DIALOGUE
ONTARIO PSYCHIATRIC ASSOCIATION
JUNE 2009

President's Message

Dr. Paul Mulzer

Greetings! I'm deeply honoured to serve as your OPA President for 2009-2010. I am humbled to follow in the wake of my distinguished colleagues who have been instrumental in restructuring the OPA to respond most effectively to its membership. The last three years have been a time of considerable change. This has not been easy for many council members but I believe it has engendered a passion, focus and direction for our association. You have clearly responded to this new direction with a substantial membership increase. We will continue this renewal with clear policies and guidelines to ensure enhanced oversight and accountability. Our commitment has been to remain a relevant and concerted voice for mental healthcare delivery in this province. Let me assure you that we will honour your confidence and continued support of this organization.

I'm delighted to work with such a talented and enthusiastic council. We collectively share a deep commitment to this year's Presidential Theme: *Dignity, Advocacy and Social Justice*. An ambitious goal, but there have been many great banners that fell short of their scribes' ideals. The American Revolution espoused Life, Liberty and the Pursuit of Happiness only to see at least another ninety years of slavery before the writ of emancipation. This was followed by a further ninety years before an African-American could choose his lunch counter or attend an unsegregated university. Freedom comes at a high price and certainly not swiftly! This is also true of the stigma of mental illness and its pervasive legacy within our healthcare system. In April, I'm sure, like me, you watched the G20 Summit to get a glimpse of the international powerbrokers. I could not help but wonder what a summit of the B20 would look like — the bottom 20 world economies. As they tackle poverty, despair and deteriorating social programming in the aftermath of the global recession. Of course, we do not need to venture beyond our own borders to address these concerns. We have our own third world crisis and, curiously enough, it is also our greatest human rights challenge. Our freedom train, march on Washington, or Alabama sit-in is found in addressing the deplorable disparity within our First Nations populations. I believe how we address these social, political, economic and health concerns will be our greatest triumph or our deepest shame. OPA is committed to fostering relationships with First Nations providers, federal, provincial representatives and other key stakeholders in renewing our commitment to address this healthcare crisis.

In the role of advocacy, it is appropriate that psychiatry stand at the forefront of medical specialties in exploring alternate models of resident on-call care delivery. Clearly, advances have been made but much still needs to be done. We know the impact of sleep deprivation on the individual, mood, and decision-making. We need to add our voice to student union groups, like PAIRO, working in concert with governing bodies and residency programs in stressing a need for reform. Psychiatry must take a leadership role in advocating for our future colleagues and continue in our efforts to emphasize humanity in residency. As a specialty, we have always looked reflectively on our history while maintaining a future focus.

2009-2010 is an exciting and ambitious year. We are already feverishly planning our Annual Conference for April 23 & 24, 2010. I'd encourage you to mark your calendar now for what promises to be our best annual event ever! I'm very excited about our Fall Conference, on September 26, 2009. Dr. Nancy McWilliams will be an excellent keynote speaker. I personally benefited in my case formulation skills from her must-read book, "*Psychoanalytic Case Formulation*". We're actively seeking a larger venue to accommodate the interest this dynamic speaker is sure to generate.

2010 will be our 90th Anniversary and it should prove to be a very exciting year leading up to this milestone celebration. *Dialogue* will highlight key excerpts from conferences of the past through our growing archives while giving you updates on our Fall and Annual Conference. Join us for what will be a very memorable year as we pay tribute to our colleagues' accomplishments over the last ninety years, their leadership, as well as the changing face of psychiatric practice throughout the province. Join us as we seek to encourage change, promote awareness and build relationships to foster care and renewed optimism.▲

Paul Mulzer, MD, FRCP(C)
President, Ontario Psychiatric Association

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Contents

From the Editor

LOOKING back to the 2009 OPA Annual Conference, I would like to take this opportunity to recognize all those that made this Conference such a success… First of all, the OPA Conference Committee co-chaired by Dr. Paul Mulzer and Dr. Jon Davine; our Sponsors and Exhibitors for their ongoing financial support; our Speakers for sharing generously their knowledge and expertise; and, of course, all of you who attended the Conference, especially those who came to the registration desk and sent in evaluation forms to share with us their feedback. Your input is always welcomed as we start planning the next Conference. I hope you will enjoy the central spread of this issue with the 2009 Conference photos.

Looking forward to the Fall Conference, we encourage you to review the Conference information on page 5 and make plans to attend this event. Dr. Nancy McWilliams is a well known and sought after speaker and we are thrilled to offer you an opportunity to meet with her this September.

The 2010 OPA Annual Conference will take place on April 23 & 24, 2010, at the Le Méridian King Edward Hotel in Toronto. It is never too early to start planning — please check out our Call for Nominations for the *T. A. Sweet Award* and Call for Abstracts on pages 10 and 11 respectively.

As the Ontario Psychiatric Association will celebrate its 90th Anniversary in 2010, we decided to establish a column on OPA history as a regular *Dialogue* feature. Dr. John Deadman has been working on the OPA archives for quite some time now, and his update is posted on page 4.

One of the main objectives of the OPA is to represent the members of the Association in their relationships with governments at all levels, universities, and other associations. OPA Council is vigilant when it comes to issues that would greatly affect OPA members. The recent OPA campaign to oppose adoption of the OMA's new relativity model (CANDI) resulted in a deferral of the OMA decision on change in position on the relativity model to November 2009. Thank you to Dr. K. Sonu Gaind for his leadership in organizing the campaign! You will find his update on recent developments on page 3.

As you review this issue's materials, I hope you will find not only useful information but also "food for thought" and consider contributing your materials for future issues — be it an article, book review, clinical case or even some old photographs related to OPA history.

Wishing you all many happy and sunny days this summer!

Halyna Troian, CAE
Editor

Update on Relativity and Fees

As discussed in the recent OPA email campaign, the Ontario Medical Association (OMA) is considering dramatic changes to the relativity allocation process in a new Comparison of Average Net Daily Income (CANDI) relativity model. However, there is no provision whatsoever in the current CANDI model for accounting for increased complexity/intensity/risk of specialized care that requires a minimum of 5 years basic post-graduate speciality training versus care requiring a minimum of 2 years basic post-graduate training. The CANDI model has not gone through full due process at the OMA, has serious methodological flaws disadvantaging psychiatry and other undervalued specialties, and **if adopted would lead to a net shift of nearly $870 million dollars (with undervalued specialties getting $435 million less, and family practice getting $434 million more than with current Relative Value Implementation Committee (RVIC) methodology).**

You will recall that the OPA and the OMA Section on Psychiatry had opposed premature adoption of the OMA's new relativity model (CANDI), and had insisted on sufficient time for review, consultation and correction of fundamental methodological flaws of CANDI. OMA General Council voted at its May 2-3 meeting to defer considering a change in the OMA's position on relativity until the November 2009 OMA Council meeting.

The actions of the OPA, the OMA Section on Psychiatry, and Ontario psychiatrists were instrumental in achieving this outcome. Thank you to all of you who took part in the OPA letter writing campaign. We received approximately 250 letters of protest from Ontario psychiatrists in less than 3 days, a remarkable response given the very short timelines. Without such opposition, all indications are that the CANDI model would have been adopted in its current flawed state at the May OMA General Council meeting; instead we were able to successfully pressure the OMA Board of Directors to bring a motion to Council advising deferral.

If the OMA adopts a revised relativity model at its November 2009 Council meeting, this could affect relativity allocations for 2010 and beyond. **Upcoming relativity allocations for October 2009 have already been determined, psychiatry will be receiving a total increase of 9.5% to its sectional allocation.** Please refer to the table at the end of this piece for a detailed breakdown of how that 9.5% will be allocated across psychiatric fees.

While we achieved our immediate goal at deferring CANDI's premature adoption at the May OMA General Council, the battle for relativity is far from over. There continues to be significant opposition of the OMA Relativity Working Group to consider any differences in complexity/intensity/risk between specialist care requiring 5 years minimum training and family practice requiring 2 years minimum training. While the Working Group cites difficulties in comparing complexity as the reason for excluding such a measure from the model, the chair of the Working Group (himself an orthopaedic surgeon) has repeatedly stated he does not see a distinction between the complexity of specialist care compared to family practice care. The Working Group's position seems to reflect this ideology rather than any actual methodological barrier.

The OPA believes it is important to properly value family practice care, but also believes failing to recognize the increased complexity/intensity/risk of specialist care requiring an additional 3 years training undervalues psychiatric care and other specialty care.

Given the ideology of the Working Group and the voting and power structure of the OMA, it is clear specialist care will not be properly valued in CANDI without significant pressure forcing improvements to the CANDI methodology. The OPA, OMA Section on Psychiatry and Coalition of Ontario Psychiatrists plan to work over the next several months to mobilize other specialty groups to have a concerted voice insisting on such improvements in the CANDI model. We will keep you apprised of future developments, and advise of any further member actions that may be helpful prior to the November OMA Council meeting.▲

K. Sonu Gaind, MD, FRCP(C)
Past President, Ontario Psychiatric Association
Tariff Chair, OMA Section on Psychiatry
e-mail: psych@rogers.com

TABLE: Distribution of October 2009 9.5% Psychiatry Sectional Allocation

Fee Code	Description	Existing Fee	Oct 2009 Fee	% increase
A195	Consult – outpatient	$ 162.95	$ 176.23	8.15
A197 / A198	Consultative interview – parent/child	$ 173.80	$ 187.96	8.15
A / C / W895	Consult – inpatient	$ 190.15	$ 205.65	8.15
A / C / W795A	Geriatric Consult	$ 195.55	$ 270.00	38
A / C / W695A	Neurodevelopmental Consult	$ 271.60	$ 324.00	19.3
K 190	Inpatient psychotherapy	$ 68.80	$ 74.41	8.15
K197 / 198	Outpatient psychotherapy/psych care	$ 65.65	$ 71.00	8.15
K199	Inpatient psychiatric care	$ 75.70	$ 81.87	8.15
G478	ECT – inpatient	$ 66.25	$ 71.65	8.15
G479	ECT – outpatient	$ 75.70	$ 81.87	8.15
K191	Family psychiatric care – inpatient	$ 68.80	$ 92.88	35
K193	Family psychotherapy – inpatient	$ 68.80	$ 84.41	22.7
K195 / 196	Outpatient family psychotherapy/care	$ 68.80	$ 80.55	17.08

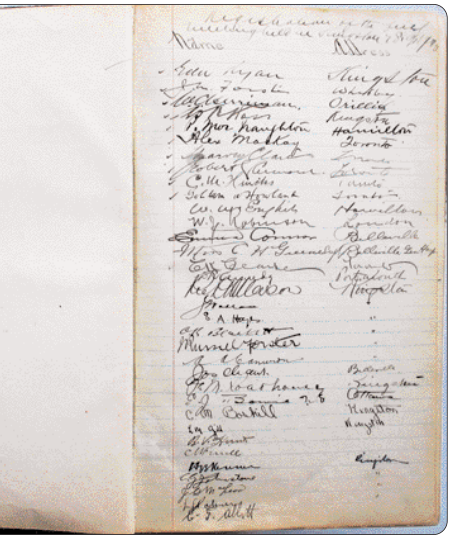
In addition, all group psychotherapy fees and certification fees will increase by 8.15%; CTO fees will increase by 6.5%; and most assessment fees will increase by 10.2%

News from the OPA Archives – Overview

We will be celebrating the 90th Anniversary of the founding of the Ontario Psychiatric Association at next year's Annual Conference in 2010. We plan to publish a series of articles on the history of the OPA in coming months to mark this significant milestone. In the archives, we have now worked through the early years up to 1956. As Archivist, I have gone through a lot of material, but there are significant gaps, particularly in the early years. I am seeking the help of some older members who may have material from that period that they would be willing to contribute to the Archives.

At the Annual Conference this year, we made a presentation about our work so far. The project started innocently enough in a conversation between the Past President, Dick O'Reilly and me about two years ago. I was complaining that when I tried to do a project on the history of the OPA, I found that the archives were in total disarray and had been consigned to dead storage — making them very difficult to retrieve. Dick invited me to join OPA Council and I was subsequently appointed Archivist of the Association.

The rest of the story is told in articles to the *Dialogue* over the past couple of years. We have been in close communication with the CAMH Mental Health Archives and they have some material that will be useful to us. In 2007 we obtained a small bursary from the *Hewson and Griffen Bursaries for Archival Research*. It got us started but because of limited time and funds, we have concentrated on the material from the *Ontario Neuro-Psychiatric Association* from 1920 to 1956 when it was renamed the *Ontario Psychiatric Association*. Most of this early material is contained in the original Minute Book and the Register of attendance at meetings, both of which are rich sources of material.



For the Annual Conference, we prepared posters showing material from these books. These are the little items of OPA's history that we want to preserve through a good archival system. We want to hear from you if you have recollections or items of this sort. Please send them to me or to the OPA:

– John Deadman, Archivist, OPA: *deadmanj@mcmaster.ca*
– Halyna Troian, CAE, OPA: *opa@eopa.ca*

John Deadman, MD, FRCP(C)
Archivist

Dr. Aldwyn B. Stokes (President 1955) in the front row (center) with members of the OPA Executive of that year, probably taken at the Annual Meeting of 1956. The composite photo below, showing OPA Presidents from 1950 to 1977, was probably prepared for the 60th Anniversary of the OPA in 1980.

OPA Psychotherapy Section's 2009 Fall Conference

The Psychotherapy Section is very pleased to bring Dr. Nancy McWilliams to Toronto for the OPA Psychotherapy Section's 2009 Fall Conference on September 26, 2009. Dr. McWilliams is a psychoanalyst and Visiting Professor of Clinical Psychology at the Graduate School of Applied and Professional Psychology, Rutgers University. She is the author of several books, including *Psychoanalytic Diagnosis: Understanding Personality Structure in the Clinical Process, Psychoanalytic Case Formulation,* and *Psychoanalytic Therapy: A Practitioner's Guide*. She is also associate editor of the *Psychodynamic Diagnostic Manual* (PDM). She is Past President of the Division of Psychoanalysis (39) of the American Psychological Association, Consulting Editor of the *Psychoanalytic Review*, and on the editorial board of *Psychoanalytic Psychology*.

Dr. McWilliams has written widely on personality structure and personality disorders, psychodiagnosis, sex and gender, trauma, intensive psychotherapy, and contemporary challenges to the humanistic tradition in psychotherapy. Her books have been translated into twelve languages, and she has lectured widely both nationally and internationally. Her book on case formulation received the Gradiva Award for best psychoanalytic clinical book of 1999; in 2004 she was given the Rosalee Weiss Award for contributions to practice by the Division of Independent Practitioners of the American Psychological Association; and in 2006 she was made an Honorary Member of the American Psychoanalytic Association. A graduate of the National Psychological Association for Psychoanalysis, she is also affiliated with the Center for Psychoanalysis and Psychotherapy of New Jersey and the National Training Program of the National Institute for the Psychotherapies in New York City. She has a private practice in Flemington, New Jersey.

Dr. McWilliams specializes in psychoanalytic psychotherapy and supervision; the relationship between psychodiagnosis and treatment; alternatives to DSM-IV diagnostic conventions; integration of feminist theory and psychoanalytic knowledge; the application of psychoanalytic understanding to the problems of diverse clinical populations; altruism; narcissism; structural diagnosis; dissociation and dissociative disorders.

More information about Dr. McWilliams and her work can be found on: *www.nancymcwilliams.com*.

TOPIC OF THE CONFERENCE

A New Look at Paranoia: Understanding and Addressing Paranoid Dynamics across the Spectrum of Mental Health and Disorder.

DESCRIPTION

Although DSM criteria for diagnosing paranoia involve *externally* observable traits such as suspiciousness, psychoanalysts have followed Freud in viewing paranoia as an *intrapsychic* process characterized by projection and disavowal. The term, whose roots suggest "a mind outside itself," refers to states in which a person finds it difficult to distinguish what is inside from what is outside the self. Phenomenologically, paranoia may represent inadequate psychological separation from a caregiver to whom the paranoid person was anxiously attached. Although most visible in psychotic conditions, paranoid states of mind are common in high-functioning people and present notable therapeutic challenges. Dr. McWilliams will review analytic theory and research on paranoia, emphasizing its origins in humiliation, and will make recommendations for therapists working with paranoid patients.

LEARNING OBJECTIVES

At the end of the conference, participants will be able to:

1. Identify not simply the more familiar persecutory paranoid dynamics (projection and denial of anger), but those involving projection and disavowal of other feelings (e.g., erotomania, paranoid jealousy, megalomania, paranoid hatred).
2. Summarize the suspected etiologies of paranoid dynamics, including experiences of being treated as a (projective) bad object by a caregiver and accordingly subjected to humiliation.
3. Avoid therapeutic attitudes that threaten paranoid patients (e.g., excessive sympathy, efforts to be neutral or abstinent to a degree that strikes the patient as inauthentic, efforts to prove one's goodness).
4. Convey attitudes that allow paranoid patients to elaborate their experience and reduce the shame that underlies paranoid adaptations (e.g., unwavering respect, ruthless honesty, clarity about boundaries, acknowledgment of the grain of truth in the patient's projections).▲

Tina Chadda, MD, FRCP

OPA Psychotherapy Section's
2009 FALL CONFERENCE
Saturday, September 26, 2009
Park Hyatt Hotel, Toronto

Guest Speaker –

Dr. Nancy McWilliams, Ph.D.

Association of General Hospital Psychiatric Services – AGHPS

New Slate of Officers

The AGHPS is pleased to announce the new slate of officers for the period February 2009 – February 2010.

- **Past President:** Dr. Gerry McNestry
- **President:** Dr. David Koczerginski
- **Vice President:** Dr. Allan Rosenbluth
- **Treasurer:** Ms. Jane Sippell

We would like to take this opportunity to thank Dr. Brian Hoffman who is completing his term on the Executive. Dr. Hoffman has been instrumental in the success of the AGHPS over the last several years.

Suicide Prevention – Presenting the Findings

The AGHPS thanks the OPA for the opportunity to share the results of the project *"People at Risk of Suicide: Identifying Activities and Opportunities in Ontario General Hospital Psychiatric Services"* at the OPA Conference held in February 2009.

This project was undertaken with one-time funding from the Ministry of Health and Long Term Care and involved a number of experts and Association members over the last two years. We believe that the information collated in the report can be helpful to clinicians, program leaders, community colleagues, system planners, and funders in continually improving the design and delivery of services to people at risk of suicide.

The report on Phases 1 and 2 was distributed to the Schedule One hospitals in Ontario. You can read the report on our web site at: *www.aghps.com*.

Jane Chamberlin Lecturer

The **Jane Chamberlin Lecturer** for 2009 was **Dr. Paul Links** who presented on his research into the prevention of suicide.

Dr. Links is the incumbent of the Arthur Sommer Rotenberg Chair in Suicide Studies, University of Toronto; the first Chair in North America dedicated to suicide research and is a Professor in the Department of Psychiatry, Faculty of Medicine, University of Toronto. Dr. Links is the Past President for the Canadian Association for Suicide Prevention and President of the Association for Research on Personality Disorders. In January 2009, Dr. Links assumed the role of Editor of the *Journal of Personality Disorders*. Also he is the Deputy Chief of Psychiatry of the St. Michael's Hospital's Mental Health Service.

Jane Chamberlin Award

The AGHPS was honored to present this year's **Jane Chamberlin Award** to **Dr. David Gotlib** on a nomination from Dr. Ty Turner.

Dr. David Gotlib is Medical Director of the Emergency Psychiatry Team, Community Mental Health and the Mobile Crisis Intervention Team at St. Joseph's Health Centre in Toronto.

Dr. Gotlib obtained his first degree, in Computer Science, from the University of Toronto, and then worked for Bell Canada's Computer Communications Group, designing business data networks. Dr. Gotlib left the computer field to attend medical school in Ottawa. He began general practice in Toronto in 1985. His practice increasingly tended towards dealing with patient's mental health issues, and he eventually left his practice in 1994 and did a residency in general and child psychiatry at Johns Hopkins Hospital in Baltimore, MD, where he served as chief resident in the child psychiatry program. He returned to Toronto in 2000 and joined the staff of St. Joseph's Health Centre as Medical Director of the emergency psychiatry team. He developed an Urgent Care Psychiatric Service at St. Joseph's, and later became Medical Director of the Mobile Crisis Intervention Team in May 2005, and added medical directorship of the Community Mental Health Centre to his responsibilities in 2007. In addition to his hospital-based duties, he serves as a consultant to the Griffin Centre's residential treatment program for dually-diagnosed youth, and since 2001 he has been active in the Collaborative Mental Health Care Network, which links Ontario family physicians with psychiatrist mentors to provide easy access to case-by-case support and ongoing professional development. He was co-chair from 2005 to 2007 and continues to serve on the Steering Committee.

Award of Honourable Mention

This year, for the first time, the AGHPS also presented an **Award of Honourable Mention** to **Dr. Greg Jaychuk**, Chief Psychiatry and **Mr. Bill Seymour**, Director Mental Health of Blue Water Health for their project *"An Evaluation of Community Based Discharge Planning"*. The nomination was received by Ms. P. Chapman. We congratulate these individuals and Blue Water Health for their innovation in meeting the needs of those in their care for issues related to mental health.▲

June Hylands
Executive Director, AGHPS

OPA 2009 Annual Conference Highlights

The 89th Annual Conference could not have succeeded without the dedication and tireless support of Dr. Jon Davine, my Co-Chair, Halyna Troian, our new management company, BB&C and our Executive Council. Our success is a direct result of their due diligence at critical times in conference planning. Although lessons have been learned for future conferences the event was a resounding educational success. I also appreciate the Educational Committee and the OPA Council's willingness to take on a new format which was well received by those in attendance. Speakers' evaluations were quite glowing with particular reference to our keynote speakers' topics which were considered "relevant, timely and of great interest to psychiatrists". Brigadier-General Hilary F. Jaeger's *"Mental Health Challenges Associated with Military Operations"* was considered thought-provoking. Many in attendance commented on their enhanced appreciation and understanding of the concerted efforts of the Department of National Defence to meet the mental health needs of military personnel. Several psychiatrists asked how they might help with transitions of those leaving active duty. This is the kind of dialogue that builds partnerships and we are very excited about future initiatives that begin with an open exchange of ideas. Of course, Dr. Janice Stein never fails to deliver a thoughtful and inspiring discussion as she successfully integrates political, social and psychological determinants of health care. The discussion that ensued was almost as lively as the presentation. Lastly, I extend my appreciate to Dr. Cornelia Wieman for her presentation on *"Mental Health Care for Aboriginal Peoples"*. I've valued Nel's mentorship in the past and her comprehensive review of this critical topic. Those in attendance appreciated her assessment of the subject matter and her emphasis on the remarkable resilience of First Nations People.

We are rebuilding the OPA and welcome your attendance at our next Conference on April 23 & 24, 2010. We have room in most of our venues for more attendees. You will be pleasantly surprised by the efforts to re-invigorate our provincial meeting and its value to our membership. Our venue, Le Méridien King Edward Hotel is a real jewel and I think you'll appreciate its history, charm, fine dining and proximity to all that this dynamic City of Toronto has to offer. Please mark your calendar and plan to join the OPA in April 2010.▲

Paul Mulzer, MD, FRCP(C)
President, Ontario Psychiatric Association

Psychoanalytic Couples Therapy: Theory and Techniques

presented by SARAH USHER at the 89th Annual Conference of the Ontario Psychiatric Association, February, 2009.

Couples, married and otherwise, usually come to a psychotherapist as a next-to-last resort, often after many years of unhappiness. They bring their most private selves, in some way urgently needing to expose problems; in another, embarrassed and shamed by what they often perceive as painful personal failure.

Although there are several methods for treating couples in difficulty, this author has found that a psychoanalytic, or psychodynamic, approach is the most useful, as it allows for interpretations of unconscious material, when appropriate, and for long-term treatment, when needed.

A psychodynamically-oriented couples therapist will be informed about, and watch for, complex transference and countertransference reactions as the therapy progresses.

The most common transference — from the patient-couple to the therapist is a parental one. This can cause sibling-like behaviour in the couple, competing for the therapist's attention, or competing to be the compliant — or the non-compliant and rebellious — one. The couples therapist provides a holding environment (Winnicott), a container (Bion), a role model for listening, and a role model for communication.

The most common countertransference is also parental, with the therapist trying to be the teacher and helper of the two partners. However, because of the triangular situation, oedipal issues can re-emerge for the therapist, who may perceive the couple as the oedipal couple, and feel either voyeuristic or even excluded. This, of course, can affect the therapy significantly, particularly if it is not attended to.

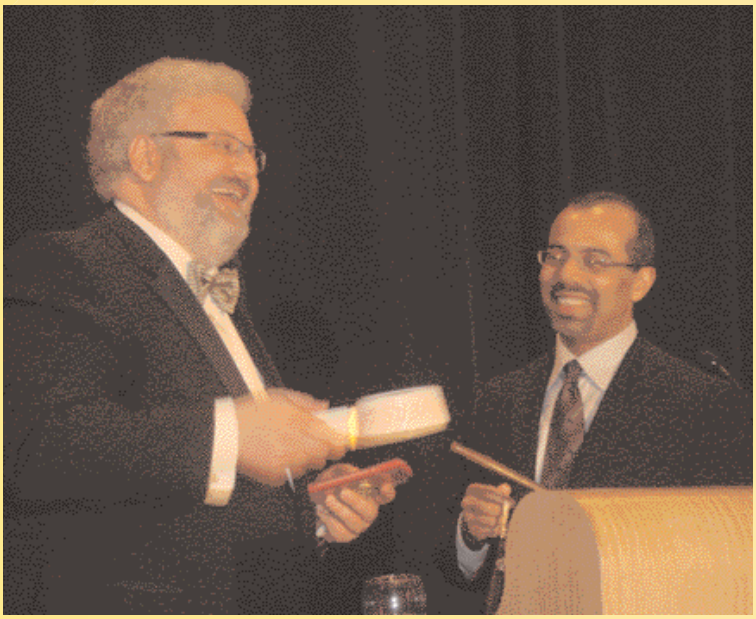
There are other transferences and countertransferences that are evoked, because of the unique triangular situation.

In terms of technique, this author always sees both partners together, the theory being that this keeps the dialogue between them, with the therapist observing. A family history is taken of each individual in the beginning sessions, with the other present. The partners' reactions to each other's histories are often interesting. Doing it this way allows for everyone to carry out, and to understand, interpretations — particularly ones that come from the individual's past.

An approach of mutual contribution, with warmth and humour, is most helpful when working with couples.▲

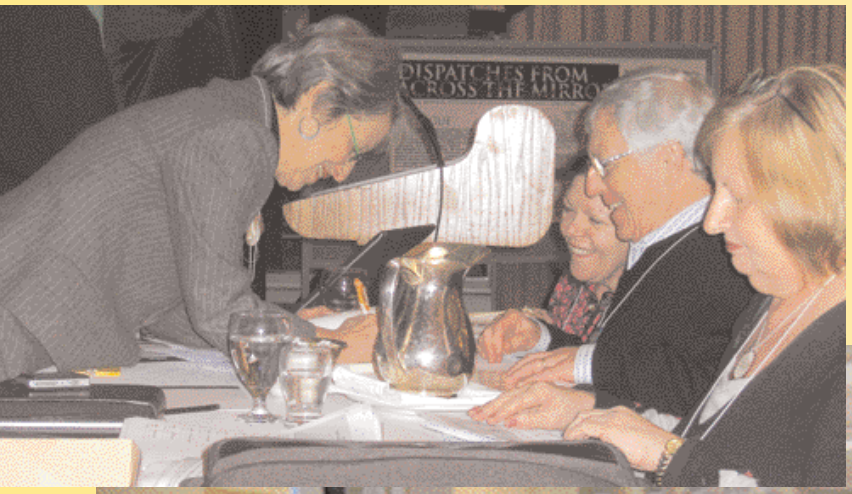
Sarah Usher, Ph.D., C.Psych., is a psychoanalyst in private practice and the author of *What is this Thing Called Love? A Guide to Psychoanalytic Therapy with Couples*, published in 2008, by Routledge.

OPA 2009 Annual Conference… *February 27 & 28, 2009*



"Passing the Torch" – Dr. Paul Mulzer, OPA newly elected President, and Dr. K. Sonu Gaind, now OPA Past President.

OPA Conference – At the podium, Dr. K. Sonu Gaind, 2008 OPA Preside
On the left: Keynote Speaker Dr. Janice Stein with OPA Conference De



Keynote Speaker Brigadier-Gen
On the left: OPA Conference Del

OPA Conference Dinner.

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OPA Conference Delegates at the Dinner.

eral Hilary F. Jaeger.
legates during a break in activities.

Please mark your calendars for the

OPA 2010 ANNUAL CONFERENCE

April 23 & 24, 2010
Toronto, Ontario
Le Méridien King Edward Hotel

Stay tuned for our further announcements of the conference program and registration form!

T. A. Sweet Award – Call for Nominations

Dr. Theodore A. Sweet

The OPA announces its Call for Nominations for the 2010 *T. A. Sweet Award* recipient. This award is presented annually to an individual who has made a major contribution to the understanding of mental illness and its impact on individuals in society.

Previous recipients have included leaders in volunteer and community activities, people from the field of journalism and individuals who suffer from mental illness. Our most recent recipients were: Ron Ellis, Lt. General (Ret.) Roméo Dallaire, Anne Murray, Phil Upshall, Senator Michael Kirby, William MacPhee, Michael Bay and Robert Munsch.

Dr. Ted A. Sweet was the Secretary of the ***Ontario Neuro-Psychiatric Association*** from 1946 until the early 1960s, well after the ONPA had changed its name to the ***Ontario Psychiatric Association*** in 1956. His characteristic signature appeared throughout the minute books of that period. He was a physician at the Ontario Hospital, Whitby, until his retirement in 1965. In his will, he left a bequest to the OPA that was to be used for a good purpose.▲

Please fax your nominations to

905-826-4873

by 5:00 pm on Friday, July 31, 2009.

Please include the following information:

- Name of nominee.
- An explanation (40 lines or less) describing in what way you think they have made a contribution to the understanding of mental illness and its impact on individuals in society.

ONTARIO PSYCHIATRIC ASSOCIATION (OPA) 2010 ANNUAL CONFERENCE CALL FOR ABSTRACTS

The OPA Conference Organizing Committee is accepting submissions in the following categories:

SYMPOSIUM (2.0 – 2.5 hours)
Ideally, a symposium should include several participants from different institutions, areas of the province or disciplines.

WORKSHOP (1.5 – 2.0 hours)
Workshops focus on specific topics and are particularly aimed at skill transmission including case analysis, skills building or role-play.

PANEL DISCUSSION (1.5 – 2.0 hours)
Two or more speakers state their respective viewpoints on a subject. The discussion is moderated, and questions from the floor may be asked.

VIDEO SESSION (45 – 60 minutes)
Videos related to psychiatric disorders and mental health issues. The presenter will be asked to introduce and lead a discussion regarding their video.

POSTER SESSION
There will be a formal poster session (time to be determined), but we ask that posters be on display throughout the meeting.

N.B. Under Maintenance of Certification (MOC) Guidelines, all submissions must allocate a minimum of 25% of the time for audience interaction (i.e. discussion period, Q & A).

DEADLINE FOR SUBMISSIONS: WEDNESDAY, SEPTEMBER 30, 2009.

The official submission form may be downloaded from the OPA web site: ***www.eopa.ca***

Our Education Is Only Limited by Our Imagination

Psychiatry residents at the University of Toronto have formed a dialogue group with "Consumer-Survivors," known as the Residents and Consumers' Initiative, RACI for short. In the fall of 2008, two first-year residents Priya Raju and Rachel Kronick were introduced to Pat Capponi and other consumers and through their imagination formed an opportunity to dissolve barriers and share stories. The evolution of this group has been fascinating. On a monthly basis a group of residents and consumers get together over a meal and discuss a variety of issues that include personal experiences and reflections on the latest newscast. Through this process residents have developed a deeper appreciation of the impact of the social determinants of health on patients with mental illness. It is clear that many individuals in our society have yet to be provided with a safe space in which to discover themselves through their illness. While we have heard of desperate measures, we have also been inspired by how communities form and prosper. One consumer for example, developed a volunteer pet adoption service that provides temporary homes for patients' pets while they are in hospital. In fact, currently the demand for this service has exceeded the supply and additional resources are being researched.

RACI continues to expand in its membership as well as its efforts. Over the past year our work has been presented at various forums including the Harvey Stancer Research Day in Toronto, June 2008; the OPA Annual Conference, February 2009 and was the heart of Advocacy Day for Residents at the University of Toronto, this past May. As a group we have also provided feedback to the Mental Health Commission of Canada and future projects include conferences, workshops and advocacy projects.

For any further information please do not hesitate to contact us by e-mail.▲

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Once Daily

Seroquel XR

quetiapine

Prescribing Summary

Patient Selection Criteria

SEROQUEL XR (quetiapine fumarate extended-release) is indicated for the management of the manifestations of schizophrenia, as monotherapy for the acute management of manic episodes associated with bipolar disorder and as monotherapy for the acute management of depressive episodes associated with bipolar I and bipolar II disorder. *Geriatrics (>65 years of age):* SEROQUEL XR is not indicated in elderly patients with dementia. *Pediatrics (< 18 years of age):* The safety and efficacy of SEROQUEL XR have not been established.

CONTRAINDICATIONS

SEROQUEL XR (quetiapine fumarate extended-release) is contraindicated in patients with a known hypersensitivity to this medication or any of its ingredients.

Special Populations:

Pregnant Women: Patients should be advised to notify their physician if they become pregnant or intend to become pregnant during treatment with SEROQUEL XR. The safety and efficacy of SEROQUEL XR during human pregnancy have not been established. Therefore, SEROQUEL XR should only be used during pregnancy if the expected benefits justify the potential risks. *Nursing Women:* The degree to which quetiapine is excreted into human milk is unknown. Women who are breastfeeding should be advised to avoid breastfeeding while taking SEROQUEL XR. *Pediatrics (< 18 years of age):* The safety and efficacy of SEROQUEL XR have not been established. *Geriatrics (≥ 65 years of age):* The number of patients ≥65 years of age exposed to SEROQUEL XR during clinical trials was limited (n=63). Mean plasma clearance of quetiapine was reduced by 30% to 50% in elderly subjects vs. younger patients. In addition, as this population has more frequent hepatic, renal, central nervous system, and cardiovascular dysfunctions, and more frequent use of concomitant medication, caution should be exercised with the use of SEROQUEL XR in the elderly patient (see ADMINISTRATION). Use in Geriatric Patients with Dementia: Overall Mortality: Elderly patients with dementia treated with atypical antipsychotic drugs showed increased mortality compared to placebo in a meta-analysis of 13 controlled trials of various atypical antipsychotic drugs. In two placebo-controlled trials with oral SEROQUEL in this population, the incidence of mortality was 5.5% for SEROQUEL-treated patients compared to 3.2% for placebo-treated patients. SEROQUEL XR is not indicated in elderly patients with dementia. *Dysphagia:* Esophageal dysmotility and aspiration have been associated with antipsychotic drug use. Aspiration pneumonia is a common cause of morbidity and mortality in elderly patients, in particular those with advanced Alzheimer's dementia. SEROQUEL XR and other antipsychotic drugs should be used cautiously in patients at risk for aspiration pneumonia.

Safety Information

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions. Increased Mortality in Elderly Patients with Dementia: Elderly patients with dementia treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo. Analyses of thirteen placebo-controlled trials with various atypical antipsychotics (mostly duration of 10 weeks) in these patients showed a mean 1.6 fold increase in death rate in the drug-treated patients. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature.

General: Body Temperature Regulation: Disruption of the body's ability to reduce core body temperature has been attributed to antipsychotic agents. Appropriate care is advised when prescribing SEROQUEL XR (quetiapine fumarate extended-release) for patients who will be experiencing conditions which may contribute to an elevation of core temperature, e.g., exercising strenuously, exposure to extreme heat, receiving concomitant medication with anticholinergic activity, or being subject to dehydration. *Acute Withdrawal (discontinuation) Symptoms:* Acute discontinuation symptoms such as, insomnia, nausea, headache, diarrhea, vomiting, dizziness and irritability, have been described after abrupt cessation of antipsychotic drugs including SEROQUEL XR. Gradual withdrawal over a period of at least one to two weeks is advisable. Symptoms usually resolved after 1 week post-discontinuation. *Cardiovascular: Hypotension and Syncope:* As with other drugs that have high α1-adrenergic receptor blocking activity, SEROQUEL XR may induce orthostatic hypotension, dizziness, and sometimes syncope, especially during the initial dose titration period. In placebo-controlled SEROQUEL XR trials, there was little difference in the adverse reaction reporting rate of syncope in patients treated with SEROQUEL XR (0.3%, 4/1239) compared to patients on placebo (0.3%, 2/619). Syncope was reported in 1% (35/4083) of patients treated with SEROQUEL (quetiapine, immediate release formulation), compared with 0.3% (3/1006) on placebo, and 0.4% (2/527) on active control drugs. SEROQUEL XR should be used with caution in patients with known cardiovascular disease (e.g., history of myocardial infarction or ischemic heart disease, heart failure, or conduction abnormalities), cerebrovascular disease, or other conditions predisposing to hypotension (e.g., dehydration, hypovolemia, and treatment with antihypertensive medications) (see OVERDOSAGE). *Cholesterol and Triglyceride Elevations:* In schizophrenia clinical trials, SEROQUEL XR treated patients had increases from baseline in mean cholesterol and triglycerides of 4% and 14%, respectively compared to decreases from baseline in mean cholesterol and triglycerides of 2% and 6% for placebo treated patients. In a 3-week bipolar mania clinical trial, SEROQUEL XR treated patients had increases from baseline in mean cholesterol and triglycerides of 2% and 20%, respectively, compared to decreases in mean cholesterol and triglycerides of 2% and 5% for placebo-treated patients. In a bipolar depression clinical trial, SEROQUEL XR treated patients had increases from baseline in mean cholesterol and increases from baseline in mean triglycerides of 2% and 11%, respectively compared to decreases in mean cholesterol and triglycerides of 3% and 2% for placebo-treated patients. Very common (≥10%) cases of elevations in serum triglyceride levels (>2.258 mmol/L on at least one occasion) and elevations in total cholesterol (predominantly LDL cholesterol) (≥6.2064 mmol/L on at least one occasion) have been observed during treatment with quetiapine in clinical trials (see ADVERSE REACTIONS). Lipid increases should be managed as clinically appropriate. Endocrine and *Metabolic: Hyperglycaemia:* As with some other antipsychotics, hyperglycaemia, and diabetes mellitus (including exacerbation of pre-existing diabetes, diabetic ketoacidosis, and diabetic coma including some fatal cases) in the aggregate have been reported rarely (≥0.01% – <0.1%) during the use of SEROQUEL in post-marketing experience, sometimes in patients with no reported history of hyperglycaemia (see ADVERSE REACTIONS, Post-Market Adverse Drug Reactions). Increases in blood glucose and hyperglycaemia, and occasional reports of diabetes, have been observed in clinical trials with quetiapine (see ADVERSE REACTIONS, Abnormal Hematologic and Clinical Chemistry Findings). Assessment of the relationship between atypical antipsychotic use and glucose abnormalities is complicated by the possibility of an increased background risk of diabetes mellitus in patients with schizophrenia and the increasing incidence of diabetes mellitus in the general population. Given these confounders, the relationship between atypical antipsychotic use and hyperglycaemia-related adverse events is not completely understood. However, epidemiological studies suggest an increased risk of treatment-emergent hyperglycaemia-related adverse events in patients treated with the atypical antipsychotics. Precise risk estimates for hyperglycaemia-related adverse events in patients treated with atypical antipsychotics are not available. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycaemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycaemia during treatment with atypical antipsychotics should undergo fasting blood glucose testing. In some cases, hyperglycaemia has resolved when the atypical antipsychotic was discontinued; however, some patients required continuation of anti-diabetic treatment despite discontinuation of the suspect drug. Patients with risk factors for diabetes mellitus (e.g., obesity, family history of diabetes) who are starting treatment with atypical antipsychotics should undergo fasting blood glucose testing at the beginning of treatment and periodically during treatment. Patients with an established diagnosis of diabetes mellitus who are started on atypical antipsychotics should be monitored regularly for worsening of glucose control. *Hyperprolactinaemia:* An elevation of prolactin levels was not demonstrated in schizophrenia clinical trials with SEROQUEL XR as compared with placebo. In bipolar disorder clinical trials with SEROQUEL XR, elevation in prolactin levels occurred in 2.4% (7/288) of patients treated with SEROQUEL XR compared to 0.7% (2/300) of patients treated with placebo. Increased prolactin levels with quetiapine were observed in rat studies. As is common with compounds which stimulate prolactin release, the administration of quetiapine resulted in an increase in the incidence of mammary neoplasms in rats. The physiological differences between rats and humans with regard to prolactin make the clinical significance of these findings unclear. To date, neither clinical nor epidemiological studies have shown an association between chronic administration of drugs that stimulate prolactin release, and mammary tumourigenesis. Tissue culture experiments, however, indicate that approximately one third of human breast cancers are prolactin dependent *in vitro*; a factor of potential importance if prescription of these drugs is contemplated in a patient with previously detected breast cancer. Possible manifestations associated with elevated prolactin levels are amenorrhea, galactorrhea, and menorrhagia. In the multiple fixed-dose schizophrenic clinical trial there were no differences in prolactin levels at study completion for SEROQUEL, across the recommended dose range, and placebo. *Hypothyroidism:* In SEROQUEL XR clinical trials, 0.5% (4/805) of patients on SEROQUEL XR compared to 0% (0/262) on placebo experienced decreased free thyroxine and 2.7% (21/786) on SEROQUEL XR compared to 1.2% (3/256) on placebo experienced increased TSH; however, no patients experienced a combination of clinically significant decreased free thyroxine and increased TSH. No patients had events of hypothyroidism. In clinical trials, on average SEROQUEL was associated with about a 20% mean reduction in thyroxine levels (both total and free). Forty-two percent of SEROQUEL-treated patients showed at least a 30% reduction in total T, and 7% showed at least a 50% reduction. Maximum reduction of thyroxine levels generally occurred during the first two to four weeks of treatment with SEROQUEL. These reductions were maintained without adaptation or progression during longer term treatment. Decreases in T_4 were not associated with systematic changes in TSH or clinical signs or symptoms of hypothyroidism. Approximately 0.4% (12/2595) of patients treated with SEROQUEL experienced persistent increases in TSH, and 0.25% of patients were treated with thyroid replacement. *Weight Gain:* In 6-week placebo-controlled schizophrenic clinical trials, for patients treated with SEROQUEL XR mean weight gain was 1.77 kg (n=951) compared to 2.19 kg (n=414) in patients treated with SEROQUEL. For patients treated with placebo the mean weight gain was 0.26 kg (n=319). In a 3-week placebo-controlled bipolar mania clinical trial, for patients treated with SEROQUEL XR mean weight gain was 1.3 kg (n=151) compared to 0.1 kg (n=160) in patients treated with placebo. In an 8-week placebo-controlled bipolar depression clinical trial, for patients treated with SEROQUEL XR mean weight gain was 1.3 kg (n=137) compared to -0.2 kg (n=140) in patients treated with placebo. *Gastrointestinal: Anticholinergic Effect:* Consistent with its dopamine antagonist effects, SEROQUEL XR may have an anticholinergic effect. Such an effect may mask signs of toxicity due to overdosage of other drugs or may mask symptoms of disease such as brain tumour or intestinal obstruction. *Hematologic: Neutropenia:* Severe neutropenia (<0.5 x 10⁹/L) has been uncommonly reported in quetiapine clinical trials. There was no apparent dose relationship. Possible risk factors for leucopenia and/or neutropenia include pre-existing low white cell count (WBC) and history of drug induced leucopenia and/or neutropenia. SEROQUEL XR should be discontinued in patients with a neutrophil count <1.0 x 10⁹/L. These patients should be observed for signs and symptoms of infection and neutrophil counts followed (until they exceed 1.5 x 10⁹/L) (see ADVERSE REACTIONS, Abnormal Hematologic and Clinical Chemistry Findings and Post-Market Adverse Drug Reactions). *Hepatic: Hepatic Impairment:* Decreased clearance of SEROQUEL was observed in patients with mild hepatic impairment. No pharmacokinetic data are available for quetiapine in patients with moderate or severe hepatic impairment. However, should clinical judgement deem treatment with SEROQUEL XR necessary, the drug should be used with great caution in patients with moderate or severe hepatic impairment (see ADMINISTRATION). *Transaminase Elevations:* Asymptomatic, transient, and reversible elevations in serum transaminases (primarily ALT) associated with SEROQUEL XR have been reported. The proportions of patients with transaminase elevations of >3 times the upper limits of the normal reference range in a pool of placebo-controlled trials ranged between 1% and 2% for SEROQUEL XR compared to 2% for placebo.

During premarketing clinical trials, therapy with SEROQUEL was associated with elevation of hepatic transaminases, primarily ALT. Within a clinical trial database of 1892 SEROQUEL-treated schizophrenic patients, with baseline ALT levels <60 IU/L, 5.3% (101/1892) had treatment-emergent ALT elevations to >120 IU/L, 1.5% (29/1892) had elevations to >200 IU/L, and 0.2% (3/1892) had elevations to >400 IU/L. No patients had values in excess of 800 IU/L. None of the SEROQUEL-treated patients who had elevated transaminase values manifested clinical symptomatology associated with liver impairment. The majority of transaminase elevations were seen during the first two months of treatment. Most elevations were transient (80%) while patients continued on SEROQUEL therapy. Of the 101 SEROQUEL-treated patients whose enzyme levels increased to >120 IU/L, 40 discontinued treatment while their ALT values were still raised. In 114 SEROQUEL-treated patients whose baseline ALT was >90 IU/L, only 1 experienced an elevation to >400 IU/L. Precautions should be exercised when using SEROQUEL XR in patients with pre-existing hepatic disorders, in patients who are being treated with potentially hepatotoxic drugs, or if treatment-emergent signs or symptoms of hepatic impairment appear. For patients who have known or suspected abnormal hepatic function prior to starting SEROQUEL XR, standard clinical assessment, including measurement of transaminase levels is recommended. Periodic clinical reassessment with transaminase levels is recommended for such patients, as well as for patients who develop any signs and symptoms suggestive of a new onset liver disorder during SEROQUEL XR therapy. **Neurologic:** ***Neuroleptic Malignant Syndrome (NMS):*** Neuroleptic Malignant Syndrome is a potentially fatal symptom complex that has been reported in association with antipsychotic drugs, including SEROQUEL XR. The clinical manifestations of NMS are hyperthermia, muscle rigidity, altered mental status, and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmia). Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis) and acute renal failure. In arriving at a diagnosis, it is important to identify cases where the clinical presentation includes both serious medical illness (e.g., pneumonia, systemic infection, etc.) and untreated or inadequately treated extrapyramidal signs and symptoms. Other important considerations in the differential diagnosis include central anticholinergic toxicity, heat stroke, drug fever and primary central nervous system pathology. The management of NMS should include immediate discontinuation of antipsychotic drugs, including SEROQUEL XR, and other drugs not essential to concurrent therapy; intensive symptomatic treatment and medical monitoring; and treatment of any concomitant serious medical problems for which specific treatments are available. There is no general agreement about specific pharmacological treatment regimens for uncomplicated NMS. If a patient requires antipsychotic drug treatment after recovery from NMS, the potential reintroduction of drug therapy should be carefully considered. The patient should be carefully monitored since recurrences of NMS have been reported. ***Tardive Dyskinesia (TD) and Extrapyramidal Symptoms (EPS):*** Tardive dyskinesia is a syndrome of potentially irreversible, involuntary, dyskinetic movements that may develop in patients treated with antipsychotic drugs. Although the prevalence of the syndrome appears to be highest among the elderly, especially elderly women, it is impossible to rely upon estimates to predict which patients are likely to develop the syndrome. In short-term placebo-controlled clinical trials in schizophrenia and bipolar mania, the aggregated incidence of EPS-related adverse events was similar to placebo (schizophrenia: 7.8% for quetiapine and 8.0% for placebo; bipolar mania: 11.2% for quetiapine and 11.4% for placebo). In short-term placebo-controlled clinical trials in bipolar depression, the aggregated incidence of EPS-related adverse events was 8.9% for quetiapine compared to 3.8% for placebo. The incidence of individual EPS-related adverse events (e.g., akathisia, extrapyramidal disorder, tremor, dyskinesia, dystonia, restlessness, muscle contractions involuntary, psychomotor hyperactivity and muscle rigidity), however was generally low and did not exceed 4% for any individual adverse event. In long-term studies of schizophrenia and bipolar disorder the aggregated exposure adjusted incidence of treatment-emergent EPS was similar between quetiapine and placebo. The risk of developing TD and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic drugs administered to the patient increase. However, the syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses. There is no known treatment for established cases of TD, although the syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn. Antipsychotic treatment, itself, however, may suppress (or partially suppress) the signs and symptoms of the syndrome and thereby may possibly mask the underlying process. The effect that symptomatic suppression has upon the long-term course of the syndrome is unknown. Given these considerations, SEROQUEL XR should be prescribed in a manner that is most likely to minimize the occurrence of TD. Chronic antipsychotic treatment should generally be reserved for patients who appear to suffer from a chronic illness that is known to respond to antipsychotic drugs, and for whom alternative, equally effective, but potentially less harmful treatments are not available or appropriate. In patients who do require chronic treatment, the smallest dose and the shortest duration of treatment producing a satisfactory clinical response should be sought. The need for continued treatment should be reassessed periodically. If signs and symptoms of TD appear in a patient on SEROQUEL XR, drug discontinuation should be considered. However, some patients may require treatment with SEROQUEL XR despite the presence of the syndrome. ***Seizures:*** In controlled clinical trials with SEROQUEL XR, there was no difference in the incidence of seizures in patients treated with SEROQUEL XR (0.1%, 1/1259) or placebo (0.5%, 3/619). Nonetheless, as with other antipsychotics, caution is recommended when treating patients with a history of seizures or with conditions associated with a lowered seizure threshold (see ADVERSE REACTIONS). ***Potential Effect on Cognitive and Motor Performance:*** Somnolence was a very commonly reported adverse event in patients treated with SEROQUEL XR, especially during the initial dose titration period. Since SEROQUEL XR may cause sedation and impair motor skill, patients should be cautioned about performing activities requiring mental alertness, such as operating a motor vehicle or hazardous machinery, until they are reasonably certain that therapy with SEROQUEL XR does not affect them adversely. **Ophthalmologic:** ***Cataracts:*** **The development of cataracts was observed in association with quetiapine treatment in chronic dog studies at 4 times the recommended lowest dose. Lens changes have also been observed in patients during long-term SEROQUEL treatment, but a causal relationship to SEROQUEL use has not been established. The possibility of lenticular changes during long-term use of SEROQUEL XR in man, thus can not be excluded at this time. Eye examinations (e.g., slit lamp exams) prior to or shortly after initiation of treatment with SEROQUEL XR and at 6-month intervals thereafter, are recommended. If clinically significant lens changes associated with SEROQUEL XR use are observed, discontinuation of SEROQUEL XR should be considered. Psychiatric: Suicide:** The possibility of suicide or attempted suicide is inherent in schizophrenia and bipolar disorder, and thus close supervision and appropriate clinical management of high-risk patients should accompany drug therapy. In a bipolar mania clinical trial, the incidence of treatment emergent suicidal ideation or suicidal behavior, as measured by the Columbia Analysis of Suicidal Behaviour, was 1.3% for SEROQUEL XR treated patients and 3.8% for placebo-treated patients. In a bipolar depression clinical trial, the incidence of treatment emergent suicidal ideation or suicidal behaviour, as measured by the Columbia Analysis of Suicidal Behaviour, was 0.7% for SEROQUEL XR treated patients and 1.4% for placebo-treated patients. **Renal:** There is little experience with SEROQUEL XR in patients with renal impairment, except in a few (subclinical) single dose study with SEROQUEL. SEROQUEL XR should thus be used with caution in patients with known renal impairment, especially during the initial dosing period (see ADMINISTRATION).

ADVERSE REACTIONS

Commonly Observed Adverse Events in Short-Term Placebo-Controlled Clinical Trials: ***Schizophrenia:*** During acute therapy with SEROQUEL XR, the most commonly observed adverse events associated with the use of SEROQUEL XR (incidence of at least 5%, and an incidence at least 5% higher than that observed with placebo) were sedation, dry mouth, somnolence, and dizziness. ***Bipolar Disorder: Bipolar Mania:*** During acute therapy with SEROQUEL XR, the most commonly observed adverse events associated with the use of SEROQUEL XR (incidence of at least 5%, and an incidence at least 5% higher than that observed with placebo) were sedation, dry mouth, somnolence, constipation, dizziness, weight gain and dysarthria. ***Bipolar Depression:*** During acute therapy with SEROQUEL XR, the most commonly observed adverse events associated with the use of SEROQUEL XR (incidence of at least 5%, and an incidence at least 5% higher than that observed with placebo) were dry mouth, somnolence, sedation, increased appetite, weight gain and dyspepsia. **Adverse Events Associated with Discontinuation in Short-Term Placebo-Controlled Clinical Trials:** ***Schizophrenia:*** In short-term, placebo-controlled schizophrenic trials, there was no difference in the incidence of adverse events associated with discontinuation of SEROQUEL XR or placebo. Overall, 6.4% of SEROQUEL XR-treated patients discontinued treatment due to adverse events compared to 7.5% of placebo-treated patients. ***Bipolar Disorder: Bipolar Mania:*** In a 3-week placebo-controlled bipolar mania trial, 4.6% of patients on SEROQUEL XR discontinued due to adverse events compared to 8.1% on placebo. ***Bipolar Depression:*** In an 8-week placebo-controlled bipolar depression trial, 13.1% of patients on SEROQUEL XR discontinued due to adverse events compared to 3.6% on placebo. Sedation (6.6%) and somnolence (3.6%) were the most common adverse events leading to discontinuation in the SEROQUEL XR treatment group (see SUPPLEMENTAL PRODUCT INFORMATION).

To report adverse events:
AstraZeneca Canada Inc.
Mississauga, Ontario L4Y 1M4
www.astrazeneca.ca T 1-800-433-0783 F 1-800-267-5743

DRUG INTERACTIONS

Drug-Drug Interactions: Given the primary central nervous system effects of quetiapine, SEROQUEL XR (quetiapine fumarate extended-release) should be used with caution in combination with other centrally acting drugs (see SUPPLEMENTAL PRODUCT INFORMATION).

8 Administration

SEROQUEL XR (quetiapine fumarate extended-release) tablets should be swallowed whole and not split, chewed, or crushed. SEROQUEL XR can be administered with or without food. SEROQUEL XR should be administered once daily, generally in the evening. **Schizophrenia:** **Usual Dose:** The titration rate, based on the clinical trials, is shown in the table below.

	Day 1	Day 2	After Day 2
Once daily dosing	300 mg	600 mg	Up to 800 mg

The dose should be adjusted within the effective dose range of 400 mg to 800 mg per day, depending on the clinical response and tolerability of the patient. In a controlled clinical trial, the treatment effect size of 600 mg and 800 mg doses of SEROQUEL XR was greater than that of the 400 mg dose. In schizophrenia, the safety of doses above 800 mg/day has not been evaluated. The need for continuing existing EPS medications should be re-evaluated periodically as SEROQUEL XR has not been associated with treatment-emergent EPS across the clinical dose range. **Bipolar Disorder: Bipolar Mania:** **Usual Dose:** The titration rate, based on the clinical trial is shown in the table below.

	Day 1	Day 2	After Day 2
Once daily dosing	300 mg	600 mg	Up to 800 mg

The dose should be adjusted within the effective dose range of 400 mg to 800 mg/day, depending on the clinical response and tolerability of the patient. In bipolar mania, the safety of doses of above 800 mg/day has not been evaluated. **Bipolar Disorder: Bipolar Depression:** **Usual Dose:** The titration rate, based on the clinical trial is shown in the table below.

	Day 1	Day 2	Day 3	Day 4 and thereafter
Once daily dosing	50 mg	100 mg	200 mg	300 mg

The usual target dose is 300 mg/day. The dose may be further increased depending on the response and tolerability of the patient. The maximum dose is 600 mg/day. In SEROQUEL clinical trials antidepressant efficacy was demonstrated with SEROQUEL at both 300 mg/day and 600 mg/day, however no additional benefit was seen in the 600 mg group during short-term treatment. In bipolar depression, the safety of doses of quetiapine above 600 mg/day has not been evaluated. **Switching patients from SEROQUEL tablets to SEROQUEL XR tablets:** For more convenient dosing, patients who are currently being treated with divided doses of SEROQUEL (quetiapine, immediate release formulation) may be switched to SEROQUEL XR

at the equivalent total daily dose taken once daily. Individual dosage adjustments may be necessary. Dosing Considerations in Special Populations: *Elderly:* As with other antipsychotics, SEROQUEL XR should be used with caution in the elderly, especially during the initial dosing period. The rate of dose titration of SEROQUEL XR may need to be slower, and the daily therapeutic target dose lower, than that used in younger patients. Elderly patients should be started on the lowest available dose (i.e., 50 mg/day) of SEROQUEL XR. The dose can be increased in increments of 50 mg/day to an effective dose, depending on the clinical response and tolerance of the individual patient. *Hepatic Impairment:* Quetiapine is extensively metabolized by the liver. Therefore, SEROQUEL XR should be used with caution in patients with mild hepatic impairment, especially during the initial dosing period. Patients with mild hepatic impairment should be started on the lowest available dose (i.e., 50 mg/day) of SEROQUEL XR. The dose should be increased daily in increments of 50 mg/day to an effective dose, depending on the clinical response and tolerance of the individual patient (see WARNINGS AND PRECAUTIONS, Hepatic). *Renal Impairment:* As clinical experience is lacking, caution is advised (see WARNINGS AND PRECAUTIONS, Renal). *Missed Dose:* SEROQUEL XR should be taken at the same time each day. If a previous days dose has been missed, administration should be resumed the next day at the normal administration time. Dosage Forms and Packaging: SEROQUEL XR (quetiapine fumarate extended-release) is available as film-coated tablets containing quetiapine fumarate equivalent to 50 mg, 200 mg, 300 mg or 400 mg of quetiapine free base as follows: 50 mg quetiapine tablets are peach coloured, capsule-shaped, biconvex, imprinted with "XR 50" on one side and plain on the other, available in high density polyethylene (HDPE) bottles of 60 tablets. 200 mg quetiapine tablets are yellow, capsule-shaped, biconvex, imprinted with "XR 200" on one side and plain on the other, available in HDPE bottles of 60 tablets. 300 mg quetiapine tablets are pale yellow, capsule-shaped, biconvex, imprinted with "XR 300" on one side and plain on the other, available in HDPE bottles of 60 tablets. 400 mg quetiapine tablets are white, capsule-shaped, biconvex, imprinted with "XR 400" on one side and plain on the other, available in HDPE bottles of 60 tablets.

SUPPLEMENTAL PRODUCT INFORMATION

ADVERSE REACTIONS

The stated frequencies of adverse events represent the proportion of individuals who experienced, at least once, a treatment-emergent adverse event of the type listed. An event was considered treatment-emergent if it occurred for the first time or worsened while receiving therapy following baseline evaluation. *Clinical Trial Adverse Drug Reactions:* The prescriber should be aware that the figures in the tables and tabulations cannot be used to predict the incidence of side effects in the course of usual medical practice where patient characteristics and other factors differ from those that prevailed in the clinical trials. Similarly, the stated frequencies cannot be compared with figures obtained from other clinical investigations involving different treatments, uses, and investigators. The figures cited, however, do provide the prescribing physician with some basis for estimating the relative contribution of drug and nondrug factors to the side effect incidences in the population studied. The information below is derived from a clinical trial database for SEROQUEL XR (quetiapine fumarate extended-release) consisting of 1329 patients exposed to SEROQUEL XR for the treatment of schizophrenia, bipolar mania and bipolar depression, in short-term placebo-controlled trials. The experience corresponds to approximately 82.9 patient-years.

Table 1 Adverse Events Reported for at Least 1% of SEROQUEL XR-Treated Subjects (Doses Ranging From 150G to 800G mg/day) and for a Higher Percentage of SEROQUEL XR-Treated Subjects than Subjects Who Received Placebo in Short-Term, Placebo-Controlled Schizophrenia Phase III Trials

Body system and MedDRA Term*	Percentage of subjects with adverse events*	
	SEROQUEL XR (n=457)	Placebo (n=319)
Whole body		
Fatigue	3	2
Anxiety	2	1
Irritability	1	0
Pyrexia	1	0
Nervous system		
Sedation	12	7
Somnolence	12	4
Dizziness	10	4
Tremor	2	1
Restlessness	2	1
Gastrointestinal system		
Dry mouth	12	1
Constipation	6	5
Dyspepsia	5	2
Cardiovascular system		
Orthostatic hypotension	7	5
Hypotension	3	1
Tachycardia	3	1
Heart rate increased	4	1
Metabolic and nutritional disorders		
Increased appetite	2	0
Special senses		
Vision blurred	2	1

* Events for which SEROQUEL XR incidence was equal to or less than placebo are not listed in the table, but included the following: headache, insomnia, and nausea.
† Patients with multiple events falling under the same preferred term are counted only once in that term.

Table 2 Adverse Events Reported for at Least 1% of SEROQUEL XR-Treated Subjects (Doses Ranging From 300G to 800G mg/day) and for a Higher Percentage of SEROQUEL XR-Treated Subjects than Subjects Who Received Placebo in a Short-Term (3-Week), Placebo-Controlled Bipolar Mania Phase III Trial

Body system and MedDRA Term*	Percentage of subjects with adverse events*	
	SEROQUEL XR (n=510)	Placebo (n=160)
General disorders and administration site conditions		
Fatigue	7	4
Contusion	1	0
Pain	1	0
Nervous system disorders		
Sedation	34	8
Somnolence	17	4
Dizziness	10	4
Dysarthria	5	0
Lethargy	2	1
Sluggishness	2	1
Dizziness postural	1	0
Gastrointestinal disorders		
Dry mouth	24	7
Constipation	10	3
Dyspepsia	7	4
Toothache	3	1
Cardiovascular disorders		
Heart rate increased	3	0
Orthostatic hypotension	3	0
Tachycardia	2	1
Metabolic and nutritional disorders		
Weight increased	7	1
Increased appetite	4	2
Musculoskeletal and connective tissue disorders		
Back pain	3	2
Arthralgia	1	0
Psychiatric disorders		
Abnormal dreams	3	0
Bipolar I disorder	1	0
Respiratory disorders		
Nasal congestion	5	1
Dry throat	1	0
Special senses		
Vision blurred	2	1

* Events for which SEROQUEL XR incidence was equal to or less than placebo are not listed in the table.
† Patients reports percentages rounded to the nearest integer.
‡ Patients with multiple events falling under the same preferred term are counted only once in that term.

Table 3 Adverse Events Reported for at Least 1% of SEROQUEL XR-Treated Subjects (Doses of 300G mg/Day) and for a Higher Percentage of SEROQUEL XR-Treated Subjects than Subjects Who Received Placebo in a Short-Term (3-Week), Placebo-Controlled Bipolar Depression Phase III Trial

Body system and MedDRA Term*	Percentage of subjects with adverse events*	
	SEROQUEL XR (n=157)	Placebo (n=140)
General disorders		
Fatigue	6	2
Irritability	4	3
Anxiety	2	1
Nervous system disorders		
Somnolence	29	6
Sedation	25	7
Dizziness	13	11
Paraesthesia	3	2
Dysarthria	2	0
Disturbance in attention	2	1
Hypersomnia	1	0
Akathisia	1	0
Akinesia	1	0
Gastrointestinal disorders		
Dry mouth	37	7
Constipation	8	4
Dyspepsia	7	1
Toothache	3	0
Cardiovascular disorders		
Heart rate increased	1	0
Infection and infestations		
Cystourethritis viral	4	1
Urinary tract infection	2	0
Metabolic and nutritional disorders		
Increased appetite	12	6
Weight increased	7	1
Decreased appetite	2	1
Musculoskeletal and connective tissue disorders		
Arthralgia	4	1
Back pain	3	1
Muscle spasms	3	1
Neck pain	1	0

Body system and MedDRA Term*	Percentage of subjects with adverse events*	
	SEROQUEL XR (n=1027)	Placebo (n=1 140)
Psychiatric disorders		
Abnormal dreams	5	0
Confusional state	1	0
Disorientation	1	0
Skin and subcutaneous tissue disorders		
Hyperhidrosis	2	1

* Events for which SEROQUEL XR incidence was equal to or less than placebo are not listed in the table.
† Table reports percentages rounded to the nearest integer.
‡ Patients with multiple events falling under the system preferred term are counted only once in that term.

Other Adverse Events: Weight Gain: In 6-week placebo-controlled schizophrenia clinical trials, for patients treated with SEROQUEL XR mean weight gain was 1.77 kg (n=451) compared to 0.19 kg (n=474) for patients treated with SEROQUEL (quetiapine, immediate release formulation). For patients treated with placebo the mean weight gain was 0.56 kg (n=311). In a 3-week placebo-controlled bipolar mania clinical trial, for patients treated with SEROQUEL XR mean weight gain was 1.5 kg (n=151) compared to 0.1 kg (n=140) in patients treated with placebo (see WARNINGS AND PRECAUTIONS). In one 3-week placebo-controlled bipolar depression clinical trial, for patients treated with SEROQUEL XR mean weight gain was 1.3 kg (n=257) compared to 0.3 kg (n=240) in patients treated with placebo (see WARNINGS AND PRECAUTIONS). Seizures: There have been uncommon reports (≥0.1% – <1%) of seizures in patients administered quetiapine, although the frequency was no greater than that observed in patients administered placebo in controlled clinical trials (see WARNINGS AND PRECAUTIONS, Neuroleptic Malignant Syndrome). Neuroleptic Malignant Syndrome: There have been uncommon cases of neuroleptic malignant syndrome in patients administered quetiapine. Priapism: There have been rare reports (≥0.01% – <0.1%) of priapism in patients administered quetiapine. Somnolence: Somnolence may occur, usually during the first two weeks of treatment, which generally resolves with the continued administration of SEROQUEL XR. Neuroleptic Malignant Syndrome: As with other antipsychotics, rare cases of neuroleptic malignant syndrome have been reported in patients treated with quetiapine (see WARNINGS AND PRECAUTIONS, Neuroleptic). Withdrawal Symptoms: As with other antipsychotics, rare cases of withdrawal symptoms have been reported in patients treated with quetiapine. Metabolic: There have been uncommon reports of diabetic ketoacidosis in patients administered quetiapine. Hyperprolactinemia: Uncommon cases of hyperprolactinemia including symptomatic have been reported. ECG Changes: 0.8% of SEROQUEL XR patients, and no placebo patients, had tachycardia (>1 20 bpm) at any time during the trials. SEROQUEL XR was associated with a mean increase in heart rate, corrected for HR, of 7 beats per minute compared to a mean decrease of 1 beat per minute for placebo. This is consistent with the rates of SEROQUEL. Thus slight monitoring of tachycardia may be relevant to the potential of SEROQUEL XR for inducing orthostatic changes (see WARNINGS AND PRECAUTIONS, Cardiovascular). Extrapyramidal Symptoms (EPS): In three short-term placebo-controlled clinical trials for the treatment of schizophrenia, utilizing doses between 1000 mg and 1800 mg of SEROQUEL XR, the incidence of any adverse events potentially related to EPS was 7.5% for SEROQUEL XR, 7.7% for SEROQUEL, and 4.7% in the placebo group and without evidence of dose response. In these studies, the incidence rates of the individual adverse events (eg, akathisia, extrapyramidal disorder, tremor, dyskinesia, dystonia, restlessness, and muscle rigidity) were generally low and did not exceed 3% for any treatment group. At the end of treatment, the mean change from baseline in SAS total score and BARS Global Assessment score was similar across the treatment groups. The use of concomitant anticholinergic medication was infrequent and similar across the treatment groups. The incidence of EPS was consistent with that seen with the profile of SEROQUEL in schizophrenic patients. The incidence of EPS did not increase with the dose of SEROQUEL XR. In short-term placebo-controlled clinical trials in schizophrenic and bipolar mania, the aggregated incidence of EPS-related adverse events was similar to placebo (schizophrenia: 7.8% for quetiapine and 8.2% for placebo; bipolar mania: 11.2% for quetiapine and 11.4% for placebo). In short-term placebo-controlled clinical trials in bipolar depression, the aggregated incidence of EPS-related adverse events was 6.9% for quetiapine compared to 5.8% for placebo. The incidence of individual EPS-related adverse events (e.g., akathisia, extrapyramidal disorder, tremor, dyskinesia, dystonia, restlessness, muscle contractions involuntary, psychomotor hyperactivity and muscle rigidity), however were generally low and did not exceed 4% for any individual adverse event. In long-term studies of schizophrenia and bipolar disorder the aggregated exposure-adjusted incidence of treatment-emergent EPS was similar between quetiapine and placebo. Dyskinesia: There have been uncommon cases of dyskinesia in patients administered quetiapine. In clinical trials, an increase in the rate of dyskinesia with quetiapine versus placebo was only observed in bipolar depression. Hypotension: There have been uncommon cases of hypotension in patients administered quetiapine. Acute Withdrawal (discontinuation): Symptoms: Acute discontinuation symptoms such as insomnia, nausea, headache, diarrhea, vomiting, dizziness and irritability, have been described after abrupt cessation of antipsychotic drugs including SEROQUEL XR. Gradual withdrawal over a period of at least one to two weeks is advisable. Symptoms usually resolved after 1 week, post-discontinuation. Abnormal Hematologic and Clinical Chemistry Findings: As with other antipsychotics, common cases of neutropenia and/or neutropenia have been observed in patients administered quetiapine. Uncommon cases of neutrophilia have been observed. In three pre-SEROQUEL XR placebo-controlled monotherapy clinical trials, among patients with a baseline neutrophil count >1.5 X 10⁹/L, the incidence of at least one occurrence of neutrophil count <1.5 X 10⁹/L was 1.8% in patients treated with SEROQUEL XR and 1.8% for SEROQUEL, compared to 0.8% in placebo-treated patients. In all placebo-controlled monotherapy clinical trials among patients with a baseline neutrophil count >1.5 x 10⁹/L, the incidence of at least one occurrence of neutrophil count <1.5 x 10⁹/L was 1.73% in patients treated with SEROQUEL, compared to 0.73% in placebo-treated patients. In clinical trials conducted prior to protocol amendment for abnormal duration of patients with treatment-emergent neutrophil count <1.0 x 10⁹/L, among patients with a baseline neutrophil count ≥1.5 x 10⁹/L, the incidence of at least one occurrence of neutrophil count <1.5 x 10⁹/L was 0.7% for patients treated with SEROQUEL and 0% in placebo-treated patients and the incidence ≥1.5 – <1.0 x 10⁹/L was 0.79% in patients treated with SEROQUEL and 0.17% in placebo-treated patients. (see WARNINGS AND PRECAUTIONS, Hematological). Common cases of asymptomatic elevations in serum transaminases (ALT, AST) or uncommon cases of γGT, bilirubin have been observed and in some patients administered quetiapine. These elevations were usually reversible on continued quetiapine treatment (see WARNINGS AND PRECAUTIONS, Hepatic). SEROQUEL treatment was associated with small dose-related decreases in thyroid hormone levels, particularly total T, and free T. The reduction in total and free T, was prevalent within the first 2 to 4 weeks of quetiapine treatment, with no further reduction during long-term treatment. There was no evidence of clinically significant changes in TSH concentration over time. In nearly all cases, cessation of quetiapine treatment was associated with a reversal of the effects on total and free T, irrespective of the duration of treatment. Smaller decreases in total T, and mean free T, were seen only at higher doses. Levels of TBG were unchanged and in general asymptomatic increases in TSH were not observed and these were no indication that SEROQUEL causes clinically relevant hypothyroidism (see WARNINGS AND PRECAUTIONS, Endocrine and Metabolism). Hyperglycemia: Mean glucose increases in hyperglycemic levels. Fasting blood glucose >7.0 mmol/L or a non-fasting blood glucose >11.1 mmol/L on at least one occasion) have been observed commonly (≥1% – <10%) with quetiapine in clinical trials. In 3 long-term bipolar maintenance placebo-controlled adjunct clinical trials, mean exposure 213 days for SEROQUEL (344 patients) and 153 days for placebo (388 patients), the sequence-adjusted rate of any increased blood glucose level (>7.0 mmol/L) for patients mean fasted 8 hours since a meal was 18.0 per 100 patient years for SEROQUEL (10.2% of patients) and 9.5 for placebo per 100 patient years (4.6% of patients). In short-term (12 weeks duration) placebo-controlled clinical trials (2945 treated with quetiapine and 1 499 treated with placebo), the percent of patients who had a fasting blood glucose >7.0 mmol/L or a non-fasting blood glucose >11.1 mmol/L was 3.5% for quetiapine and 2.1% for placebo. In a 24 week, mild (active-controlled, 115 patients treated with SEROQUEL) designed to evaluate glycemic status with oral glucose tolerance testing of all patients, at week 24 the incidence of a treatment-emergent post-glucose challenge glucose level ≥11.1 mmol/L was 1.7%, and the incidence of a fasting treatment-emergent blood glucose level >7.0 mmol/L was 7.8% (see WARNINGS AND PRECAUTIONS, Endocrine and Metabolism). Cholesterol and Triglycerides Elevations: In one 3-week clinical trial, where TBL cholesterol was clinically measured as opposed to calculated, there was a slight mean increase in total cholesterol in patients administered SEROQUEL, which was driven by increases in HDL cholesterol. The mean TBL have increased at Week 24 by 10% in patients administered SEROQUEL, which was statistically significant. The total cholesterol/HDL ratio did not change significantly during therapy with SEROQUEL. Furthermore, triglycerides did not increase significantly over the HDL cholesterol decrease during therapy (see WARNINGS AND PRECAUTIONS, Cardiovascular). Post-Marketing Adverse Drug Reactions: During post-marketing experience, leucopenia and/or neutropenia have been reported shortly SEROQUEL treatment. Rarely/rare of leucopenia and/or neutropenia have followed cessation of therapy with SEROQUEL. Possible risk factors for leucopenia and/or neutropenia include pre-existing low white cell count and history of drug induced leucopenia and/or neutropenia (see WARNINGS AND PRECAUTIONS, Hematological). As with some other antipsychotics, hyperglycaemia and/or diabetes mellitus (including exacerbation of pre-existing diabetes, diabetic ketoacidosis, and diabetic coma including some fatal cases) in the aggregate have been reported rarely (≥0.01% – <0.1%) during the use of SEROQUEL, sometimes in patients with no reported history of hyperglycaemia (see WARNINGS AND PRECAUTIONS, Endocrine and Metabolism). Angioedema: Angioedema have been reported very rarely in post-marketing reports, including a case with a fatal outcome, possibly related to SEROQUEL treatment. The reporting rate of neuroleptic associated with SEROQUEL use, which is generally accepted to be an underestimate due to underreporting, does not exceed the background incidence rate estimates. Estimates of the background incidence rate (all causes) of severe life-threatening encephalopathy in the general population range between 82 and 110 cases per million person-years, and the incidence rate of drug induced encephalopathy is reported to be 16 cases per million person-years. In addition, the all cause fatal encephalopathy rate is reported to be one per million person-years while the drug induced fatal encephalopathy is estimated to be 0.3 cases per million person-years. If a patient develops encephalopathy after treatment with SEROQUEL XR, the drug should be discontinued and an alternative treatment started.

DRUG INTERACTIONS

Drug-Drug Interactions: The Effect of SEROQUEL XR on Other Drugs: Alcohol: SEROQUEL (quetiapine, immediate-release formulation) potentiated the cognitive and motor effects of alcohol in a clinical trial in subjects with psychotic disorders. Alcoholic beverages should be avoided while taking SEROQUEL XR. Antihypertensive Agents: Because of its potential for inducing hypotension, SEROQUEL XR may enhance the effects of certain antihypertensive agents. Levodopa and Dopamine Agonists: As it antagonizes dopamine, SEROQUEL XR may antagonize the effects of levodopa and dopamine agonists. Lithium: The single dose pharmacokinetics of lithium were not affected when co-administered with SEROQUEL. Antipsychotics: SEROQUEL did not induce the hepatic enzymes involved in the metabolism of antipsychotics. Carbamazepine: SEROQUEL did not affect the single dose pharmacokinetics of lamotrigine. Divalproex: Co-administration of SEROQUEL (750 mg bid) and divalproex (500 mg bid) increased the mean oral clearance and the mean maximum plasma concentration of valproic acid (administered as divalproex) by 11%. These changes were not clinically relevant. The Effect of Other Drugs on SEROQUEL XR: Hepatic Enzyme Inducers: Concomitant use of SEROQUEL XR with hepatic enzyme inducers such as carbamazepine may substantially decrease systemic exposure to quetiapine. In a multiple dose trial in patients to assess the pharmacokinetics of SEROQUEL given before and during treatment with carbamazepine (a known hepatic enzyme inducer), co-administration of carbamazepine significantly increased the clearance of quetiapine. This increase in clearance reduced systemic quetiapine exposure (as measured by AUC) to an average of 13% of the exposure during administration of quetiapine alone; although a greater effect was seen in some patients. As a consequence of this interaction, lower plasma concentrations can occur, and hence, in such patients, consideration for a higher dose of SEROQUEL XR, depending on clinical response, should be considered. It should be noted that the recommended maximum daily dose of SEROQUEL XR is 800 mg/day and continued treatment at higher doses should only be considered as a result of careful consideration of the benefit-risk assessment for an individual patient. Co-administration of SEROQUEL and another enhanced enzyme inducer, phenytoin, caused threefold increases in the clearance of quetiapine. Increased doses of SEROQUEL XR may be required in enzyme-induced control of psychotic symptoms in patients co-administered SEROQUEL XR and phenytoin and other hepatic enzyme inducers (e.g., barbiturates, rifampicin, etc.). The dose of SEROQUEL XR may need to be reduced if phenytoin or carbamazepine or other hepatic enzyme inducers are withdrawn and replaced with a non-inducer (e.g., sodium valproate). CYP 3A4 Inhibitors: CYP 3A4 is the primary enzyme responsible for cytochrome P450-mediated metabolism of quetiapine. Thus, co-administration of ketoconazole (such as itraconazole, erythromycin, clarithromycin, diltiazem, verapamil, or nefazodone), which inhibit CYP 3A4, may increase the concentration of SEROQUEL XR. In a multiple-dose trial to healthy volunteers to assess the pharmacokinetics of SEROQUEL given before and during treatment with ketoconazole, co-administration of ketoconazole resulted in an increase in mean C_{max} and AUC of quetiapine of 235% and 522%, respectively, with a corresponding decrease in mean oral clearance of 84%. The mean half-life of quetiapine increased from 7.4 to 43 hours, but the mean t_{max} was unchanged. Due to the potential for an interaction of a similar magnitude in a clinical setting, the dosage of SEROQUEL XR should be reduced during concomitant use of quetiapine and potent CYP 3A4 inhibitors (such as azole antifungals, macrolide antibiotics, and protease inhibitors). Special consideration should be given to sedative and debilitated patients. The risk/benefit ratio needs to be considered on an individual basis. In all patients. Divalproex: Co-administration of SEROQUEL (750 mg bid) and divalproex (500 mg bid) increased the mean maximum plasma concentration of quetiapine by 17% without changing the mean oral clearance. Cimetidine: In a clinical study examining the pharmacokinetics of SEROQUEL following co-administration with cimetidine, (a non-specific P450 enzyme inhibitor), no clinically significant interaction was observed. Ritonavir/Saquinavir: Co-administration of ritonavir (200 mg bid) with SEROQUEL (300 mg bid) increased the clearance of SEROQUEL by 15%. Fluoxetine, Imipramine, Risperidone and Thioridazine: Fluoxetine (60 mg daily), imipramine (75 mg bid), risperidone (7.5 mg bid), and thioridazine (3 mg tid) did not significantly alter the steady state pharmacokinetics of SEROQUEL. Drug-Food Interactions: SEROQUEL XR can be taken with or without food. Drug-Herb Interactions: Interactions with herbal products have not been established. Drug-Laboratory Interactions: Interactions with laboratory tests have not been established.

OVERDOSAGE

Experience: Clinical Trials: One death has been reported in a clinical trial following an overdose of 13,600 mg of quetiapine alone, however, survival has also been reported in acute overdoses of up to 30,000 mg of quetiapine. Most patients who overdosed reported no symptoms events or recovered fully from the reported events. Post-Marketing: In post-marketing experience, there have been fewer cases of coma and death in patients taking a SEROQUEL (quetiapine immediate-release formulation) overdose. The lowest reported dose associated with coma was lower in a patient who took 5,000 mg and had a full recovery within 3 days. The lowest reported dose associated with a death was in a patient who took 6,000 mg. Patients with pre-existing severe cardiovascular disease may be at an increased risk of the effects of overdose (see WARNINGS AND PRECAUTIONS, Cardiovascular, Hypotension and Syncope). Symptoms: In general, reported signs and symptoms were those resulting from an exaggeration of the drug's known pharmacological effects (e.g., drowsiness and sedation, tachycardia and hypotension). Treatment: There is no specific antidote to quetiapine. In case of severe intoxication, the possibility of multiple drug involvement should be considered, and intensive care procedures are recommended, including establishing and maintaining a patent airway, securing adequate oxygenation and ventilation, and monitoring and support of the cardiovascular system. Close medical supervision and monitoring should be continued until the patient recovers.

Product monograph is available upon request from AstraZeneca Canada Inc.

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AstraZeneca

Seroquel XR
quetiapine

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For The Downs

SEROQUEL XR®: The first treatment in Canada for both poles of bipolar disorder

For The Ups

Now you can treat bipolar mania and bipolar depression with SEROQUEL XR.* Once-a-day. And SEROQUEL XR was generally well-tolerated in clinical studies including outpatients.[1∞§]

So, when it comes to treating your patients, whether they're up or down, there's SEROQUEL XR.

(Discontinuation rates due to adverse events for SEROQUEL XR vs. placebo: bipolar mania 4.6% vs. 8.1%; bipolar depression 13.1% vs. 3.6%)

SEROQUEL XR® is indicated for the management of the manifestations of schizophrenia, as monotherapy for the acute management of manic episodes associated with bipolar disorder, and as monotherapy for the acute management of depressive episodes associated with bipolar I and bipolar II disorder.[1]

The most common adverse events with incidences ≥5% and an incidence at least 5% higher than that observed with placebo: in schizophrenia – sedation (13%), somnolence (12%), dry mouth (12%), and dizziness (10%); in bipolar mania – sedation (34%), dry mouth (34%), somnolence (17%), constipation (10%), dizziness (10%), weight gain (7%), and dysarthria (5%); in bipolar depression – dry mouth (37%), somnolence (29%), sedation (23%), increased appetite (12%), dyspepsia (7%), and weight gain (7%). Please see Product Monograph before prescribing.[1]

Increases in blood glucose and hyperglycemia, and occasional reports of diabetes have been observed in clinical trials.[1]

Eye examinations are recommended prior to, or shortly after initiation of treatment, and at 6-month intervals thereafter. Caution should be used in the elderly and those with known hepatic or renal impairment.[1]

Serious Warnings and Precautions. Increased Mortality in Elderly Patients with Dementia: Elderly patients with dementia treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo. Analyses of thirteen placebo-controlled trials with various atypical antipsychotics (modal duration of 10 weeks) in these patients showed a mean 1.6-fold increase in death rate in the drug-related patients. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature.[1]

* Comparative clinical significance is unknown.

∞ 3-week placebo-controlled trial in bipolar patients with manic or mixed episodes with or without psychotic features; n=308 (patients receiving at least 1 dose with at least 1 post-baseline YMRS assessment). SEROQUEL XR was given at a dose of 300 mg on Day 1 and at 600 mg on Day 2. From Day 3 to Day 21, SEROQUEL XR was given in flexible doses of 400 to 800 mg.

§ 8-week multicenter, randomized, double-blind, parallel group, placebo-controlled study; n=280 outpatients with bipolar I and II disorder, with or without a rapid cycling course; dosages of 300 mg or placebo were administered.

1. SEROQUEL XR® (quetiapine fumarate extended-release tablets) Product Monograph, AstraZeneca Canada Inc. August 18, 2008.

AstraZeneca

Once Daily Seroquel XR® quetiapine

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