The Clinical Use of Antipsychotic Plasma Levels

As personalized medicine in the field of psychopharmacology is turning from hope to hype, the need for precision tools in clinical practice is constantly growing. Among currently available precision tools, measuring antipsychotic plasma levels in patients prescribed antipsychotic medications, a method also known as therapeutic drug monitoring (TDM), is old, but a well-established method to account for the unique characteristics of each patient to aid in appropriate dose selection. With this readily comprehensible book, Dr. Meyer provides a comprehensive overview of the theoretical and practical framework for the effective use of TDM in clinical routine to improve the efficacy and safety of antipsychotic medications. Integrating TDM evidence for use in common clinical challenges in the practice of psychopharmacology, this book comprises an essential practical guide for routine TDM practice, a must-read work for all mental health professionals prescribing antipsychotic medications.

Georgios Schoretsanitis, MD, PhD, The Zucker Hillside Hospital, Psychiatry Research, Northwell Health, Glen Oaks, New York, USA, University Hospital of Psychiatry Zurich, Zurich, Switzerland

As we redouble our efforts to achieve the goals of personalized medicine, therapeutic drug monitoring (TDM) can play a critical role. Individuals vary enormously in how they absorb and metabolize different medications and which impactful environmental factors or co-occurring conditions they might encounter. In my view, the potential value of the knowledge that can be provided by TDM has been given less attention than it deserves. Meyer and Stahl have done an excellent job of reviewing this topic. They address all necessary perspectives, from optimizing response and tolerability to better monitoring of adherence and help to explain idiosyncratic or unexpected medication effects, as well as the timing and interpretation of plasma levels. This is an extremely useful text for anyone involved in the use of antipsychotic drugs.

John M. Kane, MD, Professor and Chairman, Department of Psychiatry, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, NY, USA

Dr. Meyer and Stahl have succeeded again in providing a well-written and evidence-based handbook with a focus on the use of antipsychotic plasma levels. This book offers so much more than a comprehensive review on the topic and provides us with important clinical pearls and helpful summarized recommendations. Most importantly, we walk away with having a good understanding and solid rationale for when and why plasma levels are important, but also having a reference we can revisit time and time again.

Deanna L. Kelly, PharmD., BCPP, Professor of Psychiatry, Director, Treatment Research Program (TRP) Maryland Psychiatric Research Center (MPRC), University of Maryland School of Medicine, MD, USA

The Clinical Use of Antipsychotic Plasma Levels

Stahl's Handbooks

Jonathan M. Meyer

Clinical Professor of Psychiatry, University of California, San Diego

Stephen M. Stahl

Clinical Professor of Psychiatry and Neuroscience,
University of California, Riverside, and Adjunct Professor
of Psychiatry, University of California, San Diego

With illustrations by

Nancy Muntner

Neuroscience Education Institute

CAMBRIDGE UNIVERSITY PRESS

Shaftesbury Road, Cambridge CB2 8EA, United Kingdom

One Liberty Plaza, 20th Floor, New York, NY 10006, USA

477 Williamstown Road, Port Melbourne, VIC 3207, Australia

314–321, 3rd Floor, Plot 3, Splendor Forum, Jasola District Centre, New Delhi – 110025, India

103 Penang Road, #05–06/07, Visioncrest Commercial, Singapore 238467

Cambridge University Press is part of Cambridge University Press & Assessment, a department of the University of Cambridge.

We share the University's mission to contribute to society through the pursuit of education, learning and research at the highest international levels of excellence.

www.cambridge.org
Information on this title: www.cambridge.org/9781009009898

DOI: 10.1017/9781009002103

First published 2021

A catalogue record for this publication is available from the British Library

Library of Congress Cataloging-in-Publication data
Names: Meyer, Jonathan M., 1962– author. | Stahl, Stephen M., 1951– author.
Title: The clinical use of antipsychotic plasma levels / Jonathan M Meyer, Stephen M Stahl ; with illustrations by Nancy Munter.
Other titles: Stahl's handbooks.
Description: Cambridge ; New York, NY : Cambridge University Press, 2021. |
Series: Stahl's handbooks | Includes bibliographical references and index.
Identifiers: LCCN 2021012648 (print) | LCCN 2021012649 (ebook) | ISBN 9781009009898 (paperback) | ISBN 9781009002103 (ebook)
Subjects: MESH: Antipsychotic Agents – blood | Dose-Response Relationship, Drug | Antipsychotic Agents – therapeutic use | Dose-Response Relationship, Drug | Psychotic Disorders – drug therapy | Schizophrenia – drug therapy | BISAC: MEDICAL / Mental Health | MEDICAL / Mental Health
Classification: LCC RM333.5 (print) | LCC RM333.5 (ebook) | NLM QV 77.9 | DDC 615.7/882–dc23
LC record available at https://lccn.loc.gov/2021012648
LC ebook record available at https://lccn.loc.gov/2021012649

ISBN 978-1-009-00989-8 Paperback

Jonathan M. Meyer, MD is Clinical Professor of Psychiatry at the University of California, San Diego, and a psychopharmacology consultant to the California Department of State Hospitals. Over the past 36 months, Dr. Meyer reports having served as a consultant to Acadia Pharmaceuticals, Alkermes, Allergan, Intra-Cellular Therapies, and Neurocrine; he has served on the speakers bureaus for Acadia Pharmaceuticals, AbbVie, Alkermes, Intra-Cellular Therapies, Neurocrine, Noven Pharmaceuticals, Inc., Otsuka America Inc., Sunovion Pharmaceuticals, and Teva Pharmaceutical Industries.

Stephen M. Stahl, MD, Ph.D., D.Sc. (Hon.) is Clinical Professor of Psychiatry and Neuroscience at the University of California, Riverside; Adjunct Professor of Psychiatry at the University of California, San Diego; Honorary Visiting Senior Fellow in Psychiatry at the University of Cambridge, UK; and Director of Psychopharmacology and Senior Academic Advisor to the California Department of State Hospitals. Over the past 36 months, Dr. Stahl has served as a consultant to AbbVie, Acadia, Adamas, Alkermes, Allergan, Arbor Pharmaceuticals, AstraZeneca, Avanir, Axovant, Axsome, Biogen, Biomarin, Biopharma, Celgene, ClearView, Concert, DepoMed, Eisai Pharmaceuticals, EMD Serono, EnVivo, Ferring, Forest, Forum, Genomind, Impel, Innovative Science Solutions, Intra-Cellular Therapies, Ironshore Pharmaceuticals, Janssen, Jazz, Karuna, Lilly, Lundbeck, Merck, Neos, NeuroPharma, Novartis, Noveida, Otsuka, Perrigo, Pfizer, Pierre Fabre, Relmada, Reviva, Sage Therapeutics, Servier, Shire, Sprout, Sunovion, Takeda, Taliaz, Teva, Tonix, Tris Pharma, Trius, Vanda, Vertex, and Viforpharma; he has been a board member of RCT Logic and Genomind; he has served on speakers bureaus for Acadia, Forum, Genentech, Janssen, Lundbeck, Merck, Otsuka, Servier, Sunovion, Takeda, and Teva, and he has received research and/or grant support from Acadia, Alkermes, AssureX, Astra Zeneca, Arbor Pharmaceuticals, Avanir, Axovant, Biogen, Braeburn Pharmaceuticals, BristolMyer Squibb, Celgene, CeNeRx, Cephalon, Dey, Eli Lilly, EnVivo, Forest, Forum, GenOmind, Glaxo Smith Kline, Intra-Cellular Therapies, ISSWSH, Janssen, JayMac, Jazz, Lundbeck, Merck, Neurocrine, Neuronetics, Novartis, Otsuka, Pfizer, Reviva, Roche, Servier, Shire, Sprout, Sunovion, Takeda, Teva, TMS NeuroHealth Centers, Tonix, and Vanda.

Contents

Foreword

In 1993, John Davis, Phil Janicak, and I co-edited a book titled *Clinical Use of Neuroleptic Plasma Levels* [1]. The publication pre-dated the introduction of most of the antipsychotics that are currently in clinical use. Among the guiding principles was the conviction that the available antipsychotics had a relatively narrow therapeutic index and that plasma concentrations could be useful for making everyday clinical decisions. The most important concern at that time was focused on extrapyramidal side effects (EPS) and the challenge was to find a "therapeutic window" that was associated with clinical effectiveness and minimal discomfort. The introduction of another generation of antipsychotics – led by risperidone, olanzapine, and quetiapine – led many prescribers to believe that these medications were better tolerated and that the search for a therapeutic window was unnecessary. Unfortunately, this belief was naïve and research in the clinical use of antipsychotic plasma levels decreased substantially.

Experience with the newer drugs demonstrated that, although many patients appeared comfortable on higher doses of medications such as olanzapine, all of these medications had dose-related side effects, including metabolic effects for some and EPS for others. In other words, the use of plasma concentrations or therapeutic drug monitoring (TDM) for making clinical decisions has great promise and this volume by Jonathan Meyer in Stephen Stahl's Handbook series is very welcome. An important strength of their approach is that it provides a thoughtful framework for interpreting plasma level information under different circumstances, and for differentiating nonadherence from kinetic issues when lower-than-expected levels are encountered. In most cases, patients will benefit when they are managed with drug doses within the recommended range, so there is not always a need to search for a plasma level window. On the other hand, TDM can be helpful for providing information when there are important clinical questions, as defined in a recent expert consensus [2]. The most obvious use is when clinicians are monitoring medication adherence on an ongoing basis, or in order to determine why an individual fails to respond to what appears to be an adequate drug dose. TDM may also be helpful when patients are being treated with medications with a high side burden at doses that are clinically effective. This

is commonly the case with clozapine where there is evidence for a threshold below which patients are unlikely to respond [3]. For higher doses, this Handbook also introduces the concept of the point of futility, or a level above which there is a very low likelihood that patients will show additional improvement. Finally, TDM may also have a valuable role during long-term treatment when patients have minimal or few active symptoms and the goal is to prevent a psychotic relapse. Under these circumstances, symptoms cannot guide an assessment as to whether or not a patient is on an adequate amount of medication.

This volume addresses each of these clinical situations and others. It is also important to note that these situations are common and following the guidance provided by this volume has the potential for enhancing clinical care.

Stephen R. Marder, MD

Professor of Psychiatry and Director of the Section on Psychosis

UCLA Semel Institute for Neuroscience and Human Behavior

Director – VISN 22 Mental Illness Research, Education Clinical Center (MIRECC) for the Department of Veterans Affairs

References

1. **Marder, S. R., Davis, J. M., and Janicak, P. G., eds. (1993)**. *Clinical Use of Neuroleptic Plasma Levels*. Washington, DC: American Psychiatric Press Inc.
2. **Schoretsanitis, G., Kane, J. M., Correll, C. U., *et al.* (2020)**. Blood levels to optimize antipsychotic treatment in clinical practice: A joint consensus statement of the American Society of Clinical Psychopharmacology (ASCP) and the Therapeutic Drug Monitoring (TDM) Task Force of the Arbeitsgemeinschaft für Neuropsychopharmakologie und Pharmakopsychiatrie (AGNP). *J Clin Psychiatry*, 81, https://doi.org/10.4088/JCP.4019cs13169.
3. **Hiemke, C., Bergemann, N., Clement, H. W., *et al.* (2018)**. Consensus guidelines for therapeutic drug monitoring in neuropsychopharmacology: Update 2017. *Pharmacopsychiatry*, 51, 9–62.

Preface: How to Use This Handbook and Useful Tables for Handy Reference

To best apply the information in this handbook, chapters 1-5 are worth reading initially, as they lay out some clinically important ideas such as coefficient of variation, time to steady state, the therapeutic threshold, and point of futility. One need not be an expert in antipsychotic kinetics to treat schizophrenia patients, but questions regarding oral medication adherence, when to obtain plasma levels, how to differentiate ultrarapid metabolizers from nonadherent patients, and the point at which further titration is unlikely to yield significant improvement are basic clinical decisions made every day. The sections covering specific antipsychotics builds on concepts explained in chapters 1–5 of the handbook. Reading the first five chapters will hopefully be enlightening, and provide the reader with the necessary tools to use plasma antipsychotic levels effectively. Those five chapters cover the following topics:

1. Sampling times for oral and long-acting injectable agents
2. The therapeutic threshold and the point of futility
3. Level interpretation including laboratory reporting issues, responding to high plasma levels, and special situations (hepatic dysfunction, renal dysfunction and hemodialysis, bariatric surgery)
4. Tracking oral antipsychotic adherence; differentiating treatment resistance from kinetic failure due to genetic variation or concurrent medications / environmental exposures, or adherence failure; use of pharmacogenomics
5. What is an adequate antipsychotic trial? Using plasma levels to optimize psychiatric response and tolerability (and when to use high-dose antipsychotics)

For easy reference, the following tables discussed elsewhere in this handbook are presented here:

Table P1 – Oral dose equivalency of commonly used first- and second-generation antipsychotics in acute schizophrenia

Table P2 – Antipsychotic nmol/l to ng/ml unit conversion

Table P3 – Mean half-life of commonly used oral antipsychotics and important metabolites

Table P4 – Mean half-life and kinetic properties of commonly used long-acting injectable antipsychotics

For easy access, the Appendix contains a single table that summarizes the therapeutic threshold, point of futility, and oral antipsychotic concentration–dose relationships.

Table P1 Oral dose equivalency of commonly used first- and second-generation antipsychotics in acute schizophrenia [1, 2]

Medication	Oral equivalent (mg)
First generation	
Haloperidol	1.00
Fluphenazine	1.25
Trifluoperazine	2.50
Perphenazine	3.75
Thiothixene	3.75
Zuclopenthixol	3.75
Loxapine	12.5
Chlorpromazine	37.5
Second generation	
Amisulpride	82.4
Aripiprazole	1.82
Brexpiprazole	0.53
Cariprazine	1.21
Lurasidone	23.2
Risperidone	1.00
Olanzapine	2.15
Ziprasidone	29.5

Comments

[a] Clozapine dose equivalencies are not provided as the primary use is for treatment-resistant schizophrenia and there are no equivalent medications [3].

[b] Quetiapine dose equivalents are not provided as both naturalistic and clinical trials data raise concerns about efficacy as monotherapy for schizophrenia [4, 5]. When used at doses > 400 mg/d for schizophrenia treatment, quetiapine also has substantial metabolic adverse effects [6, 7].

Note: Other antipsychotic dose equivalencies for antipsychotics not listed here can be calculated using a spreadsheet developed by Professor Stefan Leucht and colleagues [2]. The results are reported based on a variety of methods (e.g. minimum effective dose, 95% effective dose, etc.) and the spreadsheet can be downloaded from their website:

www.cfdm.de/media/doc/Antipsychotic%20dose%20conversion%20calculator.xls

Table P2 Antipsychotic nmol/l to ng/ml unit conversion

Antipsychotic	To obtain plasma levels in ng/ml divide levels in nmol/l by the value below:
Amisulpride	2.71
Aripiprazole	2.23
Asenapine	3.50
Brexpiprazole	2.31
Cariprazine	2.34
Chlorpromazine	3.14
Clozapine	3.06
Flupenthixol	2.30
Fluphenazine	2.29
Haloperidol	2.66
Loxapine	3.05
Lurasidone	2.03
Olanzapine	3.20
Paliperidone	2.34
Perphenazine	2.48
Risperidone	2.44
Thiothixene	2.25
Trifluoperazine	2.45
Zuclopenthixol	2.49

Table P3 Mean half-life of commonly used oral antipsychotics and important metabolites [8–18, 3, 19, 20]

Drug	$T_{1/2}$ (hours)
First-generation antipsychotics	
Chlorpromazine	11.05–15
Fluphenazine	13
Haloperidol	24
Loxapine	4
7-OH loxapine	??[a]
Molindone	2[b]

Drug	$T_{1/2}$ (hours)
Perphenazine	9–12
Zuclopenthixol	17.6
Newer antipsychotics	
Amisulpride	12
Aripiprazole	75
Asenapine sublingual Asenapine transdermal patch	24 30[c]
Brexpiprazole	91
Cariprazine Desmethylcariprazine (DCAR) Didesmethylcariprazine (DDCAR)	31.6–68.4 29.7–39.5 (DCAR) 314–446 (DDCAR)
Clozapine Norclozapine	9–17 20
Iloperidone	15–22
Lumateperone	18
Lurasidone	28.8–37.4[d]
Olanzapine	30
Paliperidone (9-OH risperidone)[e]	23
Quetiapine Norquetiapine	7 12
Risperidone Paliperidone (9-OH risperidone)[f]	3 21
Sertindole	60–73
Ziprasidone	7

Comment

Half-lives may be markedly prolonged in individuals receiving metabolic inhibitors or who have lower-functioning polymorphisms of cytochrome P450 enzymes, other relevant enzymes, or transporters involved in drug disposition. Conversely, half-lives may be significantly shorter than the mean in individuals exposed to inducers, or who have higher-functioning polymorphisms of cytochrome P450 enzymes, other relevant enzymes, or transporters involved in drug disposition.

[a] Based on studies of inhaled loxapine, the half-life of 7-OH loxapine is likely to be substantially longer [21].
[b] The therapeutic effects persist for 24–36 hours despite the absence of active metabolites [18].
[c] After patch removal.
[d] Repeated dosing in adult schizophrenia patients. Single dose half-life in volunteers is 18 hours [22].
[e] When administered as oral paliperidone.
[f] When derived from orally administered risperidone.

Table P4 Mean half-life and kinetic properties of commonly used long-acting injectable (LAI) antipsychotics [23–26]

Drug	Vehicle	Dosage	T_{max}	$T_{1/2}$ multiple dosing	Able to be loaded
First-generation antipsychotics					
Fluphenazine decanoate	Sesame oil	12.5–75 mg/2 weeks **Max:** 75 mg/week	0.3–1.5 days	14 days	Yes
Haloperidol decanoate	Sesame oil	25–300 mg/4 weeks **Max:** 300 mg/2 weeks	3–9 days	21 days	Yes
Perphenazine decanoate	Sesame oil	27–216 mg/3–4 weeks	7 days	27 days	Yes
Fluphenthixol decanoate	Coconut oil	20–40 mg/2–4 weeks **Max:** 100 mg/2 weeks	4–7 days	17 days	Yes
Zuclopenthixol decanoate	Coconut oil	25–100 mg/2–4 weeks **Max:** 400 mg/2 weeks	3–7 days	19 days	Yes
Newer antipsychotics					
Risperidone subcutaneous (**Perseris®**)	Water	90–120 mg/4 weeks	7–8 days	9–11 days	Not needed
Risperidone microspheres (**Risperdal Consta®**)	Water	12.5–50 mg/2 weeks	21 days	See note [a]	**No** (21–28 days oral overlap)
Paliperidone palmitate (**Invega Sustenna®**)	Water	39–234 mg/4 weeks	13 days	25–49 days	Yes
Paliperidone palmitate (3 mo) (**Invega Trinza®**)[b]	Water	273–819 mg/12 weeks	84–95 days (deltoid) 118–139 days (gluteal)	30–33 days	No

Drug	Vehicle	Dosage	T_{max}	$T_{1/2}$ multiple dosing	Able to be loaded
Olanzapine pamoate **(Zyprexa Relprevv®)**	Water	150–300 mg/2 weeks 300–405 mg/4 weeks	7 days	30 days	Yes
Aripiprazole monohydrate **(Abilify Maintena®)**	Water	300–400 mg/4 weeks	6.5–7.1 days	29.9–46.5 days	**No** (14 days oral overlap)
Aripiprazole lauroxil **(Aristada®)**[c]	Water	441 mg, 662 mg, 882 mg/4 wks 882 mg/6 weeks 1064 mg/8 weeks	41 days (single dose) [27] 24.4–35.2 days (repeated dosing) [28]	53.9–57.2 days	**No** (Start with AL_{NC} 675 mg IM + 30 mg oral ***OR*** 21 days oral overlap)
Aripiprazole lauroxil nanocrystal **(Aristada Initio®)**[d]	Water	675 mg once	27 days (range: 16 to 35 days)	15–18 days (single dose)	–

[a] Steady state plasma levels after 5 biweekly injections are maintained for 4–5 weeks, but decrease rapidly at that point with a mean half-life of 4–6 days [29].
[b] Only for those on paliperidone palmitate monthly for 4 months. Cannot be converted from oral medication.
[c] Requires 21 days oral overlap unless starting with aripiprazole lauroxil nanocrystal (AL_{NC}) + a single 30 mg oral dose.
[d] Aripiprazole lauroxil nanocrystal (AL_{NC}) is only used for initiation of treatment with aripiprazole lauroxil, or for resumption of treatment. It is always administered together with the clinician-determined dose of aripiprazole lauroxil, although the latter can be given up to 10 days after the aripiprazole lauroxil nanocrystal (AL_{NC}) injection.

For further reading about use of LAI antipsychotics, please see the comprehensive edited book ***Antipsychotic Long-Acting Injections***, now in its 2nd edition [30].

References

1. **Leucht, S., Samara, M., Heres, S., *et al.* (2016)**. Dose equivalents for antipsychotic drugs: The DDD method. *Schizophr Bull*, 42 Suppl 1, S90–94.
2. **Leucht, S., Crippa, A., Siafis, S., *et al.* (2020)**. Dose-response meta-analysis of antipsychotic drugs for acute schizophrenia. *Am J Psychiatry*, 177, 342–353.
3. **Meyer, J. M. and Stahl, S. M. (2019)**. *The Clozapine Handbook*. Cambridge: Cambridge University Press.
4. **Asmal, L., Flegar, S. J., Wang, J., *et al.* (2013)**. Quetiapine versus other atypical antipsychotics for schizophrenia. *Cochrane Database Syst Rev*, CD006625.
5. **Vanasse, A., Blais, L., Courteau, J., *et al.* (2016)**. Comparative effectiveness and safety of antipsychotic drugs in schizophrenia treatment: A real-world observational study. *Acta Psychiatr Scand*, 134, 374–384.
6. **Meyer, J. M., Davis, V. G., Goff, D. C., *et al.* (2008)**. Change in metabolic syndrome parameters with antipsychotic treatment in the CATIE Schizophrenia Trial: Prospective data from phase 1. *Schizophr Res*, 101, 273–286.
7. **Meyer, J. M. (2010)**. Antipsychotics and metabolics in the post-CATIE era. *Curr Top Behav Neurosci*, 4, 23–42.
8. **Simpson, G. M., Cooper, T. B., Lee, J. H., *et al.* (1978)**. Clinical and plasma level characteristics of intramuscular and oral loxapine. *Psychopharmacology (Berl)*, 56, 225–232.
9. **Zetin, M., Cramer, M., Garber, D., *et al.* (1985)**. Bioavailability of oral and intramuscular molindone hydrochloride in schizophrenic patients. *Clin Ther*, 7, 169–175.
10. **Midha, K. K., Hawes, E. M., Hubbard, J. W., *et al.* (1988)**. Variation in the single dose pharmacokinetics of fluphenazine in psychiatric patients. *Psychopharmacology (Berl)*, 96, 206–211.
11. **Dahl, M. L., Ekqvist, B., Widén, J., *et al.* (1991)**. Disposition of the neuroleptic zuclopenthixol cosegregates with the polymorphic hydroxylation of debrisoquine in humans. *Acta Psychiatr Scand*, 84, 99–102.
12. **Midha, K. K., Hubbard, J. W., McKay, G., *et al.* (1993)**. The role of metabolites in a bioequivalence study I: Loxapine, 7-hydroxyloxapine and 8-hydroxyloxapine. *Int J Clin Pharmacol Ther Toxicol*, 31, 177–183.
13. **Yeung, P. K., Hubbard, J. W., Korchinski, E. D., *et al.* (1993)**. Pharmacokinetics of chlorpromazine and key metabolites. *Eur J Clin Pharmacol*, 45, 563–569.
14. **Wong, S. L. and Granneman, G. R. (1998)**. Modeling of sertindole pharmacokinetic disposition in healthy volunteers in short term dose-escalation studies. *J Pharm Sci*, 87, 1629–1631.
15. **Kudo, S. and Ishizaki, T. (1999)**. Pharmacokinetics of haloperidol: An update. *Clin Pharmacokinet*, 37, 435–456.
16. **Mauri, M. C., Volonteri, L. S., Colasanti, A., *et al.* (2007)**. Clinical pharmacokinetics of atypical antipsychotics: A critical review of the relationship between plasma concentrations and clinical response. *Clin Pharmacokinet*, 46, 359–388.
17. **Meyer, J. M. (2018)**. Pharmacotherapy of psychosis and mania. In L. L. Brunton, R. Hilal-Dandan, and B. C. Knollmann, eds., *Goodman & Gilman's The Pharmacological Basis of Therapeutics*, 13th edn. Chicago, IL: McGraw-Hill, pp. 279–302.
18. **Yu, C. and Gopalakrishnan, G. (2018)**. In vitro pharmacological characterization of SPN-810 M (molindone). *J Exp Pharmacol*, 10, 65–73.
19. **Meyer, J. M. (2020)**. Lumateperone for schizophrenia. *Curr Psychiatr*, 19, 33–39.
20. **Schoretsanitis, G., Kane, J. M., Correll, C. U., *et al.* (2020)**. Blood levels to optimize antipsychotic treatment in clinical practice: A joint consensus statement of the American Society of Clinical Psychopharmacology (ASCP) and the Therapeutic Drug Monitoring (TDM) Task Force of

the Arbeitsgemeinschaft für Neuropsychopharmakologie und Pharmakopsychiatrie (AGNP). *J Clin Psychiatry*, 81, https://doi.org/10.4088/JCP.4019cs13169.

21. **Spyker, D. A., Voloshko, P., Heyman, E. R., *et al.* (2014)**. Loxapine delivered as a thermally generated aerosol does not prolong QTc in a thorough QT/QTc study in healthy subjects. *J Clin Pharmacol*, 54, 665–674.
22. **Meyer, J. M., Loebel, A. D., and Schweizer, E. (2009)**. Lurasidone: A new drug in development for schizophrenia. *Expert Opin Investig Drugs*, 18, 1715–1726.
23. **Larsen, N. E. and Hansen, L. B. (1989)**. Prediction of the optimal perphenazine decanoate dose based on blood samples drawn within the first three weeks. *Ther Drug Monit*, 11, 642–646.
24. **Altamura, A. C., Sassella, F., Santini, A., *et al.* (2003)**. Intramuscular preparations of antipsychotics: Uses and relevance in clinical practice. *Drugs*, 63, 493–512.
25. **Spanarello, S. and La Ferla, T. (2014)**. The pharmacokinetics of long-acting antipsychotic medications. *Curr Clin Pharamacol*, 9, 310–317.
26. **Meyer, J. M. (2020)**. Monitoring and improving antipsychotic adherence in outpatient forensic diversion programs. *CNS Spectr*, 25, 136–144.
27. **Hard, M. L., Mills, R. J., Sadler, B. M., *et al.* (2017)**. Aripiprazole lauroxil: Pharmacokinetic profile of this long-acting injectable antipsychotic in persons with schizophrenia. *J Clin Psychopharmacol*, 37, 289–295.
28. **Hard, M. L., Mills, R. J., Sadler, B. M., *et al.* (2017)**. Pharmacokinetic profile of a 2-month dose regimen of aripiprazole lauroxil: A phase I study and a population pharmacokinetic model. *CNS Drugs*, 31, 617–624.
29. **Gefvert, O., Eriksson, B., Persson, P., *et al.* (2005)**. Pharmacokinetics and D2 receptor occupancy of long-acting injectable risperidone (Risperdal Consta) in patients with schizophrenia. *Int J Neuropsychopharmacol*, 8, 27–36.
30. **Haddad, P., Lambert, T., and Lauriello, J., eds. (2016)**. *Antipsychotic Long-Acting Injections*, 2nd edn. New York: Oxford University Press.