

DIALOGUE



ONTARIO PSYCHIATRIC ASSOCIATION

SEPTEMBER 2010



*OPA
Celebrates
90th Anniversary
1920-2010*

Photo © Nicholas Kolodka



**ONTARIO PSYCHIATRIC ASSOCIATION
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Contents

OPA 2010 Annual Conference Review	2
President's Message	3
The Founding of the Canadian Psychiatric Association	4
Tariff Update	5
OPA 2010 Fall Conference	6
OPA 2011 Annual Conference	6
T. A. Sweet Award – Call for Nominations	7
OPA 2011 Annual Conference – Call for Abstracts	7
90th OPA Annual Conference (2010 Photo Highlights)	8
Quality Improvement Forum	10
Dr. Ann Thomas Award Winner	10

OPA 2010 Conference Review

THIS spring marked the Ontario Psychiatric Association's 90th Annual Conference. Thank you to all who joined us at the historic Le Méridien King Edward Hotel in Toronto to help us celebrate the OPA turning 90.

The Conference opened with a keynote address by acclaimed producer, director and comedic performer Rick Green. Rick was diagnosed with ADD as an adult after struggling with symptoms for many years, and his journey from patient to passionate advocate and educator was fascinating and enlightening (and of course entertaining!) to hear. On Saturday Dr. Edward Shorter and Dr. John Deadman presented "The OPA at 90 – Win Some, Lose Some", a keynote plenary session that reviewed where psychiatry has been over the past century and encouraged us to think about where we are going. Other session highlights included the *Jane Chamberlin Memorial Lecture*, delivered by Dr. Anthony Levitt on "The Art and Science of Dosing Strategies in the Treatment of Resistant Depression", and invited sessions by Dr. Suzanne Archie on "First Episode Psychosis and Substance Abuse", Dr. Marie-France Tourigny-Rivard on "Responding to the Needs of Seniors with Mental Health Problems", Dr. Jon Hunter on "The Use of Mentalizing in Psychotherapy", and Dr. Umesh Jain on "Adult ADHD". Attendees appreciated the depth of the academic program, and could choose from a broad range of clinical sessions to sessions highlighting service delivery models, educational models, medical politics or practice management issues.

The Conference also provided attendees a chance to socialize and reconnect with colleagues from around the province. Rick Green emceed the Friday night gala dinner and his humour and passion as a mental health advocate again shone through. Sister Margaret Smith was awarded the *T. A. Sweet Award* for her long time advocacy in the area of addictions, and it was truly inspirational to meet her and hear her incredible story. It was great to see residents actively participating in the Conference as well, with several excellent sessions presented by residents, and Dr. Nikola Grujich was awarded the *Dr. Ann Thomas Award* for the Best Resident Poster for Evaluation of the Professional Role During Psychiatry Residency.

Thank you to all who made the 2010 OPA Annual Conference such a success. We are now looking forward and planning the 2011 OPA Annual Conference, which will again be held at the Le Méridien King Edward Hotel in Toronto, April 15 & 16. The program committee will be reviewing the curriculum and we are now accepting abstracts. If you have a session or poster that would be of interest to your colleagues, please contact the OPA office. I encourage you to mark your calendars and plan to join us in 2011 — it promises to be another great Conference!▲

K. Sonu Gaind, MD, FRCP(C)
OPA Continuing Education Committee Chair

President's Message



Dr. Doron Almagor

As the Ontario Psychiatric Association marks its 90th year anniversary, I am privileged and honoured to begin my term as President. Belying its venerable 90 years, our organization is more vigorous than ever, and never more vital to the needs of our members.

Our past year has been a tremendously busy and productive one. Under the guidance of our outgoing president, Dr. Paul Mulzer,

we have been able to advocate for patient care, for the dignity of those who suffer from psychiatric illness, and against the stigma of mental health issues. We have been instrumental in lobbying for our membership in critical negotiations regarding relativity adjustments with the government and the OMA. Under the direction of our Educational Chair, Dr. Sonu Gaiind, our Annual General Meeting has been the most successful one to date in both size and quality of the program. We are well positioned to tackle the challenges of the upcoming year. Our council is composed of tremendously talented and capable members and our new President-Elect, Dr. Alison Freeland, is sure to provide continued dynamic leadership.

In just 10 years' time our organization will turn 100 years of age. I hope at that time, in the year 2020, to be reading a new incoming President's message proclaiming an even healthier and more vibrant organization and profession. What actions and strategy can we take now to make this happen? That question brings me to introduce this year's Residential Theme, the title of which is, *Building a Community of Practice*.

The phrase *Community of Practice* was originally coined by cognitive anthropologists Jean Lave and Etienne Wenger in 1991, to describe groups of people who share a concern, a set of problems, or a passion about a topic, and who deepen their knowledge and expertise in this area by interacting on an ongoing basis. This model has since been extended and is widely used in both corporate and not for profit organizations as a blueprint for knowledge management, sharing of information amongst members of a particular group, and forming links between members of an organization.

It's a simple idea really. Groups of people have been doing this for thousands of years. The theory of Communities of Practice can make us actively think of the types of systems and structures we can put in place to continue promote the growth of our communities.

In the months ahead, I will outline some of the premises of the Communities of Practice model and how we might apply it to our organization. Currently, we need to admit that our organization has very few ways in which members can communicate with each other except at our Annual General Meeting and the Fall Psychotherapy Section

Meeting. I believe this is problematic for a number of reasons, not least of which is the fact that we are not fully utilizing our human resource of almost 1000 member psychiatrists. While we have been able to mobilize our membership during times of crisis — for petitions and letter writing campaigns — imagine, how much more we could achieve if we were all actively involved in our organization!

To begin addressing some of these structural issues, I suggest we start looking at the use of new technologies to facilitate member-to-member communications. Our first step, under the leadership of our Communications Chair, Dr. Patricia Cavanagh, is to begin the process of overhauling our web site. Our new web site will feature a more modern look, increased functionality, and more timely information updates for our membership. Once our website is updated, I propose that we look to further modernizing our organization and create social networking features that are secure and accessible only to members. One can imagine a wide variety of uses for a social network that is available only to our members: as a referral resource, a place for forming both on- and offline discussion and study groups, calls for political action, postings of career opportunities, and I'm sure many uses we haven't even imagined yet.

BUILDING A COMMUNITY OF PRACTICE

The other practical aspect of this model is that terminology extends to the plural: to *Communities of Practice*. Given our number, we need a number of communities within our organization in order to function well as one unit. I initially came to OPA council as a member of one of these communities, as the Chair of the Psychotherapy Section. The Psychotherapy Section is one of the most active in the OPA, and hosts the highly successful Fall Conference. It is my hope that through these technologies we can facilitate the growth of similar communities of subspecialties within the OPA.

In the days and weeks to come I invite your feedback, your ideas, your objectives, needs, and contributions. Only together as a community can we build and address our common goals. Our profession is spread throughout a large province, and for most of us, the majority of our time is dedicated to patients, apart from our colleagues. But whether we work in a downtown Toronto teaching hospital or in a solo practice in Northern Ontario, we are all connected. I hope this year to grow these connections for the benefit of ourselves, our organization, our profession, and our patients.▲

Doron Almagor, MD, FRCP(C)
President, Ontario Psychiatric Association

The Founding of the CANADIAN PSYCHIATRIC ASSOCIATION

“...it was a smoke-filled back room in the Mount Royal Hotel in Montreal, where that early group of psychiatrists joined together to create a professional association for Canadian psychiatrists.”

— WERNER PANKRATZ

from Chapter 3 of “Psychiatry in Canada: 50 Years”

The Canadian Psychiatric Association was founded in 1951. Letters patent were issued on June 1st, 1951, and an inaugural meeting was held at the Annual General Meeting of the Canadian Medical Association in Montreal later that month. The first annual scientific meeting of the CPA was held in June 1952, again in conjunction with the CMA at their AGM in Banff. The CPA is holding its 60th Annual Conference in Toronto this September.

The Ontario Neuro-Psychiatric Association — the forerunner of the OPA — held its inaugural meeting in Kingston on 28th of April 1920. We celebrated our 90th anniversary in April this year. The members of the ONPA made valuable contributions to the fledgling CPA and in turn were influenced by it.

THE EVOLUTION OF A NATIONAL PSYCHIATRIC ASSOCIATION

After the Second World War psychiatry in Canada was still divided into the two camps that had emerged from the 19th century and the First World War. These camps were quite separate and often referred to each other in disparaging terms, if they referred to each other at all. One camp was the mental hospital physicians (originally known as alienists in the 19th century) and the other the private practice neuro-psychiatrists. By 1945, both groups were known as psychiatrists, but the formal separation from neurology was still to take place. During the war, most physicians, including many psychiatrists, were in the military or otherwise involved in the war effort. By 1945, however, there were increasing discussions on the forming of a national psychiatric association.

Many Canadian psychiatrists had joined the *American Psychiatric Association* and some the *Royal Psychopathological Association* of the UK. Most were members of the Canadian Medical Association and its *Section of Psychiatry*, formed in 1945. Both the APA and the RPA (UK) had recognized Canadian psychiatrists in different ways but neither could represent Canadian psychiatrists at a national and federal level in the rapidly changing atmosphere after the war. It only further emphasized the need for a specifically Canadian association.

Many meetings were held to discuss this, notably at the APA meeting in Montreal in 1949, where an organizational committee was set up. In 1950, this committee proposed an association be created and stated four resolutions including the name, the categories of membership, an organizational committee and an annual fee of two dollars. These resolutions were adopted at the annual general meeting of the CMA in June 1950. By the next year, at the CMA AGM in June 1951, the chair of the interim committee, George Stevenson, chaired the inaugural meeting of the newly

formed *Canadian Psychiatric Association*.

The names involved in this process were people famous in Canadian Psychiatry at that time. They included Robert O. Jones, Ewen Cameron, Aldwyn Stokes, George Stevenson, Jack Griffen, Griff McKerracher, Charlie Roberts, C.B. Farrar and many others. These were the early presidents of the organization as well as people who had political and social influence far beyond psychiatry. Without this strong cadre of support, the organization may well have foundered in the early years.

For many years the meetings were held in conjunction with the CMA meetings which were usually in June. I remember a CPA meeting in Edmonton in 1966. The CPA and CMA meetings were in different hotels but there were a number of joint sessions. By resolution, the CPA decided to formally separate the meetings but this did not take place until 1973. It was at about that time that the decision was taken to charge a separate fee for attendance at the annual meeting. Prior to that, both were included in the annual membership fee. What a change today.

The need for scientific programs was recognized from the beginning. The annual meetings emphasized scientific progress in various areas — the first meeting in 1952 focused on schizophrenia — a topic that had become much more important with the translation into English of the important work of Eugen Bleuler at around the time of the First World War. The CPA began publishing *The Bulletin* from the beginning, soon followed by the *Journal of the Canadian Psychiatric Association*, now known as the *Canadian Journal of Psychiatry*. The original one day meeting soon became two and then three. The CPA has now developed a very intensive and respected CME program which holds meetings all across Canada.

CHANGES IN THE ONPA — FROM THE OPA ARCHIVES

It is noteworthy that many of the founding members of CPA had been prominent in the OPA over the years. George Stevenson was on the Executive Committee of the ONPA throughout most of the 1930s and was President in 1936. Clarence B. Farrar had been one of the founding members of the OPA in 1920. He had been active on the Editorial Board during the 1930s. Aldwyn Stokes, who replaced Farrar as Chairman of the Department of Psychiatry of the University of Toronto was also active with the ONPA, and President in 1955 at a time when the ONPA was reorganizing itself as the OPA. There were many other OPA members involved.

The ONPA executive had suggested that ONPA should join a larger national group including the APA in its earliest days but this was never accepted by the membership. This also came up when CPA was founded but no action was

Tariff Update

taken until an Executive meeting on April 10th, 1953, when it was decided that the current president of the ONPA be the representative to CPA and that ONPA would not formally join CPA but would be affiliated with it. It is noted in the minutes of November 28th, 1953, that a letter had been written to CPA advising them "...that we had decided on a loose affidavit and that we nominate our past and present president to serve on their Executive." This was to characterize OPA's association with CPA for a number of years.

The executive and the members had been talking about a reorganization of the ONPA for some time and the founding of the CPA was to trigger significant changes. At the meeting of January 12th, 1954, a committee was established to study the ONPA constitution and the status of membership. It was decided at the executive meeting of January 31st, 1955, that the ONPA would share a cocktail reception at the CPA's annual meeting at the Royal York Hotel that year. This developed into an open meeting with the CPA on June 1st, 1955, chaired by Dr. Ewen Cameron. The program for that meeting featured some of the leading lights of psychiatry at that time.

The APA and others had been pushing the ONPA for a more formal affiliation. This had always been resisted by the Executive but it did create a strong impetus to bring the oldest psychiatric association in Canada up to modern standards and to develop formal liaisons and affiliations. It was noted in the minutes of May 7th, 1956, that Dr. Stokes moved: "*Whereas changes in medical practice in Ontario both at the present time and in the anticipated future and its relationship to psychiatry should lead us to strengthen the ONPA which has the most powerful membership of any such association in Canada, that to carry on the changes the association should strengthen its internal constitution.*"

A small subcommittee was set up to review all the recommendations. It reported on May 25th. On September 29th, 1956, the name was changed to the *Ontario Psychiatric Association* and a new constitution was adopted. Subsequent changes brought about a complete updating of all aspects of the association. Although it could be thought of as the end of an era, the transition was so seamless that many people did not notice the change.▲

John C. Deadman, MD, DPsych, FRCP(C)
Archivist, Ontario Psychiatric Association

We are now midway through the current Ontario Medical Association-Ministry of Health and Long-Term Care (OMA-MOHLTC) agreement, and most psychiatrists have seen significant increases in their fee codes as a result of the 9.5% allocation psychiatry received in October 2009. You will recall this increase was comprised of the 2.5% 'across the board' allocation all sections received, plus 7% allocated to psychiatry for relativity increases (thus by comparison, sections with no relativity increase received a total increase of 2.5%). This 9.5% increase was distributed across various OHIP psychiatry codes, with the significant majority being allocated to the 'bread and butter' time based codes.

The 9.5% sectional allocation increase is also intended to "flow through" to non-fee-for-service contractual programs as well, including to APPs, AFPs, divested Provincial Psychiatric Hospitals (dPPHs), mental health sessionals, the psychiatric stipend, sessional fee supplement, ACT teams, and OPOP sessionals. While psychiatrists in many of these areas have not yet received these flow through increases, the Section understands monies due are expected to be paid this fall, subject to certain restrictions. First, the allocation applies only to the clinical portion of work performed, not to the administrative or non-clinical portion. Also, psychiatrists in dPPHs where the salary was already higher than a \$239,269 base salary are not receiving a flow-through increase. The agreement specifies that all salaries in the dPPHs are to be brought to a baseline minimum range of \$206,690 to \$239,269. When the agreement was passed, it was unclear exactly what amount of flow-through dPPH psychiatrists above this range would receive, but the Section on Psychiatry had understood that those above the range could still expect to see some increases. The OMA has acknowledged to the Section that communication around this issue was not as clear as it should have been, and has also confirmed that the baseline salary range will be increased with each flow-through increase (so the \$206,690 to \$239,269 range should increase to approximately \$226,326 to \$262,000, and for 2010 calculations dPPH psychiatrists with salaries below approximately \$262,000 should see a flow-through increase based on the October 2010 allocation).

The Section will also soon be receiving final confirmation of what the 2010 sectional allocation will be. The agreement specifies an overall 3% increase to the funding pool, with 1.5% directed equally to all sections and the remaining 1.5% targeted for relativity increases. The relativity calculations will be based on the revised CANDI relativity model using the Skills Acquisition Modifier (SAM) that the Section successfully lobbied to have added to ensure the value of specialist training was recognized. As a result psychiatry's total allocation will be approximately 5.5% for October 2010 (again, in comparison sections receiving no relativity increase will receive a total 1.5% allocation). The majority of this will be directly to increases to existing psychiatry codes, and there will also be some new codes introduced in October 2010 allowing for some form of telephone consultation with other physicians, and for extended psychiatric consultations. Details of these codes and the final allocations are being provided in a separate communication.▲

K. Sonu Gaind, MD, FRCP(C)
Tariff Chair, OMA Section on Psychiatry

FALL CONFERENCE

Mark Your Calendars!

**OPA Psychotherapy Section's
2010 Fall Conference
Saturday, November 13, 2010**



Guest Speaker

Adam Phillips

ADAM PHILLIPS is a British psychoanalyst, writer, and literary critic. He studied English at Oxford University and then pursued psychology, specializing in child psychology. For nearly a decade he held the position of Principal Child Psychotherapist at Charing Cross Hospital, London. Currently, he divides his time between writing and conducting a private psychoanalytic practice in Notting Hill.

Phillips has written fifteen books, including:
On Flirtation: Psychoanalytic Essays on the Uncommitted Life (1995),
Side Effects (2006), and *On Kindness* (with Barbara Taylor, 2009).
He reviews for *The London Review of Books*, *The Guardian*,
and *The Observer*.

Please mark your calendars for the

OPA 2011 ANNUAL CONFERENCE



April 15 & 16, 2011
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

The OPA announces its Call for Nominations for the 2011 *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, Robert Munsch and Sister Margaret Smith.

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. He was a physician at the Ontario Hospital, Whitby, until his retirement in 1965. In his will, he left a bequest to the Ontario Psychiatric Association that was to be used for a good purpose. ▲

Please fax your nominations to

905-826-4873

by 5pm on **Monday, November 1, 2010.**

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) 2011 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: MONDAY, NOVEMBER 1, 2010.

To request the official submission form, please email the OPA office at: opa@eopa.ca

90th OPA Annual Conference



OPA 2010 ANNUAL CONFERENCE held April 23 & 24 at Le Méridien King Edward Hotel in Toronto.

Top row (left to right):

Rick Green, Keynote Speaker and Dinner MC (right corner above);

Dr. Edward Shorter (left corner opposite);

Dr. John Deadman (right corner opposite).

Middle row (left to right):

Dr. Doron Almagor, OPA President;

Dr. Susan Abbey, CPA Past President, Recipient of the 2009 RCPS C RAC 3

Prix d'excellence Award;

Dr. K. Sonu Gaiind, OPA Continuing Education Committee Chair;

Sister Margaret Smith, 2010 OPA T. A. Sweet Award Winner;

Dr. Paul Mulzer, OPA Past President.





QUALITY IMPROVEMENT FORUM

Taking a Quality Improvement (QI) Approach to Reducing Emergency Department (ED) Waits and Avoidable Hospital Visits for People Living with Mental Health and Addiction Issues in Ontario

This forum held March 31st, 2010, was attended by approximately 140 people invited by the Ministry of Health and Long-Term Care (MOHLTC) to represent hospital and community sectors, consumer groups, police, LHINs, and QI groups. The OPA was represented by two members of the OPA Council.

The day began with an overview of the issues which included lengthy emergency department (ED) wait times, fragmented care and inefficient ED processes and high proportion of Mental Health (MH) and Addiction (A) visits in EDs. In 2008/09 there were 148,000 mental health and 45,000 substance use ED visits. 44% of mental health ED visits were within-year repeats and 12% were 5 or more within year visits.

Participants were then split into groups and asked to map the care of a hypothetical case of an individual with mental illness and/or an addiction starting from presentation to the ED through to discharge and follow-up, identifying what is or is not working well, as well as opportunities for quality improvement.

Subsequently the groups reported back and identified positive aspects, including use of crisis outreach, peer support in the ED, case management, and shared care. A number of issues were identified as not working well including discrepancies in approaches to care in the ED, lack of availability of psychiatric assessment and community services, the perception of some that there is a “provider hierarchy” within the medical model leading to a non-collaborative environment, lack of a person-centered approach to care; inadequate primary care services and inappropriate use of police.

Several Quality Improvement opportunities were

identified including cross ministerial collaboration, increased knowledge of community resources, improved continuum of care, clear understanding of mental health legislation and need for leadership at the system level. System redesign opportunities were highlighted which reflected the need to improve community capacity through common intake forms and collaboration between agencies, increase capacity for medical detox, integrate community workers in ED processes, develop crisis plans/medical directives for repeat visitors to ED, provide rapid, coordinated, integrated case management, and improve connections with primary care.

From the OPA delegate perspective, the day represented an opportunity to observe the direction the Ministry is taking in terms of addressing challenges in the ED and to be part of a collaborative approach to development of ideas and processes. However, it also highlighted the need for our continued concern regarding what appears to be a diminution of the importance of psychiatric assessment, diagnosis and treatment in the pathways of care for those with mental illness and concurrent addictions.

There is continued need for strong advocacy by our profession to highlight our skills in providing clinical leadership and guidance in team settings, including the ED, and to ensure we are represented at decision making tables in order for these important concerns to be integrated into any system changes developed in the next few years.▲

Dr. Alison Freeland, MD, FRCP(C)
President-Elect, Ontario Psychiatric Association



Congratulations!

to

Nikola Grujich

Winner of the

DR. ANN THOMAS AWARD

for the

Best Resident Poster

at the

OPA 2010 Annual Conference.



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 (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.

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 α_1 -adrenergic receptor blocking activity, SEROQUEL XR may induce orthostatic hypotension, dizziness and sometimes syncope, especially during the initial dose-titration period. These events may lead to falls. In placebo-controlled SEROQUEL XR trials, there was little difference in the adverse reaction reporting rate of syncope in patients treated with SEROQUEL XR (0.5%, 11/2388) compared to patients on placebo (0.3%, 4/1267). 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:** Very common ($\geq 10\%$) 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. In 6-week MDD monotherapy clinical trials, SEROQUEL XR-treated patients had increases from baseline in mean triglycerides of 8%, compared to a mean decrease of 1% for placebo-treated patients. In the same trials, both SEROQUEL XR- and placebo-treated patients had decreases from baseline in mean cholesterol of 1% and 3%, respectively. In a longer-term randomized withdrawal MDD trial, patients who completed at least 158 days of SEROQUEL XR treatment (n=196) showed mean increases from baseline in triglycerides of approximately 5% and mean decreases from baseline in cholesterol of approximately 4%. **Endocrine and Metabolism: 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 ($\geq 0.01\%$ - $< 0.1\%$) during the use of quetiapine in post-marketing experience, sometimes in patients with no reported history of hyperglycaemia (see ADVERSE REACTIONS, Post-Market Adverse Drug Reactions). Blood glucose increases to hyperglycemic levels (fasting blood glucose ≥ 7.0 mmol/L or a nonfasting blood glucose ≥ 11.1 mmol/L on at least one occasion) have been observed commonly ($\geq 1\%$ - $< 10\%$) with quetiapine in clinical trials. Occasional reports of diabetes have also 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. **Hyperprolactinemia:** During clinical



Prescribing Summary



Patient Selection Criteria

Therapeutic classification: Antipsychotic/Antidepressant agent

INDICATIONS AND CLINICAL USE

Adults: SEROQUEL XR[®] (quetiapine fumarate extended-release) is indicated for the symptomatic relief of major depressive disorder (MDD) when currently available approved antidepressant drugs have failed either due to lack of efficacy and/or lack of tolerability. While there is no evidence that the efficacy of SEROQUEL XR is superior to other antidepressants, it provides a treatment option for patients who have failed on previous antidepressant treatments. Clinicians must take into account the safety concerns associated with antipsychotic drugs, a class of drugs to which SEROQUEL XR belongs. Safety concerns of this class include: weight gain, hyperlipidemia, hyperglycaemia, tardive dyskinesia and neuroleptic malignant syndrome (see WARNINGS AND PRECAUTIONS). SEROQUEL XR should only be prescribed in patients with MDD by clinicians who are aware of the importance and are experienced in the early detection and management of the above-mentioned safety issues associated with this class. Long-term safety of SEROQUEL XR in MDD has not been systematically evaluated. Thus, the physician who elects to use SEROQUEL XR in the treatment of MDD should use SEROQUEL XR for the shortest time that is clinically indicated. When lengthier treatment is indicated, the physician must periodically re-evaluate the long-term usefulness of the drug for the individual patient keeping in mind the long-term risks (see SUPPLEMENTAL PRODUCT INFORMATION). **Geriatrics (>65 years of age):** SEROQUEL XR is not indicated in elderly patients with dementia (See Serious Warnings and Precautions box and Special Populations). **Pediatrics (<18 years of age):** The safety and efficacy of SEROQUEL XR in children under the age of 18 years have not been established.

SEROQUEL XR is also 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. Please consult the Product Monograph for complete prescribing information.

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 breast-feeding should therefore be advised to avoid breast-feeding while taking SEROQUEL XR. **Pediatrics (<18 years of age):** The safety and efficacy of SEROQUEL XR in children under the age of 18 years have not been established. **Geriatrics (≥ 65 years of age):** The number of patients 65 years of age or over exposed to SEROQUEL XR during clinical trials was limited (n=68). When compared to younger patients the mean plasma clearance of quetiapine was reduced by 30% to 50% in elderly subjects. 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). In a clinical trial that evaluated non-demented elderly patients (aged 66 to 89 years) with MDD, the tolerability of SEROQUEL XR once daily was comparable to that seen in adults (aged 18-65 years) other than the incidence of extrapyramidal symptoms (see WARNINGS AND PRECAUTIONS, Neurologic, Tardive Dyskinesia [TD] and Extrapyramidal Symptoms [EPS]). **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.

trials with quetiapine, elevation in prolactin levels occurred in 3.6% (158/4416) of patients treated with quetiapine compared to 2.6% (51/1968) on placebo (see ADVERSE REACTIONS). 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. **Hypothyroidism:** In SEROQUEL XR clinical trials, 0.2% (4/1755) of patients on SEROQUEL XR compared to 0% (0/796) on placebo experienced decreased free thyroxine and 2.7% (46/1716) on SEROQUEL XR compared to 1.4% (11/785) on placebo experienced increased TSH; however, no patients experienced a combination of clinically significant decreased free thyroxine and increased TSH. 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 T₄ 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 T₄ 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 MDD acute monotherapy clinical trials, for patients treated with SEROQUEL XR mean weight gain was 0.87 kg (n=1149) compared to 0.31 kg (n=648) in patients treated with placebo. In a longer-term randomized withdrawal MDD trial, patients who completed at least 158 days of SEROQUEL XR treatment (n=196), mean weight gain for patients in SEROQUEL XR 50, 150 and 300 mg/day groups was 1.0 kg, 2.5 kg and 3.0 kg, respectively. In these same patients the percentage of patients experiencing a weight increase of ≥7% by 158 days in SEROQUEL XR 50, 150 and 300 mg/day groups was 13%, 24% and 33%, respectively. Based on the cumulative acute placebo-controlled clinical trial database, weight gain (based on ≥7% increase in body weight from baseline) was reported in 9.6% in quetiapine-treated patients and 3.8% in placebo-treated patients, which occurs predominantly during the early weeks of treatment in adults. **Gastrointestinal: Antiemetic Effect:** Consistent with its dopamine antagonist effects, SEROQUEL XR may have an antiemetic 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 × 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 × 10⁹/L. These patients should be observed for signs and symptoms of infection and neutrophil counts followed (until they exceed 1.5 × 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 (see ACTION AND CLINICAL PHARMACOLOGY, Special Populations and Conditions). 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 were approximately 1% for both SEROQUEL XR and placebo. During premarketing clinical trials, therapy with SEROQUEL was associated with elevation of hepatic transaminases, primarily ALT. 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 monotherapy clinical trials in MDD the aggregated incidence of EPS was 5.4% for SEROQUEL XR and 3.2% for placebo. In a short-term placebo-controlled monotherapy trial in elderly patients with MDD, the aggregated incidence of EPS was 9.0% for SEROQUEL XR and 2.3% for placebo. In long-term studies of schizophrenia, bipolar disorder and MDD 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 (0.04%, 1/2388) or placebo (0.2%, 3/1267). Nevertheless, 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. Somnolence may lead to falls. **Ophthalmologic: Cataracts: The development of cataracts was observed in association with quetiapine treatment in chronic dog studies at 4 times the recommended human 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 exam) 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/Suicidal Thoughts or Clinical Worsening:** Depressive episodes are associated with an increased risk of suicidal thoughts, self-harm and suicide (suicide-related events). This risk persists until significant remission of depression occurs. As improvement may not occur during the first few weeks or more of treatment, patients should be closely monitored until such improvement occurs. It is general clinical experience that the risk of suicide may increase in the early stages of recovery. Patients with a history of suicide-related events are also known to be at a greater risk of suicidal thoughts or suicide attempts, and should receive careful monitoring during treatment. In MDD acute clinical trials, the incidence of treatment-emergent suicidal ideation or suicide attempt was 0.7% in SEROQUEL XR-treated patients and 0.7% in placebo-treated patients. In a longer-term randomized withdrawal study in patients with MDD, the incidence during randomized treatment was 0.3% for SEROQUEL XR and 0.5% for placebo. **Renal:** There is little experience with SEROQUEL XR in patients with renal impairment, except in a low (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:

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) during acute monotherapy with SEROQUEL XR were dry mouth, sedation, somnolence, dizziness and fatigue.

Adverse Events Associated With Discontinuation in Short-Term Placebo-Controlled Clinical Trials:

In placebo-controlled monotherapy MDD trials, 14.3% of patients on SEROQUEL XR discontinued due to adverse events compared to 4.5% on placebo. In a placebo-controlled monotherapy trial in elderly patients with

MDD, 9.6% of patients on SEROQUEL XR discontinued due to adverse events compared to 4.1% on placebo.

To report adverse events:

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1004 Middlegate Road
Mississauga, Ontario
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T 1-800-433-0733

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).



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 (see INDICATIONS AND CLINICAL USE). Usual Dose: The titration rate, based on the clinical trials, is shown in the table below.

	Day 1	Day 2	Day 3
Once-daily dosing	50 mg	50 mg	150 mg

The usual target dose is 150 mg. Some patients may respond to doses as low as 50 mg/day and, where clinically indicated, dose may be increased to 300 mg/day after Day 4. In clinical trials, doses between 50-300 mg/day were shown to be efficacious; however, the incidence of certain adverse events increased with dose. In MDD, the safety of doses above 300 mg/day has not been evaluated. Some of the safety concerns associated with SEROQUEL XR and this class of agents (i.e., antipsychotics) may be dose-related. The SEROQUEL XR dose should thus be periodically reassessed to achieve and maintain the lowest effective dose. Furthermore, as the long-term safety of SEROQUEL XR in MDD has not been systematically evaluated, the physician who elects to use SEROQUEL XR in the treatment of MDD should use SEROQUEL XR for the shortest time that is clinically indicated. When long-term treatment is believed to be indicated, the physician must periodically re-evaluate the long-term usefulness of the drug for the individual patient keeping in mind the long-term risks. **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. **Switching Patients From Other Antidepressants:** For many antidepressants a gradual taper is recommended prior to complete discontinuation of the drug (physicians should refer to the approved Product Monograph of the specific antidepressant). There are no systematically collected data to address switching patients from other antidepressants to SEROQUEL XR. Generally there should be no need for a wash-out period between stopping an antidepressant and starting SEROQUEL XR. The physician may elect to initiate SEROQUEL XR treatment while tapering the antidepressant; however, patients may experience additive side effects during the overlap period. **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. In clinical trials, 68 patients, 65 years of age or over, were treated with SEROQUEL XR. Given the limited experience with SEROQUEL XR in the elderly, and the higher incidence of concomitant illness and concomitant medication in this population, SEROQUEL XR should be used with caution. The mean plasma clearance of SEROQUEL was reduced by 30% to 50% in elderly subjects when compared to 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. In elderly patients with MDD, initial dosing should begin at 50 mg on Days 1-3, the dose can be increased to 100 mg on Day 4, and 150 mg on Day 8. **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 in the individual patient. No pharmacokinetic data are available for quetiapine in patients with moderate to 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 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 day's 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, 150, 200, 300 or 400 mg of quetiapine free base as follows:

50 mg quetiapine tablets are peach coloured, capsule-shaped, biconvex, intagliated with "XR 50" on one side and plain on the other, available in high-density polyethylene (HDPE) bottles of 60 tablets. 150 mg quetiapine tablets are white, capsule-shaped, biconvex, intagliated with "XR 150" on one side and plain on the other, available in HDPE bottles of 60 tablets. 200 mg quetiapine tablets are yellow, capsule-shaped, biconvex, intagliated 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, intagliated 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, intagliated with "XR 400" on one side and plain on the other, available in HDPE bottles of 60 tablets. SEROQUEL XR is available in 5 strengths containing 50, 150, 200, 300 or 400 mg quetiapine per tablet (as quetiapine fumarate). The core of the tablet contains the excipients hydroxypropyl methylcellulose, lactose monohydrate, magnesium stearate, microcrystalline cellulose and sodium citrate. The coating of the tablet contains hydroxypropyl methylcellulose, polyethylene glycol 400, red ferric oxide (50 mg tablets), titanium dioxide and yellow ferric oxide (50, 200 and 300 mg 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 cited 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 non-drug factors to the side effect incidence in the populations studied.

Table 1: Adverse Events Reported for at Least 1% of SEROQUEL XR-Treated Subjects (Doses Ranging From 50 to 300 mg/day) and for a Higher Percentage of SEROQUEL XR-Treated Subjects Than Subjects Who Received Placebo in Short-Term, Placebo-Controlled MDD Monotherapy Phase III Trials

Body System and MedDRA Term ^a	Percentage of Subjects With Adverse Events [*]	
	SEROQUEL XR (n=1149)	Placebo (n=648)
General disorders and administration site conditions		
Fatigue	7	2
Irritability	4	3
Nervous system disorders		
Sedation	28	4
Somnolence	24	7
Dizziness	14	8
Disturbance in attention	2	<1
Hypersomnia	2	<1
Lethargy	2	1
Gastrointestinal system disorders		
Dry mouth	35	8
Constipation	8	4
Vomiting	3	1
Dyspepsia	4	3
Metabolic and nutritional disorders		
Increased appetite	5	3
Weight increased	3	<1
Musculoskeletal and connective tissue disorders		
Back pain	3	2
Myalgia	3	2
Musculoskeletal stiffness	2	1
Psychiatric disorders		
Abnormal dreams	2	1
Respiratory disorders		
Nasal congestion	2	1
Special senses		
Vision blurred	3	2

^{*} Events for which SEROQUEL XR incidence was equal to or less than placebo are not listed in the table. Table reports percentage rounded to the nearest integer.

^a Patients with multiple events falling under the same preferred term are counted only once in that term.

^b The following adverse events occurred in 1% of patients treated with SEROQUEL XR compared to <1% in placebo: chills, dysarthria, dysgeusia, sluggishness, akathisia, dizziness postural, tachycardia, restless legs syndrome, gastroesophageal reflux disease, pharyngolaryngeal pain and restlessness.

Table 2: Dose-Related Adverse Events in ≥1% of Patients Treated With SEROQUEL XR (Doses 50, 150 and 300 mg/day) Where the Incidence of the Adverse Events in Patients Treated With SEROQUEL XR 150 mg and/or 300 mg was Greater Than the Incidence in SEROQUEL XR 50 mg and Placebo-Treated Patients in Short-Term Fixed-Dose, Placebo-Controlled MDD Monotherapy Phase III Trials

Body System and MedDRA Term ^a	Percentage of Subjects With Adverse Events [*]			
	Placebo (n=338)	SEROQUEL XR 50 mg (n=181)	SEROQUEL XR 150 mg (n=328)	SEROQUEL XR 300 mg (n=331)
General disorders and administration site conditions				
Pain	0	1	1	2
Chills	0	1	0	2
Nervous system disorders				
Sedation	6	27	37	34
Somnolence	9	18	22	28
Dizziness	8	9	13	15
Dysarthria	0	1	1	3

Body System and MedDRA Term ^a	Percentage of Subjects With Adverse Events*			
	Placebo (n=338)	SEROQUEL XR 50 mg (n=181)	SEROQUEL XR 150 mg (n=328)	SEROQUEL XR 300 mg (n=331)
Disturbance in attention	0	1	2	2
Hypoaesthesia	1	0	1	2
Akathisia	1	0	2	1
Lethargy	1	2	3	1
Paresthesia	1	1	2	1
Hypersomnia	0	1	2	1
Gastrointestinal system disorders				
Dry mouth	9	22	36	40
Constipation	4	7	7	9
Nausea	8	8	12	9
Vomiting	2	2	4	5
Dyspepsia	3	2	5	4
Gastroesophageal reflux disease	0	0	1	2
Abdominal distension	1	0	0	2
Abdominal pain	1	1	2	1
Cardiovascular disorders				
Tachycardia	0	1	2	1
Metabolic and nutritional disorders				
Increased appetite	3	4	5	4
Weight increased	1	1	2	3
Musculoskeletal and connective tissue disorders				
Back pain	2	2	5	5
Arthralgia	2	2	3	3
Myalgia	2	4	5	3
Muscle tightness	1	1	0	2
Psychiatric disorders				
Anxiety	2	1	2	3
Abnormal dreams	3	2	4	2
Restlessness	0	0	1	2
Nightmare	1	1	1	2
Infections and infestations				
Nasopharyngitis	3	2	4	3
Gastroenteritis	0	1	2	1
Respiratory disorders				
Nasal congestion	2	1	2	3
Sinus congestion	1	1	2	2
Dyspnoea	1	1	1	2
Epistaxis	0	1	0	2
Nasal dryness	0	0	1	1
Special senses				
Vision blurred	1	2	3	5

* Events for which SEROQUEL XR incidence was equal to or less than placebo are not listed in the table.

^a 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 Ranging From 50 to 300 mg/day) and for a Higher Percentage of SEROQUEL XR-Treated Subjects Than Subjects Who Received Placebo in a Short-Term, Placebo-Controlled Elderly MDD Monotherapy Phase III Trial

Body System and MedDRA Term ^a	Percentage of Subjects With Adverse Events*	
	SEROQUEL XR (n=166)	Placebo (n=172)
General disorders and administration site conditions		
Fatigue	8	3
Asthenia	4	1
Nervous system disorders		
Somnolence	33	8
Headache	19	14
Dizziness	18	15
Sedation	5	1
Dysgeusia	2	1
Balance disorder	2	1
Dizziness postural	2	1
Akathisia	2	1
Gastrointestinal disorders		
Dry mouth	20	10
Constipation	5	2
Abdominal pain upper	3	2
Dyspepsia	2	1
Cardiovascular system disorders		
Hypotension	2	0
Metabolic and nutritional disorders		
Weight increased	5	4
Weight decreased	2	1
Musculoskeletal and connective tissue disorders		
Back pain	2	1
Extrapyramidal disorder	4	1

Body System and MedDRA Term ^a	Percentage of Subjects With Adverse Events*	
	SEROQUEL XR (n=166)	Placebo (n=172)
Pain in extremity	2	1
Respiratory disorders		
Nasal congestion	2	0

* Events for which SEROQUEL XR incidence was equal to or less than placebo are not listed in the table. Table reports percentage rounded to the nearest integer.

^a Patients with multiple events falling under the same preferred term are counted only once in that term.

^b The following adverse events occurred in 1% of patients treated with SEROQUEL XR compared to <1% in placebo: hypersomnia, restless legs syndrome, joint sprain, muscular weakness, pharyngolaryngeal pain and vision blurred.

Other Adverse Events: Weight Gain: In placebo-controlled MDD acute monotherapy clinical trials, for patients treated with SEROQUEL XR mean weight gain was 0.87 kg (n=1149) compared to 0.31 kg (n=648) in patients treated with placebo. In a longer-term randomized withdrawal MDD trial, patients who completed at least 158 days of SEROQUEL XR treatment (n=196), mean weight gain for patients in SEROQUEL XR 50, 150 and 300 mg/day groups was 1.0 kg, 2.5 kg and 3.0 kg, respectively. In these same patients the percentage of patients experiencing a weight increase of $\geq 7\%$ by 158 days in SEROQUEL XR 50, 150 and 300 mg/day groups was 13%, 24% and 33%, respectively (see WARNINGS AND PRECAUTIONS). Based on the cumulative acute placebo-controlled clinical trial database, weight gain (based on $\geq 7\%$ increase in body weight from baseline) was reported in 9.6% in quetiapine-treated patients and 3.8% in placebo-treated patients, which occurs predominantly during the early weeks of treatment in adults (see WARNINGS AND PRECAUTIONS). **Seizures:** There have been uncommon reports ($\geq 0.1\%$ - <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, Neurologic). **Restless Legs Syndrome:** There have been uncommon cases of restless legs syndrome in patients administered quetiapine. **Priapism:** There have been rare reports ($\geq 0.01\%$ - <0.1%) of priapism in patients administered quetiapine. **Somnolence:** Somnolence may occur, usually during the first 2 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, Neurologic). **Vital Signs:** As with other antipsychotics with α -adrenergic blocking activity, SEROQUEL XR may induce postural hypotension, associated with dizziness, tachycardia and, in some patients, syncope, especially during the initial dose-escalation period (see WARNINGS AND PRECAUTIONS, Cardiovascular). SEROQUEL XR was associated with a mean baseline to endpoint increase in heart rate of 3.9 beats per minute, compared to 1.6 beats per minute among placebo-treated patients. **Peripheral Edema:** As with other antipsychotics, common cases ($\geq 1\%$ - <10%) of peripheral edema have been reported in patients treated with quetiapine. **Mild Asthenia:** As with other antipsychotic agents, common cases of mild asthenia have been reported in patients treated with quetiapine. **Rhinitis:** There have been common reports of rhinitis in patients administered quetiapine. **Hypersensitivity:** Uncommon cases of hypersensitivity including angioedema have been reported. **ECG Changes:** In MDD monotherapy trials, 0.2% of SEROQUEL XR patients, and no placebo patients, had tachycardia (>120 bpm) at any time during the trials. SEROQUEL XR was associated with a mean increase in heart rate, assessed by ECG, 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 XR. This slight tendency to tachycardia may be related to the potential of SEROQUEL XR for inducing orthostatic changes (see WARNINGS AND PRECAUTIONS, Cardiovascular). **Extrapyramidal Symptoms (EPS):** In short-term placebo-controlled monotherapy clinical trials in MDD, the aggregated incidence of EPS was 5.4% for SEROQUEL XR and 3.2% for placebo. In a short-term placebo-controlled monotherapy trial in elderly patients with MDD, the aggregated incidence of EPS was 9.0% for SEROQUEL XR and 2.3% for placebo. In long-term studies of schizophrenia, bipolar disorder and MDD, the aggregated exposure-adjusted incidence of treatment-emergent EPS was similar between quetiapine and placebo. **Dysphagia:** There have been uncommon cases of dysphagia in patients administered quetiapine. **Dysarthria:** There have been uncommon cases of dysarthria in patients administered quetiapine. **Acute Withdrawal (Discontinuation) Symptoms:** In acute placebo-controlled monotherapy clinical trials, which evaluated discontinuation symptoms, the aggregated incidence of discontinuation symptoms after abrupt cessation was 12.1% for quetiapine and 6.7% for placebo. The aggregated incidence of the individual adverse events (e.g., insomnia, nausea, headache, diarrhea, vomiting, dizziness and irritability) did not exceed 5.3% in any treatment group and usually resolved 1 week after discontinuation. **Abnormal Dreams and Nightmares:** There have been common cases of abnormal dreams and nightmares in patients administered quetiapine. **Suicide-Related Events:** In these trials of patients with MDD the incidence of suicide-related events was 2.1% (3/144) for quetiapine and 1.3% (1/75) for placebo in patients 18-24 and 0.6% (11/1798) for quetiapine and 0.7% for placebo (7/1054) in patients ≥ 25 years of age. **Irritability:** There have been common cases of irritability in patients administered quetiapine. **Increased Appetite:** There have been common cases of increased appetite in patients administered quetiapine. **Abnormal Hematologic and Clinical Chemistry Findings:** As with other antipsychotics, common cases of leucopenia and/or neutropenia have been observed in patients administered quetiapine. Uncommon cases of eosinophilia and thrombocytopenia (platelet count decreased, $\leq 100 \times 10^9/L$ on at least one occasion) have been observed. Based on clinical trial adverse event reports not associated with neuroleptic malignant syndrome, rare cases of elevations in blood creatine phosphokinase have been reported in patients administered quetiapine. Common cases of elevations in serum prolactin levels have been observed ($>20 \mu g/L$ in males and $>30 \mu g/L$ in females) (see WARNINGS AND PRECAUTIONS, Hyperprolactinemia). In three-arm SEROQUEL XR placebo-controlled monotherapy clinical trials, among patients with a baseline neutrophil count $\geq 1.5 \times 10^9/L$, the incidence of at least one occurrence of neutrophil count $<1.5 \times 10^9/L$ was 1.5% in patients treated with SEROQUEL XR and 1.5% for SEROQUEL XR, compared to 0.8% in placebo-treated patients. In all placebo-controlled monotherapy clinical trials among patients with a baseline neutrophil count $\geq 1.5 \times 10^9/L$, the incidence of at least one occurrence of neutrophil count $<1.5 \times 10^9/L$ was 1.72% in patients treated with SEROQUEL XR, compared to 0.73% in placebo-treated patients. In clinical trials conducted prior to a protocol amendment for discontinuation of patients with treatment-emergent neutrophil count $<1.0 \times 10^9/L$, among patients with a baseline neutrophil count $\geq 1.5 \times 10^9/L$, the incidence of at least one occurrence of neutrophil count $<0.5 \times 10^9/L$ was 0.21% in patients treated with SEROQUEL XR and 0% in placebo-treated patients and the incidence ≥ 0.5 - $<1.0 \times 10^9/L$ was 0.75% in patients treated with SEROQUEL XR and 0.11% in placebo-treated patients (see WARNINGS AND PRECAUTIONS, Hematologic). Common cases of asymptomatic elevations in serum transaminases (ASAT, ALT) or uncommon cases of γ -GT levels have been observed in some patients administered quetiapine. These elevations were usually reversible on continued quetiapine treatment (see WARNINGS AND PRECAUTIONS, Hepatic). SEROQUEL XR treatment was associated with small dose-related decreases in thyroid hormone levels, particularly total T_4 and free T_4 . The reduction in total and free T_4 was maximal 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_4 , irrespective of the duration of treatment. Smaller decreases in total T_3 and reverse T_3 were seen only at higher doses. Levels of TBG were unchanged and in general reciprocal increases in TSH were not observed and there was no indication that SEROQUEL XR causes clinically relevant hypothyroidism (see WARNINGS AND PRECAUTIONS, Endocrine and Metabolism). **Hyperglycemia:** Blood glucose increases to hyperglycemic levels (fasting blood glucose ≥ 7.0 mmol/L or a nonfasting blood glucose ≥ 11.1 mmol/L on at least one occasion) have been observed commonly ($\geq 1\%$ - <10%) with quetiapine in clinical trials. In short-term (12 weeks duration or less) placebo-controlled clinical trials (3342 treated with quetiapine and 1490 treated with placebo), the percent of patients who had a fasting blood glucose ≥ 7.0 mmol/L or a nonfasting blood glucose ≥ 11.1 mmol/L was 3.5% for quetiapine and 2.1% for placebo. In a 24-week trial (active-controlled), 115 patients treated with SEROQUEL XR 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 2.6% (see WARNINGS AND PRECAUTIONS, Endocrine and Metabolism). **Cholesterol and Triglyceride Elevations:** Very common ($\geq 10\%$) 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 WARNINGS AND PRECAUTIONS, Cardiovascular). Lipid increases should be managed as clinically appropriate. In one 24-week clinical trial, where LDL cholesterol was directly measured as opposed to calculated, there was a slight mean increase in total cholesterol in patients administered SEROQUEL XR, which was driven by increases in LDL cholesterol. The mean LDL level increased at Week 24 by 10% in patients administered SEROQUEL XR, which was statistically significant. The total cholesterol/HDL ratio did not change significantly during therapy with SEROQUEL XR. Furthermore, triglycerides did not increase significantly nor did HDL cholesterol decrease during therapy (see WARNINGS AND PRECAUTIONS, Cardiovascular). **Post-Market Adverse Drug Reactions:** During post-marketing experience, leucopenia and/or neutropenia have been reported during SEROQUEL XR treatment. Resolution of leucopenia and/or neutropenia has followed cessation of therapy with SEROQUEL XR. 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, Hematologic). As with some other antipsychotics, hyperglycemia 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 ($\geq 0.01\%$ - <0.1%) during the use of SEROQUEL XR, sometimes in patients with no reported history of hyperglycemia (see WARNINGS AND PRECAUTIONS, Endocrine and Metabolism). Anaphylactic reactions have been reported very rarely in post-marketing reports, including a case with a fatal outcome, possibly related to SEROQUEL XR. The reporting rate of anaphylaxis associated with SEROQUEL XR, 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 anaphylaxis in the general population range between 80 and 210 cases per million person-years, and the incidence rate of drug-induced anaphylaxis is reported to be 16 cases per million person-years. In addition, the all-cause fatal anaphylaxis rate is reported to be one per million person-years while the drug-induced fatal anaphylaxis is estimated to be 0.3 cases per million person-years. If a patient develops anaphylaxis after treatment with SEROQUEL XR, the drug should be discontinued and an alternative treatment started. Based on post-marketing reports, galactosemia has been reported rarely.

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 exhibits *in vitro* dopamine antagonism, SEROQUEL XR may antagonize the effects of levodopa and dopamine agonists. **Lithium:** The single dose pharmacokinetics of lithium were not altered when coadministered with SEROQUEL. **Antipyrene:** SEROQUEL did not induce the hepatic enzyme systems involved in the metabolism of antipyrene. **Lorazepam:** SEROQUEL did not affect the single-dose pharmacokinetics of lorazepam. **Divalproex:** Coadministration of SEROQUEL (150 mg bid) and divalproex (500 mg bid) increased the mean oral clearance and the mean maximum plasma concentration of total 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), coadministration 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 each patient, 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. Coadministration of SEROQUEL and another microsomal enzyme inducer, phenytoin, caused five-fold increases in the clearance of quetiapine. Increased doses of SEROQUEL XR may be required to maintain control of psychotic symptoms in patients coadministered 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, coadministration of compounds (such as ketoconazole, erythromycin, clarithromycin, diltiazem, verapamil or nefazodone), which inhibit CYP 3A4, may increase the concentration of SEROQUEL XR. In a multiple-dose trial in healthy volunteers to assess the pharmacokinetics of SEROQUEL given before and during treatment with ketoconazole, coadministration 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 2.6 to 6.8 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 in elderly and debilitated patients. The risk/benefit ratio needs to be considered on an individual basis in all patients. **Divalproex:** Coadministration of SEROQUEL (150 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 coadministration with cimetidine (a non-specific P450 enzyme inhibitor), no clinically significant interaction was observed. **Thioridazine:** Coadministration of thioridazine (200 mg bid) with SEROQUEL (300 mg bid) increased the clearance of SEROQUEL by 65%. **Fluoxetine, Imipramine, Haloperidol and Risperidone:** Fluoxetine (60 mg daily), imipramine (75 mg bid), haloperidol (7.5 mg bid) and risperidone (3 mg bid) did not significantly alter the steady state pharmacokinetics of SEROQUEL. **In patients taking the following antidepressants:** amitriptyline, bupropion, citalopram, duloxetine, escitalopram, fluoxetine, paroxetine, sertraline and venlafaxine, addition of SEROQUEL XR (150 mg or 300 mg/day; for up to 4 weeks) did not appear to have a consistent overall effect on the trough or pre-dose plasma concentrations of the antidepressant. **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

For management of suspected drug overdose, contact your regional Poison Control Centre.

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 adverse events or recovered fully from the reported events.

Post-Marketing: In post-marketing experience, there have been cases of coma and death in patients taking a SEROQUEL (quetiapine, immediate-release formulation) overdose. The lowest reported dose associated with coma has been in a patient who took 5000 mg and had a full recovery within 3 days. The lowest reported dose associated with a death was in a patient who took 6000 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 cases 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, ensuring 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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SEROQUEL XR (quetiapine fumarate extended-release) is indicated for the symptomatic relief of major depressive disorder (MDD) when currently available approved antidepressant drugs have failed either due to lack of efficacy and/or lack of tolerability.

While there is no evidence that the efficacy of SEROQUEL XR is superior to other antidepressants, it provides a treatment option for patients who have failed on previous antidepressant treatments. Clinicians must take into account the safety concerns associated with antipsychotic drugs, a class of drugs to which SEROQUEL XR belongs. Safety concerns of this class include: weight gain, hyperlipidemia, hyperglycaemia, tardive dyskinesia and neuroleptic malignant syndrome (see WARNINGS AND PRECAUTIONS). SEROQUEL XR should only be prescribed in patients with MDD by clinicians who are aware of the importance and are experienced in the early detection and management of the above-mentioned safety issues associated with this class.

Long-term safety of SEROQUEL XR in MDD has not been systematically evaluated. Thus, the physician who elects to use SEROQUEL XR in the treatment of MDD should use SEROQUEL XR for the shortest time that is clinically indicated. When lengthier treatment is indicated, the physician must periodically re-evaluate the long-term usefulness of the drug for the individual patient keeping in mind the long-term risks.

SEROQUEL XR is also 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. Please consult the Product Monograph for complete prescribing information.

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

During acute MDD 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 as follows: *Adults*: dry mouth (35%), sedation (28%), somnolence (24%), dizziness (14%) and fatigue (7%). *Elderly*: somnolence (33%), dry mouth (20%), headache (19%) and fatigue (8%).

Increases in blood glucose and hyperglycaemia, and occasional reports of diabetes have been observed in clinical trials.

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 and renal impairment.

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.

Please consult the Product Monograph for warnings, precautions and adverse events.

Reference: 1. SEROQUEL XR® Product Monograph. AstraZeneca Canada Inc. May 27, 2009.

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