

The Maudsley®

Prescribing Guidelines in Psychiatry

15TH EDITION

David M. Taylor
Thomas R. E. Barnes
Allan H. Young

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**The Maudsley®
Prescribing Guidelines
in Psychiatry**

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15th Edition

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Preface

The *Maudsley® Prescribing Guidelines in Psychiatry* is now just one of several books in the Maudsley® *Guidelines* series. Since the publication of the 14th edition of the ‘big’ MPG, it has been joined by the *Maudsley® Deprescribing Guidelines: Antidepressants, Benzodiazepines, Gabapentinoids and Z-drugs* and by the *Maudsley® Prescribing Guidelines for Mental Health Conditions in Physical Illness*. These books cover some of the ground usually tackled in the main MPG but in much greater detail. In an effort to reduce repetition we have, in this 15th edition, left out (or let out) sections on such subjects as delirium, psychotropics in surgery and alternative routes of antidepressant administration and considerably reduced the size of sections on stopping psychotropics. What space has been made available by these changes has been filled by new sections on, for example, premenstrual syndrome, menopause, gambling disorder, ADHD in adults and relational aspects of prescribing practice.

This 15th edition of the MPG appears at a time when there is a growing antipathy towards the use of psychotropic drugs in mental illness. The prescribing advice given here assumes a decision to prescribe has already been made and so, to a large extent, we skirt the issue of whether or not prescribing is necessarily the right thing to do. Nonetheless, we do acknowledge that drug treatment is not always the best treatment for everyone in every situation. There are of course a range of effective non-drug treatments for mental health problems. The advice and guidance given in this and previous editions is aimed at optimising prescribing practice rather than promoting prescribing *per se*.

As ever, I and my fellow authors are indebted to a large number of expert contributors who have enabled us to provide information and guidance on such a wide range of topics; a feature that is possibly unique to the *Maudsley® Prescribing Guidelines in Psychiatry*. Sincere thanks are also due to Ivana Clark, the managing editor of this edition.

Even though some sections have been transplanted to other books in *The Guidelines* series, the scope of this edition is greater than the last and, as a consequence, it is a weightier book. It is probably worth pointing out that a special effort has been made to be economic with words and references although I suspect this is of little consolation to those lugging the book from ward to ward or home to hospital. It is the ‘big’ MPG, after all.

David M. Taylor
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Contributors' conflict of interest

Many of the contributors to *The Guidelines* have received funding from pharmaceutical manufacturers for research, consultancy or lectures. Readers should be aware that these relationships inevitably colour opinions on such matters as drug selection or preference.

We cannot therefore guarantee that guidance provided here is free of indirect influence of the pharmaceutical industry but hope to have mitigated this risk by providing copious literature support for statements made. As regards direct influence, no pharmaceutical company has been allowed to view or comment on any drafts or proofs of *The Guidelines* and none has made any request for the inclusion or omission of any topic, advice or guidance. To this extent, *The Guidelines* have been written independent of the pharmaceutical industry.

List of abbreviations

5HT3	5-hydroxytryptamine 3	AF	atrial fibrillation
22q11.2DS	22q11.2 deletion syndrome	AIDS	acquired immune deficiency syndrome
%w/v	percentage weight per volume	ALAI	aripiprazole long-acting injection
AACAP	American Academy of Child and Adolescent Psychiatry	ALP	alkaline phosphate
ACE	angiotensin-converting enzyme	ALT	alanine aminotransferase
Ach	acetylcholine	AMPA	alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid
AChE	acetylcholinesterase	AN	anorexia nervosa
AChE-I	acetylcholinesterase inhibitors	ANC	absolute neutrophil count
ACOG	American College of Obstetricians and Gynecologists	ANI	asymptomatic neurocognitive impairment
AD	Alzheimer's disease	APP	amyloid precursor protein
ADAPT	Adolescent Depression Antidepressants and Psychotherapy Trial	ARIA	amyloid-related imaging abnormality
ADAS-cog	Alzheimer's Disease Assessment Scale – cognitive subscale	ART	antiretroviral therapy
ADH	alcohol dehydrogenase	ASD	autism spectrum disorder
ADHD	attention deficit hyperactivity disorder	AST	aspartate
ADIS	Anxiety Disorders Interview Schedule	aminotransferase	aminotransferase
ADL	activities of daily living	ATPase	adenosine triphosphatase
ADR	adverse drug reactions	AUD	alcohol use disorder
AEC	Anticholinergic Effect on Cognition Scale	AUDIT	Alcohol Use Disorders Identification Test
		Aβ	beta amyloid
		BAC	blood alcohol concentration
		BAP	British Association for Psychopharmacology
		BBB	blood–brain barrier
		bd	twice a day
		BDD	body dysmorphic disorder

BDNF	brain-derived neurotrophic factor	CNS	central nervous system
BED	binge eating disorder	COCP	combined oral contraceptive pill
BEN	benign ethnic neutropenia	COMT	catechol-O-methyltransferase
BMI	body mass index	COPD	chronic obstructive pulmonary disease
BN	bulimia nervosa	COWS	Clinical Opiate Withdrawal Scale
BNF	<i>British National Formulary</i>	CQC	Care Quality Commission
BP	blood pressure	CrCl	creatinine clearance
BPD	Borderline personality disorder	CRLTA	clozapine-related life-threatening agranulocytosis
BPSD	behavioural and psychological symptoms of dementia	CRP	C-reactive protein
BuChE	butyrylcholinesterase	CTO	Community Treatment Order
CAMS	Childhood Anxiety Multimodal Study	CUtLASS	Cost Utility of the Latest Antipsychotic Drugs in Schizophrenia Study
CATIE	Clinical Antipsychosis Trials of Intervention Effectiveness	CVD	cardiovascular disease
CBT	cognitive behavioural therapy	CY-BOCS	Children's Yale-Brown Obsessive Compulsive Scale
CDRS	Children's Depression Rating Scale	CYP	cytochrome P450
CDR-SB	Clinical Dementia Rating Scale – Sums of Boxes	DAI	Drug Attitude Inventory
CDRS-R	Children's Depression Rating Scale-Revised	DBM	dibenzoylmethane
CGAS	Children's Global Assessment Scale	DBT	dialectical behaviour therapy
CGI	Clinical Global Impression	DEXA	dual-energy x-ray absorptiometry
CI	confidence interval	DHA	docosahexaenoic acid
CIBIC-plus	Clinician's Interview-Based Impression of Change plus caregiver input	DHEA	dehydroepiandrosterone
CIGH	clozapine-induced GI hypomotility	DIVA-5	Diagnostic Interview for ADHD in Adults
CIWA-Ar	Clinical Institute Withdrawal Assessment of Alcohol Scale Revised	DLB	dementia with Lewy bodies
CK	creatine kinase	DMDD	disruptive mood dysregulation disorder
CKD	chronic kidney disease	DMq	dextromethorphan and low-dose quinidine
CKD-EPI	Chronic Kidney Disease Epidemiology Collaboration	DOACs	direct-acting oral anticoagulants
		DoLS	Deprivation of Liberty Safeguards

DSM-5	<i>Diagnostic and Statistical Manual of Mental Disorders</i> , 5th edition	GGT	gamma-glutamyl transferase
DVLA	Driver and Vehicle Licensing Agency	GHB	gamma-hydroxybutyrate
ECG	electrocardiogram	GHB/GBL	gamma-hydroxybutyrate/ gamma-butyrolactone
ECT	electroconvulsive therapy	GI	gastrointestinal
EEG	electroencephalogram	GLP-1	glucagon-like peptide-1
eGFR	estimated glomerular filtration rate	GP	general practitioner
EMDR	eye movement desensitisation and reprocessing	GRDS	gastric reduction duodenal switch
EOSS	early-onset schizophrenia spectrum	GSM	genitourinary symptoms of menopause
EPA	eicosapentaenoic acid	HAD	HIV-associated dementia
EPS	extrapyramidal symptoms	HAM-D	Hamilton Depression Rating Scale
EPSE	extrapyramidal side effect	HAND	HIV-associated neurocognitive disorders
ER	extended release	HbA _{1c}	glycated haemoglobin
ERK	extracellular signal-regulated kinase	HCl	hydrogen chloride
ES	effect size	HD	Huntington's disease
EU	European Union	HDL	high-density lipoprotein
FBC	full blood count	hERG	human ether-a-go-go-related gene
FDA	Food and Drug Administration	HIV	human immunodeficiency virus
FGA	first-generation antipsychotic	HLA	human lymphocyte antigen
FPG	fasting plasma glucose	HPA	hypothalamic–pituitary–adrenal
FRAMES principles	feedback, responsibility, advice, menu, empathy, self-efficacy	HR	hazard ratio
FSH	follicle-stimulating hormone	HRT	hormone replacement therapy
FTI	Fatal Toxicity Index	IADL	instrumental activities of daily living
GABA	gamma-aminobutyric acid	ICD-10	<i>International Classification of Diseases 10</i>
GAD	generalised anxiety disorder	ICH	intracranial/intracerebral haemorrhage
GASS	Glasgow Antipsychotic Side-effect Scale	IGSLI	International Study Group on Lithium
GBL	gamma-butyrolactone	IHD	ischaemic heart disease
G-CSF	granulocyte colony-stimulating factor	IM	intramuscular
GERD	gastro-esophageal reflux disease	INR	international normalised ratio
GFR	glomerular filtration rate	IR	immediate release

ISBD	International Society for Bipolar Disorders	MR	modified release
ISTSS	International Society for Traumatic Stress Studies	MS	mood stabilisers/multiple sclerosis
IV	intravenous	MSM	men who have sex with men
Kiddie-SADS	Kiddie-Schedule for Affective Disorders and Schizophrenia	NAPLS	North American Prodromal Longitudinal Studies
LAI	long-acting injection	NaSSA	noradrenergic and specific serotonergic antidepressant
LC-MS	liquid chromatography and mass spectrometry	NbN	neuroscience-based nomenclature
LD	learning disabilities	NEET	not in education, employment or education
LDL	low-density lipoprotein	NICE	National Institute for Health and Care Excellence
LFT	liver function test	NIMH	National Institute of Mental Health
LGIB	lower gastrointestinal bleeding	NMDA	N-methyl-D-aspartate
LMP	last menstrual period	NMDAR	N-methyl-D-aspartate receptor
MADRS	Montgomery–Asberg Depression Rating Scale	NMS	neuroleptic malignant syndrome
MAO	monoamine oxidase	NNH	number needed to harm
MAOI	monoamine oxidase inhibitor	NNT	number needed to treat
MARS	Medication Adherence Rating Scale	NPIS	National Poisons Information Service
MASC	Multidimensional Anxiety Scale for Children	NPS	new psychoactive substances
MCA	Mental Capacity Act	NPV	negative predictive value
MCI	mild cognitive impairment	NRT	nicotine replacement therapy
MDD	major depressive disorder	NSAID	non-steroidal anti-inflammatory drug
MDMA	3,4-methylenedioxymethamphetamine	OCD	obsessive compulsive disorder
MDRD	Modification of Diet in Renal Disease	od	once daily
MDT	multidisciplinary team	OGTT	oral glucose tolerance test
MFQ	Mood and Feelings Questionnaire	on	at night
MHA	Mental Health Act	OOWS	Objective Opiate Withdrawal Scale
MHRA	Medicines and Healthcare products Regulatory Authority	OR	odds ratio
MI	myocardial infarction	OST	opioid substitution treatment
MMSE	Mini Mental State Examination		
MND	mild neurocognitive disorder		
MoCA	Montreal Cognitive Assessment		

PAIN	Peri-operative Pain and Addiction	PTSD	post-traumatic stress disorder
PANDAS	Interdisciplinary Network paediatric autoimmune neuropsychiatric disorder associated with <i>Streptococcus</i>	PUFA	polyunsaturated fatty acid
PANS	paediatric acute-onset neuropsychiatric syndrome	PWE	people with epilepsy
PANSS	Positive and Negative Syndrome Scale	RANZCP	Royal Australian and New Zealand College of Psychiatrists
PAWS	post-acute withdrawal syndrome	RC	Responsible Clinician
PBA	pseudobulbar affect	RCADS	Revised Children's Anxiety and Depression Scale
PD	Parkinson's disease	RCT	randomised controlled trial
PDSS	post-injection delirium sedation syndrome	REM	rapid eye movement
PE	pulmonary embolism	RID	relative infant dose
PET	positron emission tomography	RIMA	reversible inhibitor of monoamine oxidase A
PG	propylene glycol	RLAI	risperidone long-acting injection
P-gp	P-glycoprotein	ROMI	Rating of Medication Influences
PHQ-9	Patient Health Questionnaire-9	RR	respiratory rate/risk ratio
PLWH	people living with HIV	RRBI	restricted repetitive behaviours and interests
PMDD	premenstrual dysphoric disorder	RT	rapid tranquillisation
PMR	postmortem redistribution	RTA	road traffic accident
PMS	premenstrual syndrome	rTMS	repetitive transcranial magnetic stimulation
po	by mouth	RUPP	Research Units on Paediatric Psychopharmacology
POI	premature ovarian insufficiency	RYGB	Roux-en-Y gastric bypass
PORT	Program of Rehabilitation and Therapy	SADQ	Severity of Alcohol Dependence Questionnaire
PP1M	paliperidone long-acting injection 1-monthly	SAWS	Short Alcohol Withdrawal Scale
PP3M	paliperidone long-acting injection 3-monthly	SC	subcutaneous
PPH	postpartum haemorrhage	SCARED	Screen for Child Anxiety and Related Emotional Disorders
PPI	proton pump inhibitor	SCRA	synthetic cannabinoid receptor agonist
PPV	positive predictive value	SD	sexual dysfunction
prn	as required	SERM	selective oestrogen receptor modulators
PSSD	post-SSRI sexual dysfunction	SERT	serotonin receptor
PT	prothrombin time		

SGA	second-generation antipsychotic	tMS	transcranial magnetic stimulation
SIADH	syndrome of inappropriate secretion of antidiuretic hormone	TORDIA	Treatment of Resistant Depression in Adolescents
SIB	Severe Impairment Battery	TRBD	treatment-resistant bipolar disorder
SJW	St John's wort	TRD	treatment-resistant depression
SNRI	serotonin–noradrenaline reuptake inhibitor	TREC	Tranquilização Rápida-Ensaio Clínico [Rapid Tranquillisation Clinical Trial]
SOAD	Second Opinion Appointed Doctor	TRS	treatment-resistant schizophrenia
SPC	Summary of Product Characteristics	TS	Tourette syndrome
SROM	slow-release oral morphine	U&Es	urea and electrolytes
SSRI	selective serotonin reuptake inhibitor	UDP	uridine diphosphate
STAR*D	Sequenced Treatment Alternatives to Relieve Depression	UGT	UDP-glucuronosyltransferase
STOP-PD II	Study of the Pharmacotherapy of Psychotic Depression II	UGIB	upper gastrointestinal bleeding
SUD	stimulant use disorder	UGT	UDP-glucuronosyltransferase
TADS	Treatment of Adolescents with Depression Study	UKTIS	UK Teratology Information Service
TCA	tricyclic antidepressant	VaD	vascular dementia
TD	tardive dyskinesia	VG	vegetable glycerine
tDCS	transcranial direct current stimulation	VHR	Vienna High Risk
TDM	therapeutic drug monitoring	VMAT-2	vesicular monoamine transporter 2
TdP	torsades de pointes	VNS	vagal nerve stimulation
tds	three times a day	VTE	venous thromboembolism
TF-CBT	trauma-focused cognitive behavioural therapy	WBC	white blood cell
TFT	thyroid function test	WCC	white cell count
TIA	transient ischaemic attack	WHO	World Health Organization
		YMRS	Young Mania Rating Scale
		ZA	zuclopenthixol acetate

Chapter 1

Schizophrenia and related psychoses

ANTIPSYCHOTIC DRUGS

General introduction

Classification of antipsychotics

Before the 1990s, antipsychotics (or major tranquillisers as they were then known) were classified according to their chemistry. The first antipsychotic, chlorpromazine, was a phenothiazine compound – a tricyclic structure incorporating a nitrogen and a sulphur atom. Further phenothiazines were generated and marketed, as were chemically similar thioxanthenes such as flupentixol. Later, entirely different chemical structures were developed according to pharmacological paradigms. These included butyrophenones (haloperidol), diphenylbutylpiperidines (pimozide) and substituted benzamides (sulpiride, amisulpride).

Chemical classification remains useful but is rendered somewhat redundant by the broad range of chemical entities now available and by the absence of any clear structure–activity relationships for newer drugs. The chemistry of some older drugs does relate to their propensity to cause movement disorders. Piperazine phenothiazines (e.g. fluphenazine, trifluoperazine), butyrophenones and thioxanthenes are most likely to cause extrapyramidal effects, while piperidine phenothiazines (e.g. pipotiazine) and benzamides are the least likely. Aliphatic phenothiazines (e.g. chlorpromazine) and diphenylbutylpiperidines (pimozide) are perhaps somewhere in between.

Relative liability for inducing extrapyramidal side effects (EPSEs) was originally the primary factor behind the typical/atypical classification. Clozapine had long been known as an atypical antipsychotic on the basis of its low liability to cause EPSEs and its failure in animal-based antipsychotic screening tests. Its remarketing in 1990 signalled the beginning of a series of new medications, all of which were introduced with claims (to varying degrees of accuracy) of ‘atypicality’. Of these medications, perhaps only clozapine, and possibly quetiapine, is completely atypical, seemingly having a

very low or zero liability for extrapyramidal symptoms (EPS). Others show dose-related effects, although, unlike with typical drugs, therapeutic activity can usually be achieved without EPSEs. This is possibly the real distinction between typical and atypical drugs: the ease with which a dose can be chosen within the licensed dosage range that is effective but does not cause EPSEs (for example, compare haloperidol with olanzapine).

The typical/atypical dichotomy does not lend itself well to classification of antipsychotics in the middle ground of EPSE liability. Thioridazine was widely described as atypical in the 1980s but is a ‘conventional’ phenothiazine. Sulpiride was marketed as an atypical but is often classified as typical. Risperidone, at its maximum dose of 16mg/day, is just about as ‘typical’ as a drug can be. Alongside these difficulties is the fact that there is nothing either pharmacologically or chemically which clearly binds these so-called atypicals together as a group, save perhaps a general but not universal finding of preference for D2 receptors outside the striatum. Nor are atypicals characterised by improved efficacy over older drugs (clozapine and one or two others excepted) or the absence of hyperprolactinaemia (which is usually worse with risperidone, paliperidone and amisulpride than with typical drugs). Lastly, some more recently introduced agents (e.g. pimavanserin, xanomeline) have antipsychotic activity and do not cause EPS but have almost nothing in common with other atypicals in respect to chemistry, pharmacology or adverse-effect profile.

In an attempt to get round some of these problems, typicals and atypicals were reclassified as first- or second-generation antipsychotics (FGA/SGA). All drugs introduced since 1990 are classified as SGAs (i.e. all atypicals) but the new nomenclature dispenses with any connotations regarding atypicality, whatever that may mean. However, the FGA/SGA classification remains problematic because neither group is defined by anything other than time of introduction – hardly the most sophisticated pharmacological classification system. Perhaps more importantly, date of introduction is often wildly distant from date of first synthesis. Clozapine is one of the oldest antipsychotics (synthesised in 1959) while olanzapine is hardly in its first flush of youth, having first been patented in 1971. These two drugs are of course SGAs, apparently the most modern of antipsychotics.

In this edition of the *Maudsley Prescribing Guidelines*, we conserve the FGA/SGA distinction more because of convention than some scientific basis. Also, we feel that most people know which drugs belong to each group – it thus serves as a useful shorthand. However, it is clearly more sensible to consider the properties of *individual* antipsychotics when choosing drugs to prescribe or in discussions with patients and carers. With this in mind, the use of Neuroscience-based Nomenclature (NbN)¹ – a naming system that reflects pharmacological activity – is strongly recommended.

Choosing an antipsychotic

In the UK, the National Institute for Health and Care Excellence (NICE) guideline for medicines adherence² recommends that patients should be as involved as possible in decisions about the choice of medicines that are prescribed for them, and that clinicians should be aware that illness beliefs and beliefs about medicines influence adherence. Consistent with this general advice that covers all healthcare, the NICE guideline for schizophrenia emphasises the importance of patient choice rather than specifically recommending a class or individual antipsychotic as first-line treatment.³

Antipsychotics are effective in both the acute and maintenance treatment of schizophrenia and other psychotic disorders. They differ in their pharmacology, pharmacokinetics, overall efficacy/effectiveness and tolerability, and, perhaps more importantly, response and tolerability differ between patients. This variability of individual response means that there is no clear first-line antipsychotic medication that is preferable for all.

Relative efficacy

After the publication of the independent CATIE⁴ and CUtLASS⁵ studies, the World Psychiatric Association reviewed the evidence relating to the relative efficacy of 51 FGAs and 11 SGAs and concluded that, if differences in EPS could be minimised (by careful dosing) and anticholinergic use avoided, there was no convincing evidence to support any advantage for SGAs over FGAs.⁶ As a class, SGAs may have a lower propensity for EPS and tardive dyskinesia (TD),⁷ but this was somewhat offset by a higher propensity to cause metabolic adverse effects. A meta-analysis of antipsychotic medications for first-episode psychosis⁸ found few differences between FGAs and SGAs as groups of drugs but minor advantages for olanzapine and amisulpride individually. A later network meta-analysis of first-episode studies found small efficacy advantages for olanzapine and amisulpride and overall poor performance for haloperidol.⁹

When individual non-clozapine SGAs are compared, summary data suggest that olanzapine is marginally more effective than aripiprazole, risperidone, quetiapine and ziprasidone, and that risperidone has a minor advantage over quetiapine and ziprasidone.¹⁰ FGA-controlled trials also suggest an advantage for olanzapine, risperidone and amisulpride over older drugs.^{11,12} A network meta-analysis¹³ broadly confirmed these findings, ranking amisulpride second behind clozapine and olanzapine third. These three drugs were the only ones to show clear efficacy advantages over haloperidol. The magnitude of differences was again small (but potentially substantial enough to be clinically important)¹³ and must be weighed against the very different adverse effect profiles associated with individual antipsychotics. A 2019 network meta-analysis of 32 antipsychotics¹⁴ ranked amisulpride as the most effective drug for positive symptoms and clozapine as the best for both negative symptoms and overall symptom improvement. Olanzapine and risperidone were also highly ranked for positive symptom response. The greatest (beneficial) effect on depressive symptoms was seen with sulpiride, clozapine, amisulpride, olanzapine and the dopamine partial agonists, perhaps reflecting the relative absence of neuroleptic-induced dysphoria common to most FGAs.¹⁵ In the longer term, olanzapine may have advantages over some other antipsychotics.¹⁶ There was a tendency for more recently introduced drugs to have a lower estimated efficacy – a phenomenon that derives from the substantial increase in placebo response since 1970.¹⁷

Clozapine is clearly the drug of choice in refractory schizophrenia,¹⁸ although bizarrely, this is not a universal finding,¹⁹ probably because of the biased nature and quality of many active-comparator trials.^{20,21}

Both FGAs and SGAs are associated with a number of adverse effects. These include weight gain, dyslipidaemia, increases in plasma glucose/diabetes,^{22,23} hyperprolactinaemia, hip fracture,²⁴ sexual dysfunction, EPS including neuroleptic malignant syndrome,²⁵ anticholinergic effects, venous thromboembolism (VTE),²⁶ sedation and postural hypotension. The exact profile is drug specific (see individual sections on

specific adverse effects), although comparative data are not robust²⁷ (see large-scale meta-analyses^{13,28} for rankings of some adverse-effect risks).

Adverse effects are a common reason for treatment discontinuation,²⁹ particularly when efficacy is poor.¹³ Patients do not always spontaneously report adverse effects, however,³⁰ and psychiatrists' views of the prevalence and importance of adverse effects differ markedly from patient experience.³¹ Systematic enquiry, together with a physical examination and appropriate biochemical tests, is the only way accurately to assess their presence and severity or perceived severity. Patient-completed checklists such as the Glasgow Antipsychotic Side-effect Scale (GASS)³² can be a useful first step in this process. The clinician-completed Antipsychotic Non-Neurological Side-Effects Rating Scale facilitates more detailed and comprehensive assessment.³³

Non-adherence to antipsychotic treatment is common and here the guaranteed medication delivery associated with depot/long-acting injectable antipsychotic preparations (LAIs) is unequivocally advantageous. In comparison with oral antipsychotics, there is strong evidence that depots are associated with a reduced risk of relapse and rehospitalisation,^{34–36} although randomised controlled trials (RCTs) do not always reflect this difference.³⁷ Any logical assessment of the benefits of LAIs and the damage caused by relapse would conclude that LAIs should be first-line treatments, rather than reserved for those who have already relapsed on oral medication. Moreover, the wider use of SGA LAIs has to some extent changed the image of depots, which were sometimes perceived as punishments for miscreant patients. Their tolerability advantage probably relates partly to the better definition of their therapeutic dose range, meaning that the optimal dose is more likely to be prescribed (compare aripiprazole, with a licensed dose 300mg or 400mg/month, with flupentixol, which has a licensed dose in the UK of 50mg every 4 weeks to 400mg/week). The optimal dose of flupentixol is around 40mg every 2 weeks²⁸ – just 5% of the maximum allowed.

As already mentioned, for patients whose symptoms have not responded sufficiently to adequate, sequential trials of two or more antipsychotic drugs, clozapine is the most effective treatment.^{38–40} Its use in these circumstances is recommended by NICE³ and probably every schizophrenia guideline besides. The biological basis for the superior efficacy of clozapine is uncertain.⁴¹ Olanzapine should probably be one of the two drugs used before clozapine.^{10,42} A case might also be made for a trial of amisulpride: it has a uniformly high ranking in meta-analyses and one trial found continuation with amisulpride to be as effective as switching to olanzapine.⁴³ This same trial also suggested clozapine might be best placed as the second drug used, given that switching provided no benefit over continuing with the first prescribed drug.

This chapter covers the treatment of schizophrenia with antipsychotic drugs, the relative adverse effect profile of these drugs and how adverse effects can be managed.

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