modifying anti-rheumatic drugs

DVT deep vein thrombosis
ECG electrocardiogram
ECT electroconvulsive therapy
EFAD essential fatty acid deficiency
eGFR estimated glomerular filtration rate
EMD electromechanical dissociation

EPSE extrapyramidal side-effects (e.g. muscle shakes and tremor)

ESR erythrocyte sedimentation rate

FBC full blood count FU fluorouracil

G6PD glucose-6-phosphate dehydrogenase

GCS Glasgow Coma Scale

G-CSF granulocyte colony-stimulating factor

GFR glomerular filtration rate GGT gamma-glutamyl transpeptidase

GH growth hormone
GI gastrointestinal

Gluc glucose

GORD gastro-oesophageal reflux disease

GP glycoprotein

GVHD graft-versus-host disease HACA human anti-chimeric antibody

Hartmann's Sodium lactate intravenous infusion, compound

Hb haemoglobin

HbA1c glycosylated (glycated) haemoglobin

HBV hepatitis B virus

HCG human chorionic gonadotrophin

HCO₃ bicarbonate

HDL high-density lipoprotein

HHS hyperosmolar hyperglycaemic state (formerly HONS or HONK)

HIPAA heparin-induced platelet activation assay

HIT heparin-induced thrombocytopenia HIV human immunodeficiency virus HRT hormone replacement therapy

HSCT haematopoietic stem cell transplantation

HSV herpes simplex virus

IBW ideal bodyweight (see Appendix 10 for calculation)

IgΕ immunoglobulin E insulin-like growth factor IGF IgG immunoglobulin G IHD ischaemic heart disease

intramuscular IM

international normalised ratio INR

IV intravenous

IVP jugular venous pressure

K potassium

potassium chloride KC1

KGF human keratinocyte growth factor

LDL low-density lipoprotein LFTs liver function tests

LHRH luteinising hormone releasing hormone

LMWH low-molecular-weight heparin LRTI lower respiratory tract infection left-ventricular ejection fraction LVEF

LVF left ventricular failure

monoamine oxidase inhibitor MAOI

MCV mean cell volume Mg magnesium

MHRA Medicines and Healthcare products Regulatory Agency

ΜI myocardial infarction

MIC minimum inhibitory concentration

min minute

millimetres of mercury (used in blood pressure readings) mmHg

MRSA methicillin-resistant Staphylococcus aureus

sodium Na

NaCl sodium chloride NBM nil by mouth NG nasogastric

NICE National Institute for Health and Clinical Excellence

NIHSS NIH Stroke Scale

neuroleptic malignant syndrome e.g. hyperthermia, muscle rigidity & NMS

altered consciousness

National Poisons Information Service (tel: 0844 892 0111) NPIS

NPSA National Patient Safety Agency NOMI non-Q wave myocardial infarction NRTI nucleoside reverse transcriptase inhibitor NSAID non-steroidal anti-inflammatory drug

NSTEMI non ST-segment elevation myocardial infarction

NYHA New York Heart Association

 O_2 oxygen

OHSS ovarian hyperstimulation syndrome PA tissue plasminogen activator PBPC peripheral blood progenitor cell

xx | Abbreviations

PEA.

PCA patient-controlled analgesia

PCI percutaneous coronary intervention

PCV packed cell volume PE pulmonary embolism

PE phenytoin sodium equivalents (only in the

Fosphenytoin monograph) pulseless electrical activity

PICC peripherally inserted central intravenous catheter

PML progressive multifocal leucoencephalopathy

PN parenteral nutrition

PO₄ phosphate

PONV postoperative nausea and vomiting PPH primary pulmonary hypertension

PPI proton pump inhibitor
PRCA pure red cell aplasia
PSA prostate-specific antigen
PT prothrombin time
PTH parathyroid hormone
PVC poly(vinyl chloride)
r-DNA recombinant DNS

RIE right-sided infective endocarditis
Ringer's Ringer's solution for injection

SA sinoatrial

SBECD sulfobutylether beta cyclodextrin sodium

SC subcutaneous

SIADH syndrome of inappropriate ADH secretion

SLE systemic lupus erythematosus SPC summary of product characteristics

STEMI ST-segment elevation myocardial infarction

 $\begin{array}{lll} SVT & supraventricular tachycardia \\ T_3 & tri-iodothyronine; liothyronine \\ T_4 & tetra-iodothyronine; levothyroxine \\ \end{array}$

TFTs thyroid function tests
TIA transient ischaemic attack
TIH tumour-induced hypercalcaemia

TIVAD totally implantable venous access device

TNF tumour necrosis factor
TPN total parenteral nutrition
TRH thyrotrophin-releasing hormone

TSH thyroid-stimulating hormone, thyrotrophin

U urea

UA unstable angina
U&Es urea and electrolytes
UFH unfractionated heparin
ULN upper limit of normal
VEP visual evoked potentials
VT ventricular tachycardia
VTE venous thromboembolism

WCC white cell count
WFI water for injections

WPW Wolff-Parkinson-White syndrome