

DIALOGUE



ONTARIO PSYCHIATRIC ASSOCIATION

AUGUST 2011



In this issue:

**2011 ANNUAL CONFERENCE REVIEW
TARIFF UPDATE
UPCOMING EVENTS**

Photo © Nicholas Kolodka



**ONTARIO PSYCHIATRIC ASSOCIATION
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The views expressed in this newsletter do not necessarily reflect the views of the OPA Council.

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*Mark Your Calendars!
Mark Your Calendars!
Mark Your Calendars!*

**Ontario
Psychiatric
Association**



Psychotherapy Section's 2011 FALL CONFERENCE



Jessica Benjamin

**PLAYING AT THE EDGE:
Creating an Interactive Form
for Working with
Traumatized Patients**

Saturday, October 29, 2011

**THE FACULTY CLUB
UNIVERSITY OF TORONTO
41 Willcocks St., Toronto, Ontario**

President's Message: ENGAGING THE PROFESSION



Dr. Alison Freeland

Psychiatrists in Ontario are a diverse group that provides specialized assessment and treatment to an incredibly wide range of illnesses that result in varying degrees of disability for both short and long periods of time to people across the lifespan. With this in mind it is not surprising that we have been challenged to find a unified voice that represents our many interests and concerns at a provincial level. However, there are

a number of current issues that require us to unite and advocate for our unique role in the delivery of mental health services.

**THERE ARE ISSUES
THAT REQUIRE US TO
UNITE AND ADVOCATE FOR
OUR UNIQUE ROLE IN
THE DELIVERY OF
MENTAL HEALTH SERVICES**

We anticipate that very soon, the Ontario Ministry of Health will be unveiling its 10 year Mental Health and Addictions strategy. This will likely be based on the December 2010 report entitled “*Respect, Recovery, Resilience: Recommendations for Ontario’s Mental Health and Addictions Strategy*”. Although there are many commendable recommendations within this report, there is a noticeable absence of the role of psychiatrists as being uniquely trained to provide assessment and treatment for those with mental illness and substance use disorders. We will need to advocate and educate regarding our role as medical experts and clinical leaders in the provision of treatment for mental illness. Additionally we need to be prepared to embrace positive change in delivery of health care services, but also challenge recommendations that do not value the necessity for psychiatric expertise in assessment and care of illnesses that can result in considerable disability and morbidity if not properly treated.

In 2012, the OMA will begin to negotiate a new Physician Services Agreement with the government. Given the strained economic environment we can anticipate that this will be quite challenging. Ongoing dialogue to ensure our profession is resourced adequately and on par with other medical specialists will require psychiatrists to remain current and informed regarding how negotiations progress.

Our engagement in this issue is essential to ensure adequate resources for the wide range of psychiatric services needed to provide highest quality care for Ontario’s residents.

There is a third issue that we must address in the very near future. Ontario, and in fact most of Canada, is anticipating a significant psychiatrist shortage in the next few years. Recruitment of medical graduates into psychiatry training programs remains a priority issue and will require



**IGNITE YOUR INTEREST
IN THE POLITICAL LANDSCAPE
AND ENGAGE YOUR IDEAS
IN CONSIDERING THE
CHALLENGES THAT LIE AHEAD
FOR US AS A GROUP**

a unified effort by all of us to articulate our pride in our profession and the unique role we play in the mental health care system.

The Ontario Psychiatric Association will continue to work to advocate for psychiatrists in Ontario with respect to these issues. Through ongoing communication with members we hope to ignite your interest in the political landscape and engage your ideas in considering the challenges that lie ahead for us as a group.▲

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



Dr. K. Sonu Gaind

By now you would have received notice of the September 1, 2011 changes and increases to OHIP psychiatry codes based on the OMA Section on Psychiatry's proposals to the OMA-Ministry Medical Services Payment Committee (MSPC). The current OMA-Ministry Agreement provides for a global 4.25% increase to OHIP Schedule of Benefits funding (2.125% provided to all Sections equally, 2.125% for relativity corrections). The

Comparison of Average Net Daily Income (CANDI) relativity formula with Skills Acquisition Modifier (SAM factor) is again being used to determine relativity allocations. *For September 2011, psychiatry's funding allocation increase is 8.649%, or approximately \$28 million increased ongoing annualized funding for psychiatric services.* This 8.649% increase consists of the 2.125% "across the board" increase all sections receive, plus a 6.524% relativity increase for psychiatry.

Most existing time-based psychiatric K-codes and consultation codes will be increased by 7.5%. The MSPC also approved the introduction of several new psychiatry codes. In particular I would highlight codes associated with the new Clinical Care Modifier Model (which has evolved from the Complexity Model that was first presented by the Section to the OMA several years ago). As the significant majority of psychiatric services are provided through generic time-based codes, historically there has been little ability to differentiate the types of psychiatric services being provided. This has resulted in systemic disincentives to provide more complex or intense psychiatric care, especially in the face of already undervalued psychiatric fees. The Clinical Care Modifier Model aims to identify and incentivize more complex and intense psychiatric care by identifying particularly complex clinical situations. The MSPC approved the Section's evidence-based tariff proposals to introduce premiums for psychiatric services provided in the community to patients identified as being at high-risk/high-complexity as follows: a 15% premium payment for psychiatric services provided to patients following recent (within 4 weeks) psychiatric hospitalization; a 15% premium payment for psychiatric services after a recent (within 6 months) suicide attempt; and an urgent community psychiatric follow-up premium of \$200 for a new psychiatric patient consultation within 4 weeks of psychiatric hospitalization discharge.

The Clinical Care Modifier Model represents an important precedent in better identifying and incentivizing high-risk/high-intensity psychiatric care, as the incentives are clinically context sensitive and not limited to particular settings or practice models. We will continue to evolve this model with feedback from membership, and at the same time can take satisfaction that the Section's work over

several years has led to Ontario being the first jurisdiction anywhere to implement such a model for psychiatric care, which will likely serve as a precedent for influencing the development of such models elsewhere.

**ONTARIO IS THE FIRST
JURISDICTION ANYWHERE
TO IMPLEMENT THE
CLINICAL CARE
MODIFIER MODEL
FOR PSYCHIATRIC CARE**

Several other changes are also being implemented, including: a Psychiatric Consultation Extension code (for remunerating additional amounts for lengthy psychiatric consultations); Consultative Interview with Patient and Caregiver codes for patients age 65 and older, or patients with dementia, that parallel the existing A198/A197 Consultative Interview with Child/Parent codes; and extension of the current A198/A197 Consultative Child/Parent Interview codes to adolescents less than 22 years of age.

I would like to thank the Coalition of Ontario Psychiatrists and all the psychiatrists across the province who have helped bring about these positive changes. You will recall our successful member campaign to pressure the OMA to add the SAM factor to CANDI (to account for increased skills acquired with minimum required length of basic specialist training). **The resulting psychiatry relativity allocations have been over 50% higher than had otherwise been estimated prior to SAM being introduced (11.024% [4.5% and 6.524% in 2010 and 2011, respectively] vs the estimated 6.9% [3% plus 3.9%] prior to SAM). This total 4.124% higher allocation alone over the past 2 years represents over \$12 million additional ongoing annualized funding for improving psychiatric services and patient care.**

For details of billing rules for all these codes and the specific increases to existing codes, please refer to the separate OMA and MOHLTC communications regarding the September 1, 2011 changes. As always, if you have any questions please feel free to contact me at psych@rogers.com. ▲

K. Sonu Gaind, MD, FRCP(C)
*Medical Practice and Tariff Chair,
Ontario Medical Association Section on Psychiatry
OPA Council Member*

OPA 2012 ANNUAL CONFERENCE

March 30 & 31, 2012

CALL FOR ABSTRACTS

The OPA Conference Organizing Committee
is accepting submissions for the
2012 Annual Conference Educational Program.

For more information and to submit your abstract,
please visit www.eopa.ca

Deadline for Submissions:
Saturday, October 15, 2011

T. A. SWEET AWARD CALL FOR NOMINATIONS

The OPA announces its
Call for Nominations for the
2012 *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.

For more information and to submit your nomination,
please visit www.eopa.ca

Deadline for Nominations:
Thursday, September 15, 2011

OPA 2011 Annual Conference

R E V I E W

This Ontario Psychiatric Association's 91st Annual Conference took place this April at the historic Le Méridien King Edward Hotel in Toronto. The two day event once again provided members an opportunity to reconnect with colleagues across the province while enjoying a diverse and impressive academic programme.

The theme of this year's conference was *Engaging the Profession*, which ties in with OPA President Dr. Alison Freeland's presidential theme for this coming year. Given the increasing level of interest and public awareness of mental health and illness, the development of the government's proposed "10 year plan" for mental health services in Ontario, and as OMA-Ministry negotiations appear on the horizon, it is particularly timely to ensure we are all engaged in examining psychiatry's role in society, and active in advocating for our profession and our patients.

The conference opened with a keynote address, "*Is Diagnosis Useful? A Journey of Personal Experience, Societal Views and Medical Perceptions*" by Dr. Mark Vonnegut, a Massachusetts paediatrician and son of iconic author Kurt Vonnegut. Dr. Vonnegut has written two books on his personal experiences with mental illness, *The Eden Express: A Memoir of Insanity* and *Just Like Someone Without Mental Illness Only More So*. Dr. Vonnegut's session was both stimulating and eye-opening. Dr. Vonnegut shared insights gained through his unique journey, from developing psychotic symptoms, to enduring public reactions to his illness, to entering medical school at Harvard and working as a paediatrician. The thought-provoking discussion raised particularly helpful points as we consider how best to engage the public on mental illness issues.

The remainder of the programme included a diverse range of submitted sessions and renowned invited speakers, including Dr. Zindel Segal on Mindfulness-Based Cognitive Therapy, Dr. Peter Selby on Smoking Cessation, Dr. Claudio Soares on New Treatments for Mood Disturbances Across the Reproductive Cycle, Drs. Elliott Lee & Alan Douglass on the Interface Between Sleep Disorders and Mental Illness, and Drs. Keith Connors, Doron Almagor & Russell Schachar on Recent Advances in the Diagnosis and Management of ADHD in Children and Adolescents. Attendees had the opportunity to hear from Department Chairs across the province their visions of the future of academic psychiatry during a panel session on Friday, and enjoyed a stimulating session by Dr. Susan Abbey during the Jane Chamberlin Lecture on Saturday. Other sessions focussed on clinical issues, practice management, negotiations and the medical-political landscape, and health systems and service delivery.

Attendees also had a chance to unwind and mix with colleagues and OPA Council members during the Friday



Dr. Mark Vonnegut, keynote speaker; and Margaret Trudeau, T. A. Sweet Award recipient. Opposite page: Highlights from the OPA 2011 Annual Conference.

night Gala Dinner, emceed by Dr. Susan Abbey and Dr. Gary Chaimowitz. Dr. Alfred Amaladoss was awarded the *Dr. Ann Thomas Award* for the Best Resident Poster for Repetitive Transcranial Magnetic Stimulation a Novel Approach in Obsessive Compulsive Disorder, and Margaret Trudeau accepted the *T. A. Sweet Award* for her advocacy on mental health issues. The evening was a memorable one as Ms. Trudeau and a hardy group of stalwarts danced late into the night to the live band.

It truly was a wonderful conference, and I want to thank the Education Committee, OPA Council and especially our Association Manager Halyna Troian for making the 2011 OPA Annual Conference such a success.

We are now looking forward and planning the 2012 Annual Conference, which will be held on March 30 & 31, 2012, in Toronto. The program committee will be reviewing the curriculum and for 2012 we will have a streamlined and improved online submission process for abstracts. If you have a session or poster that would be of interest to your colleagues I would encourage you to submit it for consideration, and I hope you mark your calendars and plan to join us in 2012 — it promises to be another great conference!▲

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



OPA 2011
Annual Conference
ENGAGING the
PROFESSION



OPA 2011 Annual Conference REVIEW

– Dr. Soares's Presentation –

Dr. Claudio Soares from McMaster University gave an excellent keynote address on “*New Treatments for Mood Disturbances Across the Reproductive Cycle*”. Women’s mental health issues have garnered significant attention in the last few years and the importance of gender specific care in the treatment of mental illnesses has become part of evidenced based treatment. Mood disorders are of particular interest as women are at increased risk of depression compared to men throughout most of their lives. Dr. Soares led the audience through a presentation that reviewed the potential role of abrupt changes in sex steroids and how that can influence the development of depression at different reproductive stages. Of particular interest was the presentation of new research that suggests that rather than having an excess of hormones, women may have an increased sensitivity to hormones at the receptor level, and this may explain why some women may be at increased risk for depression at each key reproductive stage during their lives.

Dr. Soares spent some time presenting research that defines the role of antidepressants in treating not just the depressive symptoms that may occur in the perimenopause, but also the vasomotor symptoms. He reviewed the options available for treating perimenopausal symptoms and discussed the current evidence that supports deciding



Dr. Claudio Soares giving his address at the plenary session.

whether or not to use HRT or SSRIs/SNRIs.

The presentation was very well received, and prompted many members of the audience to engage in the question period at the end. There is clearly much to research and learn in this area, and participant feedback indicated that this will be a welcome topic at future OPA conferences.▲

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

OPA 2011 Annual Conference REVIEW

– A Resident's Perspective –

Although I have been an MIT member of the OPA for three years, this was the first Annual Conference that I have attended — and what a great initiation to this event! In the fall of 2009 I saw Nancy McWilliams speak at the annual fall psychotherapy conference, so I had high expectations for my second OPA event. Looking at the program for this year’s “*Engaging the Profession*” conference, I was interested in listening to several of the invited speakers. Having been a fan of Kurt Vonnegut, I was really looking forward to seeing his son, keynote speaker Dr. Mark Vonnegut, discuss his personal journey with mental illness. I was not disappointed. Hearing his perspective and lived experience on mental illness was not only entertaining, but thought provoking, and will influence my future practice. Although I have not read his book, I look forward to reading it now.

The content of the conference was varied and truly educational. From Treatments of Mood Disturbances Across the Reproductive Cycle, to Mindfulness-Based Cognitive Therapy, to Sleep Disorders, to Somatoform Disorders, there were so many sessions I wanted to attend

that it became difficult to choose! Not only were the talks given by experts in the field, but each provided information that will help shape my future practice. Learning relevant “clinical pearls” really set this conference apart.

Aside from the talks given, I had the opportunity to meet and talk with psychiatry residents from other schools, something I rarely have the opportunity to do. There was an increase in resident representation this year, with participants from University of Ottawa, University of Toronto, and University of Western Ontario. Many residents enjoyed the gala dinner, and dancing, which featured *T. A. Sweet Award* winner Margaret Trudeau. Hearing about how other programs work and catching up with old friends were some of the unexpected benefits of the event. The residents I spoke with plan on attending again, and I’m already looking forward to next year’s conference.▲

Dr. Jennifer Tiffney, MD
OPA Council Member

OPA 2011 Annual Conference REVIEW

– Managing Risk in Mental Health Settings –



Presenters (left to right) – Dr. Soojin Chun, Dr. Robert Swenson and Dr. Gary Chaimowitz.

This year's OPA Annual Conference highlighted some very topical themes in the area of patient safety and risk management. This comes at a time when the Ontario government has introduced significant legislative changes in the provision of hospital care, and the management of violence risk within the workplace.

The Excellent Care for All Act was introduced in 2010 with the goal to improve the quality and value of the patient experience through the application of evidence-based care. It mandated each hospital to have a quality committee, annual quality improvement plans, and executive compensation (including senior physician leaders) tied to improvement targets. The challenge has been the relative lack of structured tools and strategies to improve quality and promote patient safety within a mental health setting. Soojin Chun, a second year psychiatry resident at the University of Ottawa, and Robert Swenson, Chief of Psychiatry from the Ottawa Hospital, presented on a multi-pronged approach to improve patient safety within their mental health setting. They utilized a novel prospective surveillance approach to identify the frequency and type of adverse events through the examination of patient based, system based and pharmacy based variables. This was followed by the voluntary reporting of adverse events into a Patient Safety Learning System, and a subsequent review by physicians, clinical staff, senior program leadership and risk management to identify systemic issues and opportunities for improvement.

In 2009, Bill 168 amended the Occupational Health and Safety Act. This legislation requires employers to prepare and implement policies that address workplace violence and harassment; within the healthcare sector this includes the requirement to assess and communicate the risk of violence from patients. Mental health settings have been struggling to delineate a process to meet this requirement. Gary Chaimowitz and Mini Mamak's presentation on "How to Assess and Manage Inpatient Violence – The AIS and HARM" provided some answers on how to approach this

problem. They highlighted the need for accurate violence risk assessment within mental health facilities, and described the approach they have been using at SJHC Hamilton. They use the Aggressive Incident Scale (AIS) which allows for standardized communication and documentation of aggressive incidents within an inpatient setting, together with the Hamilton Anatomy of Risk Management (HARM). The HARM provides a structured approach to assess the risk of violence and guide both individual treatment planning, and operational risk management of patients who have been identified as being at risk for violence.

Both of these presentations provided important contributions to the area of patient safety and risk management within mental health, and we look forward to further development of these topics and others at next year's conference.▲

Sarah Jarmain, MD, FRCP(C)

President-Elect, Ontario Psychiatric Association



Congratulations!

to

Dr. Alfred Amaladoss

Winner of the

DR. ANN THOMAS AWARD

for the

Best Resident Poster

at the

OPA 2011 Annual Conference.

The OPA Questionnaire ... with apologies to Proust*

OPA's Dialogue has developed this variation on the famous Marcel Proust Questionnaire* about one's personality, tailored to the Ontario Psychiatrist. Selections from different members' responses will be featured every issue.



Dr. ALISON FREELAND

Dr. Alison Freeland is the current president of the OPA. She trained at the University of Saskatchewan as an undergraduate and then at the University of Western Ontario and University of Ottawa to complete her training in psychiatry.

What is your idea of perfect professional happiness?

I'm not sure that I want to aspire to perfect professional happiness, as I think we constantly need different experiences and emotions in order to keep us challenged with coming up with new ideas and creative solutions for patients, families and health care systems.

What is your greatest fear?

I am not a big fan of flying. It's very hard work to be solely responsible for mentally keeping a plane in the air for several hours at a time.

What is the trait in yourself that you value most as a psychiatrist?

My patients have told me that I am a good listener with a good memory. I think those are pretty basic but important traits in a psychiatrist.

What is the trait in yourself that gives you the greatest challenge as a psychiatrist?

I have to curb my natural impatience on a regular basis. Ask my teenagers... they will tell you all about it!

What do you consider the most overrated virtue?

Sobriety. There are too many good wines out there.

What is your greatest regret?

I don't really have any regrets. Well, maybe one or two, but they are in the vault!

What or who is the greatest love of your life?

Pretty straight forward... my family and my dog Aggie.

What is your current state of mind?

It's been a hectic week so my head is a little frazzled today. But overall I feel pretty good and after recharging this weekend I'll be looking forward to next week's challenges.

What do you consider your greatest professional achievement?

I love being a psychiatrist and all the positives that my job brings, but I have to say I will never forget the first time I

delivered a baby by myself as an intern and how amazing that was for the parents. That was quite a feeling!

What is your most treasured possession that you keep in your office?

A ceramic penguin made by one of my patients and given with appreciation for my help at the time of discharge, despite the fact that I had used every piece of mental health legislation possible during his admission to treat him, and he had gone to every available consent and capacity board to try and deter me!

What makes you the most unhappy about your work?

Getting behind with dictating discharge summaries and then having to go in on the weekend to catch up.

Where in Ontario would you most like to live and practice?

Ottawa. It's the perfect size and has lots of activities and opportunities for everyone. And I work with some great colleagues at the Royal Ottawa Mental Health Centre. For now I have no plans to leave!

What is your favorite occupation?

I have lots depending on my mood and where I am. But I love to be in a new city with a friend, walking around all day with no specific agenda, and experiencing all the different sites and sounds that it has to offer.

What do you most value in your colleagues?

Fairness, working hard, being upfront about problems and solutions, and a great sense of humour.

Who are your favorite authors?

Well, my all time favourite book is *Lucky Jim* by Kingsley Amis. I reread it every couple of years and enjoy it immensely every single time.

Who is your favorite hero of fiction?

Jim in *Lucky Jim*.

Who are your psychiatric heroes in real life?

I really admire all the people with mental illness that I see living and working in the community successfully despite their ongoing symptoms and challenges.

How would you like to retire?

I plan on winning the lottery, buying a villa on the mediterranean coast with a fabulous view, travelling around Europe in a Porsche convertible to see as many works of art as I can, taking painting classes and learning how to cook (which is something I currently do not do well). If I don't win the lottery I suspect I will come up with an equally fun although somewhat cheaper plan.



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. Cerebrovascular adverse events:** An increased risk of cerebrovascular adverse events has been seen in the dementia population with some atypical antipsychotics. The mechanism for this increased risk is not known. There is insufficient data with quetiapine to know if there is an increased risk of cerebrovascular events associated with quetiapine. An increased risk, however, cannot be excluded. SEROQUEL XR is not

indicated in patients with dementia. **Vascular disease:** SEROQUEL XR should be used with caution in patients with risk factors for stroke or with a history of stroke. **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 (see WARNINGS AND PRECAUTIONS, and ADVERSE REACTIONS).



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 (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 (≥10%) cases of elevations in serum triglyceride levels (≥2.258 mmol/L on at least one occasion) and decreases in HDL cholesterol (<1.025 mmol/L males; <1.282 mmol/L females at any time) have been observed during treatment with quetiapine in clinical trials (see ADVERSE REACTIONS). Lipid changes 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%. **QT Prolongation:** In clinical trials, quetiapine was not associated with a persistent increase in absolute QT intervals. However, in post-marketing experience, there were cases reported of QT prolongation with overdose (see OVERDOSAGE). As with other antipsychotics, caution should be exercised when quetiapine is prescribed in patients with cardiovascular disease or family history of QT prolongation. Also caution should be exercised when quetiapine is prescribed either with medicines known to increase QT interval or with concomitant neuroleptics, especially for patients with increased risk of QT prolongation, i.e., the elderly, patients with congenital long QT syndrome, congestive heart failure, heart hypertrophy, hypokalemia or hypomagnesemia (see DRUG INTERACTIONS). **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 (≥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 (≥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 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 tumorigenesis. 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 schizophrenia 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, 0.2% (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 T_4 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 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. 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. **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. **Dysphagia and Aspiration Pneumonia:** Dysphagia and aspiration have been reported with quetiapine. Although a causal relationship with aspiration pneumonia has not been established, SEROQUEL XR should be used with caution in patients at risk for aspiration pneumonia (see WARNINGS AND PRECAUTIONS, Special Populations and ADVERSE REACTIONS). **Hematologic: Neutropenia:** Severe neutropenia ($<0.5 \times 10^9/L$) 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 $<1.0 \times 10^9/L$. These patients should be observed for signs and symptoms of infection and neutrophil counts followed (until they exceed $1.5 \times 10^9/L$) (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 including quetiapine. 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 placebo-controlled clinical trials for schizophrenia and bipolar mania the incidence of EPS was no different from that of placebo across the recommended therapeutic dose range. It has been hypothesized that agents with a lower EPS liability may also have a lower liability to produce TD. This relationship predicts that quetiapine should have less potential than typical antipsychotic agents to induce TD in schizophrenia and bipolar mania patients. In short-term, placebo-controlled clinical trials for bipolar depression and major depressive disorder, the incidence of EPS was higher in quetiapine treated patients than in placebo treated patients. See ADVERSE REACTIONS. 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, dose reduction or drug discontinuation should be considered. Some patients may require treatment with SEROQUEL XR despite the presence of the syndrome. The symptoms of TD can worsen or even arise after discontinuation of treatment (see ADVERSE REACTIONS). **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 short-term placebo-controlled clinical trials across all indications and ages, the incidence of suicide-related events (suicidal thoughts, self-harm and suicide) was 0.9% for both quetiapine (61/6270) and for placebo (27/3047). 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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DRUG INTERACTIONS

Drug-Drug Interactions: Given the primary central nervous system effects of quetiapine, SEROQUEL XR should be used with caution in combination with other centrally acting drugs. Caution should be exercised when quetiapine is used concomitantly with drugs known to cause electrolyte imbalance or to increase QT interval (see WARNINGS AND PRECAUTIONS, Cardiovascular).

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

Body System and MedDRA Term ^a	Percentage of Subjects With Adverse Events*	
	SEROQUEL XR (n=1149)	Placebo (n=648)
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				
	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				
Disturbance in attention	0	1	2	2
Hypoesthesia	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		
	SEROQUEL XR (n=166)	Placebo (n=172)
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 ≥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 ≥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 (≥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 (≥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 α₁-adrenergic blocking activity, SEROQUEL XR may induce postural hypotension, associated with dizziness, tachycardia and, in some patients, syncope, especially during the initial dose-titration 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 (≥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). **Tardive Dyskinesia:** There have been uncommon cases of tardive dyskinesia reported in patients administered quetiapine (see WARNINGS AND PRECAUTIONS, Neurologic). **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 (see WARNINGS AND PRECAUTIONS, Neurologic). **Dysphagia:** There have been uncommon cases of dysphagia in patients administered quetiapine (see WARNINGS AND PRECAUTIONS, Gastrointestinal and Special Populations). **Dysarthria:** There have been common 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 leukopenia and/or neutropenia have been observed in patients administered quetiapine. Uncommon cases of eosinophilia and thrombocytopenia (platelet count decreased, ≤100 × 10⁹/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 µg/L in males and >30 µg/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 ≥1.5 × 10⁹/L, the incidence of at least one occurrence of neutrophil count <1.5 × 10⁹/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 ≥1.5 × 10⁹/L, the incidence of at least one occurrence of

neutrophil count $<1.5 \times 10^7/L$ was 1.72% in patients treated with SEROQUEL, 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 $<1.0 \times 10^7/L$, among patients with a baseline neutrophil count $\geq 1.5 \times 10^7/L$, the incidence of at least one occurrence of neutrophil count $<0.5 \times 10^7/L$ was 0.21% in patients treated with SEROQUEL and 0% in placebo-treated patients and the incidence $\geq 0.5 - <1.0 \times 10^7/L$ was 0.75% in patients treated with SEROQUEL and 0.11% in placebo-treated patients (see WARNINGS AND PRECAUTIONS, Hematologic). Common cases of asymptomatic elevations in serum transaminases (AST, 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 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 causes clinically relevant hypothyroidism (see WARNINGS AND PRECAUTIONS, Endocrine and Metabolism). **Hyperglycaemia:** 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) 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), and decreases in HDL cholesterol (<1.025 mmol/L males; <1.282 mmol/L females at any time) have been observed during treatment with quetiapine in clinical trials (see WARNINGS AND PRECAUTIONS, Cardiovascular). Lipid changes 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, which was driven by increases in LDL cholesterol. The mean LDL level 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 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 treatment. Resolution of leucopenia and/or neutropenia has 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, Hematologic). 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 SEROQUEL, sometimes in patients with no reported history of hyperglycaemia (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 treatment. The reporting rate of anaphylaxis 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 cause) 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 case 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, galactorrhea 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, 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 $t_{1/2}$ 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:** zimipramine, 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 were cases reported of QT prolongation with overdose. 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.



This Prescribing Summary provides you with the most current information at the time of printing. For the most current information, the full Product Monograph prepared for health professionals can be found at www.astrazeneca.ca.

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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. February 17, 2010.

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SEROQUEL XR®: For the treatment of Major Depressive Disorder¹

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