CNS SPECTRUMS Academic Supplement

The International Journal of Neuropsychiatric Medicine

The Biological and Clinical Significance of Single Isomers

Based on the proceedings of a roundtable discussion on single-isomer drug development held on March 28–29, 2001, in Washington, DC

Single-Isomer Science: The Phenomenon and Its Terminology

Joseph Gal, PhD

The Development of Single-Isomer Molecules: Why and How Andrew J. Hutt, PhD

Single Isomer Versus Racemate: Is There a Difference? Clinical Comparisons in Allergy and Gastroenterology David A. Flockhart, MD, PhD, and Harold S. Nelson, MD

Great Expectations in Stereochemistry: Focus on Antidepressants
C. Lindsay DeVane, PharmD, and David W. Boulton, PhD

Escitalopram: A Second-Generation SSRI Michael J. Owens, PhD, and Jerrold F. Rosenbaum, MD

Efficacy Comparison of Escitalopram and Citalopram in the Treatment of Major Depressive Disorder: Pooled Analysis of Placebo-Controlled Trials

Jack M. Gorman, MD, Andrew Korotzer, PhD, and Guojin Su, PhD

New Single-Isomer Compounds on the Horizon Joseph Gal, PhD

Conclusion: The Future of Single-Isomer Pharmacology

Jerrold F. Rosenbaum, MD



Brought to you by an unrestricted educational grant from

FOREST PHARMACEUTICALS, INC. Pharmaceuticals • Therapeutics • Healthcare • Managed Care • Specialty Sales

DISCLAIMER

This academic supplement is provided as a service to medicine by Forest Pharmaceuticals, Inc. Sponsorship of this review does not imply the sponsor's agreement with the views expressed herein.

Although every effort has been made to ensure that drug doses and other information are presented accurately in this publication, the ultimate responsibility rests with the prescribing physician. Neither the publisher, the sponsor, nor the authors can be held responsible for errors or for any consequences arising from the use of information contained herein. Readers are strongly urged to consult any relevant primary literature. No claims or endorsements are made for any drug or compound currently under clinical investigation.

Copyright ©2002, MedWorks Media, LLC. 333 Hudson St., New York, NY 10013. Printed in the USA. All rights reserved, including the right of reproduction, in whole or in part, in any form.

CNS SPECTRUMS

The International Journal of Neuropsychiatric Medicine

EDITOR

Jack M. Gorman, MD College of Physicians and Surgeons, Columbia University New York, NY

INTERNATIONAL EDITOR

Joseph Zohar, MD Chaim Sheba Medical Center Tel Aviv, Israel

ASSOCIATE INTERNATIONAL EDITORS

<u>EUROPE</u>

Donatella Marazziti, MD University of Pisa Pisa, Italy

MID-ATLANTIC

Dan J. Stein, MB University of Stellenbosch Tygerberg, South Africa

FAR EAST

Shigeto Yamawaki, MD, PhD Hiroshima University School of Medicine Hiroshima, Japan

EDITORIAL DIRECTOR
James M. La Rossa Jr.

FOUNDING EDITOR
Eric Hollander, MD

BOARD OF ADVISORS

Margaret Altemus, MD Cornell University Medical Center New York, NY

Mitchell F. Brin, MD Mount Sinai School of Medicine New York, NY

Dennis S. Charney, MD Yale University New Haven, CT

Jeffrey L. Cummings, MD University of California Los Angeles, CA

Dwight L. Evans, MD University of Pennsylvania Philadelphia, PA

Mark George, MD Medical University of South Carolina Charleston, SC

Thomas R. Insel, MD Yerkes Primate Labs Emory University School of Medicine Atlanta, GA

Lorrin M. Koran, MDStanford University Medical School Stanford, CA

Herbert Y. Meltzer, MD Vanderbilt University Medical Center Nashville, TN

Stuart A. Montgomery, MD St. Mary's Hospital Medical School London, United Kingdom

Dennis L. Murphy, MD
National Institute of Mental Health
Bethesda, MD

Charles B. Nemeroff, MD, PhD Emory University School of Medicine Atlanta, GA

Humberto Nicolini, MD, PhD Instituto Mexicano de Psiquiatria Mexico City, Mexico

Katharine Phillips, MD Brown University Providence, RI

Harold A. Pincus, MD Western Psychiatric Institute & Clinic Pittsburgh, PA

Scott L. Rauch, MD Massachusetts General Hospital Charlestown, MA

Alan Schatzberg, MD Stanford University Medical School Stanford, CA

Norman Sussman, MD New York University Medical School New York, NY

Neal R. Swerdlow, MD, PhD University of California, San Diego La Jolla, CA

Michael Trimble, MD National Hospital for Neurology and Neurosurgery London, United Kingdom

Herman G.M. Westenberg, MD University Hospital Utrecht Utrecht, The Netherlands

Richard Wyatt, MD National Institute of Mental Health Bethesda, MD

Stuart Yudofsky, MD Baylor College of Medicine Houston, TX

MEDWORKS MEDIA Corporate Staff

VICE PRESIDENTS AND ASSOCIATE PUBLISHERS Imre Balanli Genevieve Romano

MANAGING EDITOR Christopher Naccari

SENIOR EDITOR, INTERNATIONAL Amanda Schoenberg

DEPUTY EDITORS
Susan Curry
Deborah Hughes
José R. Ralat
Craig McRea Seip

CME PROJECTS EDITOR
Kadrin Wilfong

SENIOR ACQUISITIONS EDITOR Caroline Carlin Risman

ACQUISITIONS EDITOR Lisa Arrington

ART DIRECTION & DESIGN Anthony J. Korsak

PRODUCTION COORDINATOR
Lila Moses

ASSISTANT TO THE PUBLISHER Lowell Yaeger

DESIGNER, MULTIMEDIA Michael Mosley

ADMINISTRATIVE ASSISTANT Claudette Crawford

CORPORATION COUNSEL
Kevin F. Saer, Esq.
Davis, Wright & Tremaine

DIRECTOR OF ADVERTISING SALES Darren L. Brodeur

DIRECTOR, ONCOLOGY SALES Paul McDaniel

MARKETING DIRECTOR, GLOBAL James Kassaris

PUBLISHER & FOUNDER James M. La Rossa Jr.

CNS SPECTRUMS

The International Journal of

Neuropsychiatric Medicine Volume 7 • Number 4

> Supplement 1 April 2002

The Biological and Clinical Significance of Single Isomers

- **Participant Biographies**
- Single-Isomer Science: The Phenomenon and Its Terminology By Joseph Gal, PhD
- 14 The Development of Single-Isomer Molecules: Why and How By Andrew J. Hutt, PhD
- 23 Single Isomer Versus Racemate: Is There a Difference? **Clinical Comparisons in Allergy and Gastroenterology** By David A. Flockhart, MD, PhD, and Harold S. Nelson, MD
- 28 Great Expectations in Stereochemistry: Focus on Antidepressants By C. Lindsay DeVane, PharmD, and David W. Boulton, PhD
- 34 Escitalopram: A Second-Generation SSRI By Michael J. Owens, PhD, and Jerrold F. Rosenbaum, MD
- 40 Efficacy Comparison of Escitalopram and Citalopram in the Treatment of Major Depressive Disorder: Pooled Analysis of Placebo-Controlled Trials By Jack M. Gorman, MD, Andrew Korotzer, PhD, and Guojin Su, PhD
- 45 New Single-Isomer Compounds on the Horizon By Joseph Gal, PhD
- 55 Conclusion: The Future of Single-Isomer Pharmacology By Jerrold F. Rosenbaum, MD





MEMBER SINCE 2001

CNS Spectrums is a peer-reviewed journal indexed in EMBASE/Excerpta Medica, DIALOG, SilverPlatter, OVID, and Lexis-Nexis. CNS Spectrums is endorsed by, and is the official journal of, the International Neuropsychiatric Assoc., with members in 30 countries. CNS Spectrums (ISSN: 1092-8529) is published monthly by MedWorks Media, Inc., 333 Hudson St., 7th Floor, New York, NY 10013. Periodicals postage paid at New York, NY, and at additional mailing offices. One year subscription rates: Domestic \$90; Foreign \$145; in-training \$50. For subscriptions, fax us at: (212) 328-0600. E-mail: publisher@medworksmedia.com

For editorial and advertising inquires:

Telephone: (212) 328-0800; Facsimile: (212) 328-0600

E-mail: publisher@medworksmedia.com; Web site: www.medworksmedia.com

Opinions and views expressed by authors are their own and do not necessarily reflect the views of the publisher, MedWorks Media, or the editorial advisory board. Advertisements in CNS Spectrums are accepted on the basis of adherence to ethical medical standards, but acceptance does not imply endorsement by CNS Spectrums, or the publisher MedWorks Media.

CNS Spectrums[®] is a registered trademark of CNS Spectrums, LLC, New York, NY.

Permission to reproduce articles in whole or part must be obtained in writing from the publisher. Copyright© 2002 by MedWorks Media. All right reserved. Printed in the United States.