DIALOGUE
ONTARIO PSYCHIATRIC ASSOCIATION
MARCH 2010

President's Message

Dr. Paul Mulzer

I'm mindful of the old adage "may you live in interesting times". When I first heard this expression in my late teens I questioned if it was penned by a humourist, a cynic or a sage. Perhaps in a tangible manner the author was all three. We certainly can see its applicability in the dramatic events of 2009. We saw an intense drive to reform the mental health and addiction system with both a National Commission and a dramatic Provincial Initiative which began with a roar of media fanfare but appears to be going out with a diminutive whimper. It was followed by the monumental mismanagement that became the eHealth saga and the unfulfilled promise of more titillating disclosures to come. We ushered in a new Health Minister who echoed the party line of austerity. This, of course, was preceded by a massive bailout of multi-national corporations.

Never has this year's Presidential Theme of *Dignity, Advocacy and Social Justice* been more appropriate than now and never has a need for grassroots political activism been more desperately required. I'm not a political zealot but the events of the last few years have shaken me from my apathetic slumber. I think the collective wisdom and experience of many of our members is desperately required to balance the often well intended but brash policy initiatives. I am old enough to remember implementing ineffective health unit policies and receiving prompt and often colourful feedback on my naïveté from more seasoned clinicians. At present there are too many degrees of separation between an idea at a Ministry or LHIN level and the stark reality on the clinical front. I'd encourage all members to advise where you can, challenge where you must and serve where you are able.

> *ADVISE WHERE YOU CAN, CHALLENGE WHERE YOU MUST AND SERVE WHERE YOU ARE ABLE.*

This invitation, of course, includes consideration of allowing your name to stand as a potential Council member of the OPA. Your wisdom is an asset that is highly valued, indeed.

I'm leaving my role as President just at the point I think I'm beginning to get good at it! This is certainly ironic. I could not be more delighted to introduce your incoming President, Dr. Doron Almagor, who has been a very active Council member at critical times in our recent history. He has a keen intellect and a thoughtful manner that will honour the trust we've placed in him. I hope you will attend our 90th Annual Conference on April 23 and 24, 2010, and speak with our Council members in attendance. Council members like our Treasurer, Dr. Deborah Elliott, who has served in this critical, but often thankless role, and Dr. Anne Hennessy, who is the very human face of the OPA in her duties as membership committee chair. Our communication committee is ably lead by Dr. Patricia Cavanagh.

The delightfully distractible and incorrigibly inattentive Rick Green will entertain you. You will also enjoy our walk through the OPA timeline with Dr. John Deadman and historical scholar, Dr. Edward Shorter. Dr. Sonu Gaind has served you well as educational committee chair and Past President with an excellent selection of thought provoking topics. I'd like to thank him for his leadership during challenging times. Our venue, Le Méridien King Edward Hotel, was well received last year and promises to showcase another great CME event. I'd encourage you to join with your Council and OPA Manager, Halyna Troian, as we respectfully recognize our past, advocate to meet the challenges of the present and pursue social justice for our future to enhance and enrich the lives of the vulnerable patients we serve.▲

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

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From the Editor

Coming together is a beginning.
Keeping together is progress.
Working together is success.
— Henry Ford

THIS YEAR the Ontario Psychiatric Association celebrates its 90th Anniversary. One of the oldest associations in Canada, it went through challenging times during its long history, dealing with issues of great importance to its members and the Canadian population in general. But at all times it remained a society of professionals that had two main objectives: to maintain the highest standards of the profession of psychiatry, and to advocate on behalf of the mentally ill and their families. Let us celebrate together this milestone anniversary at the Annual Conference in April! What could be a better opportunity to meet your colleagues and friends, to share your experience with your peers and to learn from your mentors.

In this issue of *Dialogue* Dr. J. Deadman continues to reflect on OPA history in his column. His article on educational programs at past OPA conferences is most informative.

Earlier this year we experienced first hand the nationwide response to the devastating earthquake in Haiti. We were all struck by the magnitude of the Haiti disaster, and the enormous need for help. In his article, Dr. A. Howlett explores the ways in which our members may offer support to relief efforts in Haiti.

This issue also features Dr. S. Jarmain's article on the role of seclusion and restraint in an era of recovery; Dr. A. Howlett's update on PAIRO and physician wellness; an update on tariffs by Dr. K. Sonu Gaind; and Dr. A. Hennessy's thoughts on the meaning of being a member of the OPA.

We encourage you, our members, to share with us your memories of the OPA, stories about your mentors, people that influenced your career choice and served as role models for your professional development. As always, we welcome your articles, book reviews and clinical cases.

Look forward to seeing many of you at our not-to-be-missed history making 90th OPA Annual Conference!▲

Halyna Troian, CAE
Editor

OPA 2010 Annual Conference Update

We are eagerly looking forward to the upcoming Ontario Psychiatric Association Annual Conference, on April 23-24. This conference marks the OPA's 90th Anniversary, and following the positive feedback from last year's conference we are pleased to be returning to the elegant and historic Le Méridien King Edward Hotel in Toronto to celebrate turning 90!

The Education Committee has worked hard to bring you a strong and diverse program, which will start off with a keynote address, "My Award-Winning, Coast-to-Coast Mental Disorder", by acclaimed producer, director and comedic performer Rick Green. Rick has been diagnosed with adult ADD. He produced the award-winning documentary *ADD & Loving It?!* and recently launched the website *TotallyADD.com*. We are thrilled that Rick will also be emcee'ing the Friday night gala dinner, where Sister Margaret Smith of North Bay will be receiving the *T.A. Sweet Award* for her longstanding work in the field of addictions. Other program highlights will include the Jane Chamberlin Memorial Lecture, delivered by Dr. Anthony Levitt on *The Art and Science of Dosing Strategies in the Treatment of Resistant Depression*, a keynote on *The History of Psychiatry and the OPA* by Dr. Edward Shorter and Dr. John Deadman, invited sessions on first episode psychosis by Dr. Suzanne Archie, child psychiatry by Dr. Umesh Jain, geriatric psychiatry by Dr. Marie-France Tourigny-Rivard, and others.

Finally, you will note we have moved the conference into the spring, a wonderful time to visit Toronto. Please join us for the conference and the Friday night gala dinner and meet up with your colleagues from around the province, it promises to be a great program.▲

K. Sonu Gaind, MD, FRCP(C)
Past President, Ontario Psychiatric Association
OPA Education Committee Chair

The Annual General Meeting (AGM) of the Ontario Psychiatric Association will be held at 12:00 noon on Friday, April 23, 2010, at Le Méridien King Edward Hotel (Vanity Fair Ballroom) 37 King Street East Toronto, Ontario

I PROXY ELIGIBILITY

Full Members, Life Members and Members-in-Training who are in good standing are entitled to vote at the OPA's Annual General Meeting. If you are unable to attend the meeting, you may request another person to represent you and your vote.

II VOTING CARD

Voting card(s) will be issued to each voting member on April 23, 2010, just prior to the meeting.

III SUBMISSION OF PROXIES

All those who will be exercising a proxy for a member must hand in a completed proxy form. One voting card per proxy will be issued at the OPA Annual General Meeting registration desk.

IV CONSULTATION WITH THE PERSON EXERCISING YOUR PROXY

Voting members should inform their proxy of their preferred stand on each topic under consideration.

ONTARIO PSYCHIATRIC ASSOCIATION
Annual General Meeting

PROXY

I, _____
(Please print your name)
will be unable to attend the April 23, 2010, Annual General Meeting of the Ontario Psychiatric Association, and hereby designate,

_____
(Name of proxy)

OR

☐ OPA Secretary
to act at this meeting with the same power as if I personally attended.

Signature _____

Date _____

Please submit the completed proxy form to the OPA office by Monday, April 19, 2010, by mail (2233 Argentia Road, Suite 100, Mississauga, ON L5N 2X7), fax (905-826-4873) or e-mail *opa@eopa.ca*.

Reaching Out to Haiti

Following the disastrous earthquake in Haiti, a number of medical organizations, including the Royal College of Physicians and Surgeons of Canada, the Canadian Medical Association, the Ontario Medical Association, and the American Psychiatric Association, wrote to their members offering their condolences and response plans. The OPA would also like to offer its condolences to all those who have been affected by this tragedy. As physicians we are concerned about the well-being and mental health of our patients, neighbours, and communities and we know that this will greatly affect all of us. We hope to do our best to react swiftly to an anticipated increase in demands for psychiatric services.

New information with regards to needs and support options come forward every day and we recommend that you follow these updates online. All organizations indicate that financial donations remain the most effective way to contribute at this time. Our Canadian Government has removed its $50-million dollar cap and will match dollar-for-dollar every donation made by individual Canadians. The OPA would like to thank our members who have already found a way to support relief for Haiti.

If you wish to provide a charitable donation, there are many organizations involved in providing aid to Haiti. Proceeds from the nation-wide program Canada For Haiti (*www.canadaforhaiti.com*) go toward a coalition of Canadian NGOs, including Canadian Red Cross Society, Care Canada, Free the Children, Oxfam Canada, Oxfam Quebec, Plan Canada, Save the Children Canada, UNICEF Canada and World Vision Canada. Additional information on other charities and how to evaluate charities before making a donation can be found at *www.cbc.ca/haitirelief*.

Physicians have also asked how they can assist with on-site relief efforts. Physicians have been recruited through organizations such as Médecins Sans Frontières/Doctors Without Borders. The role of psychiatry on the ground has yet to be determined. The APA, for instance, is not yet recruiting volunteers. Those interested in volunteering should refer to these organizations above; however, the APA Guidelines on Mental Health and Psychosocial Support in Emergency Settings (Action Sheet 4.1 Point 7, pages 73-74) state the following: *Well-intending foreign mental health professionals (who are not affiliated to any organization) should be discouraged from traveling to disaster affected regions unless they meet the following criteria:*

- *Previous work in emergency settings;*
- *Previous work outside own socio-cultural setting;*
- *Basic competence in interventions covered in guidelines understanding of either community psychology or public health principles;*
- *Written invitation from a national or established international organization to work in the country;*
- *Invited to work as part of an organization that is likely to maintain a sustained community presence in the emergency area;*
- *Not focus work on implementing interventions themselves (e.g. clinical work), but rather providing support to programs on a general level, including the transfer of skills to local staff, so that interventions and supports are implemented by local staff.*

To assist in the mental health response, the APA has many resources on disaster psychiatry and disaster mental health care and services posted on their web site, including: Disaster Resources for First Responders, and Providing Assistance to Victims.

Here at home, the Ottawa Sun reported that Haitian-born Psychiatrist, Dr. Pierre Monpremier, and colleagues are offering free psychiatric treatment and counseling over the next six months for those with family and friends in Haiti.

The OPA would be pleased to hear from you about your stories, ideas and efforts to bring relief to those affected. Please write to us at *opa@eopa.ca*.

Andrew L. Howlett, MD
PGY-3 / University of Toronto
OPA Council Member

Tariff Update

As reported in the last issue of *Dialogue*, the proposed new relativity model, the Comparison of Average Net Daily Income (CANDI) model, had finally been modified to include a "Skills Acquisition Modifier", or SAM, which placed a value on additional years of minimum required post-graduate specialty training. This revised CANDI model with SAM modifier was approved in November by OMA General Council, and thus will form the basis for the OMA's proposals for determining 2010 and 2011 relativity allocations. The Ministry of Health and Long Term Care has also identified several priority areas it wishes to discuss with Sections and address for 2010 and 2011 allocations. While the Section will of course engage in discussions to improve patient care in areas of need, we are also very aware of the need to ensure sectional allocations negotiated on behalf of members are directed in ways to also address our members' needs. Once more information is available we are planning to survey members for their opinions regarding possible options for future allocations.

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

TRANSFORMING MENTAL HEALTH CARE
the role of seclusion and restraint in an era of recovery

On October 10, 2008, The Globe and Mail reported: *"Mental health workers should avoid using physical restraint to control combative patients and adhere to far stricter standards when there is no other option but to use them."* This was a recommendation that came out of the Jeffrey James Coroner's Inquest, which looked into the death of a 34 year old male with a long and complex history of schizophrenia. Jeffrey James was transferred from Penatanguishine to CAMH, and died of a pulmonary embolism after 5 days of restraint use. The inquest identified a number of concerns including inadequate physician assessment for both mental and physical status of the patient while in restraint. They issued 65 recommendations with far reaching implications for the standards of practice around restraint use. Specific organizations named in the report included Accreditation Canada, CAMH, Psychiatric and Schedule 1 facilities, LHIN's, RNAO and the Psychiatric Patient Advocate Office (PPAO). As a result of these recommendations, psychiatric facilities have had to reexamine their restraint policies, and often make significant changes in the level of observation and frequency of reassessment of patients by physicians.

The Jeffrey James inquest comes at a time when there has been increasing focus on restraint use in psychiatric facilities across North America, and a concern about the morbidity and mortality related to prolonged use of restraint. In 1998, a team of Hartford Courant reporters and researchers compiled a national database (US) to shed light on deaths that occurred during or shortly after psychiatric or developmentally disabled patients were restrained or secluded. The database documented 142 deaths from 1988 to the 1998, as identified by public agencies, advocacy offices and news accounts. This triggered a report to the US Congress, and subsequently a commissioned report outlining the need for transformation within the mental health system. A Cochrane Review in 2000 supported the concerns about restraint use when it stated:

> *"No controlled studies exist that evaluate the value of seclusion or restraint in those with serious mental illness. There are reports of serious adverse effects for these techniques in qualitative reviews. Alternative ways of dealing with unwanted or harmful behaviours need to be developed."*
>
> (Sailas EES, Fenton M. Seclusion and restraint for people with serious mental illnesses. Cochrane Database of Systematic Reviews 2000, Issue 1.)

In 2003 the Substance Abuse and Mental Health Services Administration (SAMHSA) launched "A National Call to Action: Eliminating the Use of Seclusion and Restraint". Their National Action Plan has included state incentive grants to identify alternatives to restraint use. They have adopted the "The Six Core Reduction Strategies ©" – Huckshorn, K. (NTAC, 2006) as an evidence-based approach to work towards elimination of seclusion and restraint:

1. Leadership toward Organization Change
2. Use of Data to Inform Practice
3. Workforce Development
4. Use of Seclusion and Restraint Prevention Tools
5. Full Inclusion of Consumers and Families
6. Rigorous Debriefing [incident review].

One of the most successful examples of significant reduction of seclusion and restraint is the Pennsylvania State Hospital System's Seclusion and Restraint Reduction Program (Psychiatric Services, September 2005), in which they dramatically reduced the use of seclusion and restraint from 1990 to 2000 — over 90% in some cases.

Canada has lagged behind the US in its lack of a national strategy to reduce the use of seclusion and restraint, but within Ontario there have been a number of significant task forces examining the issues. In 2000, the PPAO completed a Review of Seclusion and Restraint Practices in Ontario Provincial Psychiatric Hospitals in which they identified significant concerns in the use of seclusion and restraint within Ontario. CAMH issued a Restraint Minimization Taskforce Report in 2008 *(http://www.camh.net)* which outlines key components of restraint use minimization that can be used by mental health institutions. The Canadian Patient Safety Institute and the OHA sponsored a paper "Patient Safety in Mental Health" *(http://www.patientsafetyinstitute.ca)* which is the first compendium of information in the area of patient safety and mental health within Canada, and includes a review of the relevant literature. In September 2009 the Ontario Hospital Association (OHA) and Ontario Shores cosponsored a Mental Health Thought Leadership Forum to look at "transforming current practices in the use of restraint and seclusion." Discussion identified that in order for there to be elimination or even significant reduction in seclusion and restraint use, there needs to be a cultural transformation — where leaders, staff, physicians, clients and families work together to prevent conflict from occurring in the first place, use a trauma-informed approach, and attend to concepts of resiliency and recovery. For physicians in Ontario, it is important to be aware of the changing standards of practice in this area and to actively engage in transforming the system so that our clients receive the highest quality of care possible, while maintaining safety for all involved.▲

Sarah Jarmain, MD, FRCP(C)
OPA Council Member

New and Relevant from PAIRO

The Provincial Association of Interns and Residents of Ontario (PAIRO) remains active in ensuring that residents across the province continue to receive high standard education, opportunities and value for their efforts in serving the people of Ontario. Here are a few highlights from PAIRO's activities that I thought might be of importance and interest to our OPA members.

1. RESTRICTED REGISTRATION

Informally known as "moon-lighting", restricted registration is a program being piloted for residents who wish to work during off-hours. While some provinces enable residents to work as primary care givers, cover in-patient units or community call-shifts over weekends, Ontario removed this privilege for their residents years ago. Given an increase in demand for physician services and a request from members of PAIRO to provide this option, the restricted registration program is bridging this gap. There is a fairly formal process in place for residents to receive restricted registration. For those OPA members who are interested in finding out more about this program, or to post job opportunities for residents, please visit *www.restrictedregistrationontario.ca* or contact me through the OPA office for more details.

2. DEBT DEFERRAL

Still somewhat buried behind red-tape, residents will soon be able to hold off paying interest or any principal payment on their federal and provincial student loans during residency through the Resident Loan Interest Relief Program. The Ministry of Health and Long Term Care has agreed to temporarily pay the bill. The catch — residents participating in this program will be required to practice in Ontario for five full years after completing their residency, while at the same time paying off their loans.

3. H1N1 PANDEMIC RESPONSE

PAIRO has agreed that their residents would respond in any fashion necessary to help prevent or manage a H1N1 pandemic outbreak. This may include working outside the general expectations and responsibilities of one's training program such as psychiatry residents operating primary care or vaccine clinics. However, it has not come to this, and in fact, preparation for a H1N1 pandemic response seems almost trivial now given the recent disaster in Haiti. PAIRO has not made a statement with regards to the Haiti disaster, although you may refer to my comments on page 5 of this issue of *Dialogue*.

4. PHYSICIAN HEALTH & WELLNESS RESOURCE

This resource (*www.ePhysicianHealth.com*) is available to all physicians and I strongly encourage you to visit this site and review its services. More details about *www.ePhysicianHealth.com* can be found in the article below.

5. OTHER PAIRO PROJECTS

Please visit *www.pairo.org* for the latest details on PAIRO activities. Funding for residents is available for enhancing resident programs as well as new patient care initiatives that provide non-clinical benefits for patients served by residents.▲

Andrew L. Howlett, MD
PGY-3 / University of Toronto
OPA Council Member

The Latest in Physician Wellness

Physicians may be the most difficult patient population to treat. Although they share many illnesses with other patient populations, doctors' professional demands and pride may interfere with timely recognition and management of conditions. These may ultimately become quite costly to their health and their ability to practice. Mental health conditions are one of the most serious and under-recognized ailments of physicians. To improve physician wellness a number of experts in the area, including members of the OPA, have spear-headed an e-based wellness program for all physicians. *ePhysicianhealth.com* is now free and accessible on the Internet. I encourage you to peruse the site and review the variety of modules: from managing appropriate life style behaviours, to more serious conditions such as disruptive behaviour of physicians and substance abuse problems. This will be of value to physicians who are well, and also when you find yourself under stress. When I read through this site I was surprised to discover many familiar faces including my OPA colleagues as well as Dr. Yoni Freedhoff from the Bariatric Medical Institute in Ottawa. These prompted me to remember just how important it is to remain connected to those invested in healthy living and in particular, physician wellness. As a psychiatrist in training, it is critical to mold one's practice into a healthy and sustainable one.▲

Andrew L. Howlett, MD
PGY-3 / University of Toronto
OPA Council Member

90 YEARS OF PROFESSIONAL EDUCATION

The Ontario Psychiatric Association and its predecessor, the Ontario Neuro-Psychiatric Association will be officially 90 years old at the time of our Annual Meeting in April. The meeting will be held at Le Méridien King Edward Hotel on the 23rd and 24th of April which is only a few days before the anniversary of the first meeting on the 28th of April, 1920. Throughout those 90 years, the ONPA and the OPA have always included scientific papers and presentations in their general meetings. For a time in the 1920s, the ONPA published a journal consisting of papers presented at recent meetings. There was an attempt to restart the journal after the Second World War. A mimeographed document did come out a few times but the costs and long delays in commercial printing in those years meant that this journal was short-lived.

1920-2010

The Evolution of the Annual General Meeting

The Annual General Meeting was the focus of the presentations, but from the early years, a Fall Meeting was also held. These were held in the various Ontario Hospitals in the system with occasional meetings at the Toronto Psychiatric Hospital or the Homewood Sanatorium. Several meetings after the war were held at Sunnybrook or Westminster because the mental health of returning veterans was a big concern as it is now. These were afternoon or one day meetings depending on the length of the program. The fall clinical meeting on 28th of September, 1956, was held at the Park Plaza Hotel and for several years after that, annual meetings were held at the King Edward Hotel. By this time, there was a growing program that meant that the presentations were sometimes spread out over two days.

I attended my first OPA annual meeting at the Park Plaza Hotel in January 1966. I remember that there were paper sessions and symposia by different sections and usually a keynote speaker on a topic of the day. It was a Friday and Saturday meeting, but that year the Community Psychiatry Section held a panel discussion on the Thursday evening before. I have only missed two OPA annual meetings since then.

The January meeting was gradually extended to three days. Dr. Stanley Greben was Program Chair at that time and he can be credited with creating an annual meeting that was the equal of any in Canada. As the program got busier, the Park Plaza could no longer accommodate us and the meeting was moved to the Sheraton Centre. We had a couple of years at the Royal York. One of those years was the big blizzard which closed down the downtown of Toronto for almost a day. This led people to comment that there always seemed to be a big snowstorm at the time of the OPA meeting. It was then at the King Edward, the Delta Chelsea and the Eaton Centre Marriott until last year when we returned to the King Edward Hotel.

Let every student of nature
take this as his rule,
that whatever the mind seizes upon
with particular satisfaction,
is to be held in suspicion.
— FRANCIS BACON (1561-1620)
from *Novum Organum*, 1620

...FROM THE OPA ARCHIVES

Some Topics of Discussion over the Years

In the early years there was a heavy emphasis on medical and neurological topics. The 1925 meetings had presentations on the diagnosis of frontal lobe tumours, and acute haemorrhagic encephalitis. The one psychiatric paper, presented by Professor Humphries of Queens University, was entitled: *"Some Criticisms of the Freudian Concept of the Preconscious."*

In 1926 there was much discussion on Dementia Praecox and the new term, Schizophrenia that was then beginning to appear in the literature. Dr. W.E. Blatz, for many years chair of the Department of Psychology at the University of Toronto, gave a paper on Mental Hygiene. Dr. C.B. Farrar, Chair of the Department of Psychiatry described the community services available at the Toronto Psychiatric Hospital.

In 1927, the spring meeting was at the Ontario Hospital for Epileptics in Woodstock, and the fall meeting was at the Ontario Hospital for the Feeble Minded in Orillia with topics related to those facilities.

A paper in 1928 was: *"The Intensive Use of Bromides in the Treatment of the Functional Neuroses."* Another topic was: *"Post-encephalitic Paralysis Agitans."* Does anyone know what that condition is?

The eugenic sterilization of the feeble-minded was discussed at the meeting of 27th of May, 1930. The outcome of the discussion is not recorded. In 1932, the psychiatric examination for deportation was discussed. The ONPA seemed to get into loaded socio-political topics at that time. There were also discussions on neuro-syphilis and general paresis of the insane (GPI) which were filling the back wards of all the hospitals in those days. This was in the days before penicillin. How quickly we forget.

A sample program from 1934 has much about it that is familiar although the terminology has changed:

"Encephalography"
— Dr. D.R. Gunn, Ontario Hospital, Toronto.
"Analysis of Death Resulting from Acute Mental Excitement"
— Dr. G.H. Hutton, Ontario Hospital, Hamilton.
"Psychoneurosis and Conjugal Psychopathy"
— Dr. H.C. Moorehouse, Ontario Hospital, Brockville.
"Psychiatry and the Criminal Code"
— Dr. K.G. Gray, Ontario Hospital, Mimico.
"Current Trends in Mental Hygiene"
— Dr. C.M. Hincks (Guest Speaker), General Director National Committee for Mental Hygiene.

Some names from the past. I don't remember Dr. Hutton, but all of the others were still active when I was a student.

The topics continued in this vein throughout the 1930s and 1940s. At the June 1938 meeting, Dr. Norm Easton, who just retired from the Ontario Hospital, New Toronto in the early 1960s, gave a paper: *"The Insulin Shock Treatment of Schizophrenia."* This is the first mention of Insulin Coma in the minutes.

No meetings were held in 1940, 1941 or 1942 because of the extreme shortages of psychiatrists and physicians during the Second World War. At the meeting of 15th January, 1943, members were given the opportunity of witnessing a leucotomy operation at the Toronto General Hospital and a long discussion followed. It was performed by neurosurgeon Dr. K.G. McKenzie who worked in many hospitals in the system over the next 20 years. A quote in those minutes. The final sentence is a harbinger of things to come: *The afternoon session was held at the Psychiatric Hospital and Dr. L.D. Proctor of the Research Unit presented post-operative cases, all of whom have received Metrazole, Insulin or Electro-Shock without definite improvement.*

After the Second World War, the topics begin to take on a more familiar tone although there is an increasing awareness of the happenings in psychiatry by the general public. The Canadian Psychiatric Association was founded in 1951 and discussions as to whether the ONPA should amalgamate with it resulted in a decision to affiliate but not amalgamate. A joint meeting between CPA and ONPA in 1955 at the Royal York Hotel was chaired by Dr. Ewen Cameron of McGill University, and Sir Aubrey Lewis from the Maudsley Hospital in London England was the discussant.

On September 29th, 1956, the name was changed to the Ontario Psychiatric Association and a new constitution was adopted. 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

Membership of OPA: What does membership mean?

In these times of Internet connectivity, when it is easy to reach half way across the world with a couple of keyboard clicks many groups are having a tough time getting people together to connect, discuss issues and support each other.

Membership means being part of a group but I like the derivation where a member is a supporting strut holding up an edifice. Without you, the members, the whole house will fall down for the Ontario Psychiatric Association.

This organization has been around for 90 years arising from the Ontario Neuro-Psychiatric Association.

The council represents all university faculties of Ontario and community based psychiatrists and liaises with the OMA through the Coalition of Ontario Psychiatrists. We also have a healthy relationship with the CPA.

The OPA has the mandate to enhance scientific discourse between members, and through its Annual Meeting and the meeting of the psychotherapy section it endeavours to meet this mandate.

Membership is under pressure because of many factors:

- *The greying of the psychiatric profession.*
- *Difficulty recruiting younger psychiatrists.*
- *A plethora of meetings and associations competing for a shrinking market (pun intended).*

As a member of the OPA Council I am aware of the constant need to be relevant, responsive to members and recruitment focused.

The OPA has been a constant part of my professional life; the meetings are friendly, collegial and allow residents and younger members to meet and connect with friends and colleagues and to learn at the same time.

We welcome your input, your voice and thank you for your ongoing MEMBERSHIP!▲

Anne Hennessy, MD, FRCP(C)
OPA Member Services Committee Chair

AGHPS – Connecting through Technology

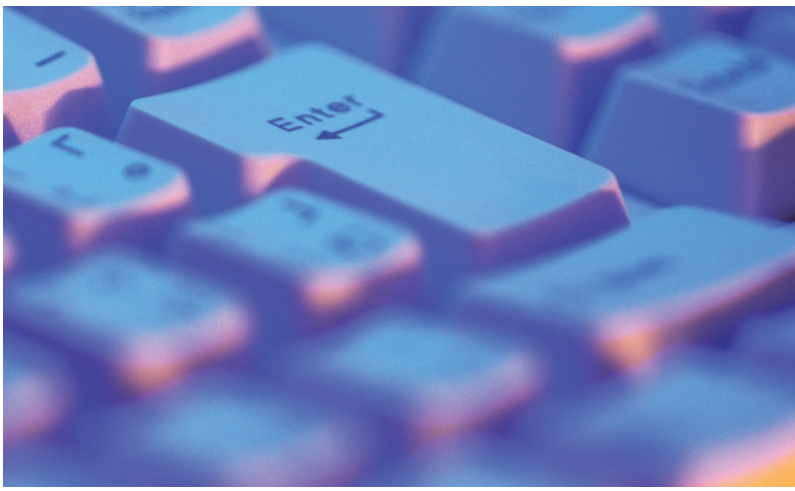
The Association of General Hospital Psychiatric Services (AGHPS) is pleased to have this opportunity to provide a brief summary of our activity in 2009 and some of the planning for 2010.

With the *People at Risk of Suicide Project* completed, the AGHPS focused attention in 2009 to complete extensive work on our web site in order to be increasingly helpful to Ontario's Schedule I hospitals.

The AGHPS has always been a pragmatic Association interested in making a difference to the front line mental health professionals in Ontario. Throughout our work with the Prevention of Suicide Project and in various surveys over the last few years we have asked our members how we can be more helpful to them. Repeatedly we were asked to play a lead role in bringing the hospitals together — to act as a "hub" that would allow the collecting and sharing of good ideas and best practices across Ontario. As we worked through the Project we were struck with the number of excellent initiatives and practices at individual hospitals and the inability to share our collective work in a simple and effective manner.

The AGHPS took this vision forward and has now developed an interactive web site that will allow General Hospitals to easily ask questions, post comments, attach policies, guidelines and other documents — to interact with their peers.

In practical terms, we are now in a position to be able to send an e-mail blast to Chiefs of Psychiatry and/or Directors of Mental Health in all Schedule I facilities in Ontario. We can ask them directly to advise us on their priorities (needs assessments), survey the province on



specific questions ranging from administrative issues (e.g. office rents) to practice guidelines. We can ask those professional leaders to post comments and share their policies and documents with others.

To assist with the launch of the web site, the AGHPS had USB flash drives with *www.aghps.com* made and a tutorial about how to use the web site. These are being mailed to Chiefs of Psychiatry and Directors of Mental Health throughout the province. We will also hold online educational sessions through March 2010. We encourage everyone to take advantage of this new interactive site and we welcome your comments.▲

June Hylands
Executive Director, AGHPS

Seroquel XR

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 reevaluate 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.

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 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 (≥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 hyperglycaemic 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 hyperglycaemic during treatment with atypical antipsychotics should undergo fasting blood glucose testing. In some cases, hyperglycaemia has resolved when the atypical antipsychotic was discontinued; however, some patients required continuation of anti-diabetic treatment despite discontinuation of the suspect drug. Patients with risk factors for diabetes mellitus (e.g., obesity, family history of diabetes) who are starting treatment with atypical antipsychotics should undergo fasting blood glucose testing at the beginning of treatment and periodically during treatment. Patients with an established diagnosis of diabetes mellitus who are started on atypical antipsychotics should be monitored regularly for worsening of glucose control. ***Hyperprolactinaemia:*** 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 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 mastodynia. **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 ≥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 x 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 x 10^9/L. These patients should be observed for signs and symptoms of infection and neutrophil counts followed (until they exceed 1.5 x 10^9/L) (see ADVERSE REACTIONS, Abnormal Haematologic 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%, 1/2588) 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 exams) prior to or shortly after initiation of treatment with SEROQUEL XR and at 6-month intervals thereafter, are recommended. If clinically significant lens changes associated with SEROQUEL XR use are observed, discontinuation of SEROQUEL XR should be considered. Psychiatric: Suicide/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 few (subclinical) single-dose study with SEROQUEL. SEROQUEL XR should thus be used with caution in patients with known renal impairment, especially during the initial dosing period (see ADMINISTRATION).

ADVERSE REACTIONS

Commonly Observed Adverse Events in Short-Term Placebo-Controlled Clinical Trials:

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:
AstraZeneca Canada Inc.
1004 Middlegate Road
Mississauga, Ontario
L4Y 1M4
www.astrazeneca.ca
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, imprinted 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, imprinted 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, imprinted with "XR 200" on one side and plain on the other, available in HDPE bottles of 60 tablets. 300 mg quetiapine tablets are pale yellow, capsule-shaped, biconvex, imprinted with "XR 300" on one side and plain on the other, available in HDPE bottles of 60 tablets. 400 mg quetiapine tablets are white, capsule-shaped, biconvex, imprinted with "XR 400" on one side and plain on the other, available in HDPE bottles of 60 tablets. 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 population 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 II Trials

Body System and MedDRA Term[a]	Percentage of Subjects With Adverse Events[b]	
	SEROQUEL XR (n=1149)	Placebo (n=440)
General disorders and administration site conditions		
Fatigue	7	2
Irritability	4	3
Nervous system disorders		
Sedation	28	6
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

[a] 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.

[b] Patients with multiple events falling under the same preferred term are counted only once in that term.

[c] The following adverse events occurred in 1% of patients treated with SEROQUEL XR compared to <1% in placebo: chills, dysarthria, dyspepsia, sluggishness, diarrhea, dizziness postural, tachycardia, restless legs syndrome, gastroesophageal reflux disease, pharyngolaryngeal pain and melaena.

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[b]			
	Placebo (n=330)	SEROQUEL XR 50 mg (n=151)	SEROQUEL XR 150 mg (n=328)	SEROQUEL XR 300 mg (n=311)
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	10	15
Dysarthria	0	1	1	2

Body System and MedDRA Term[a]	Percentage of Subjects With Adverse Events*			
	Placebo (n=3339)	SEROQUEL XR 50 mg (n=181)	SEROQUEL XR 150 mg (n=1204)	SEROQUEL XR 300 mg (n=1311)
Dizziness in attention	0	1	2	2
Hypoesthesia	1	0	1	2
Akathisia	1	0	2	1
Lethargy	1	2	3	1
Paraesthesia	1	1	2	1
Hypersomnia	0	1	2	1
Gastrointestinal system disorders				
Dry mouth	9	22	36	43
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	0
Musculoskeletal and connective tissue disorders				
Back pain	2	2	5	5
Arthralgia	2	2	3	0
Myalgia	2	4	5	0
Muscle tightness	1	1	0	2
Psychiatric disorders				
Anxiety	2	1	2	0
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	5
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 extrapyramidal events occurred in 1% of patients treated with SEROQUEL XR compared to <1% in placebo: hypersomnia, restless legs syndrome, joint stiffness, muscular weakness, pharyngeal/laryngeal pain and vision blurred.

Other Adverse Events: *Weight Gain:* In placebo-controlled MDD and schizophrenia clinical trials, the patients treated with SEROQUEL XR whose weight gain was 0.87 kg (n=1149) compared to 0.31 kg (n=4410) in patients treated with placebo. In a long-term randomized withdrawal MDD trial, patients who completed at least 156 days of SEROQUEL XR treatment (n=196), whose 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 156 days in SEROQUEL XR 50, 150 and 300 mg/day groups were 13%, 24% and 32%, 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 3.0% in placebo-treated patients, which occurs predominantly during the early weeks of treatment in adults (see WARNINGS AND PRECAUTIONS). *Sedation:* 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. *Somnambulism:* Somnambulism 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 was associated with a mean baseline to endpoint increase in heart rate of 2.9 beats per minute, compared to 1.4 beats per minute in placebo-treated patients. *Peripheral Edema:* As with other antipsychotics, common cases (≥1% - <10%) of peripheral edema have been reported in patients treated with quetiapine. *Allelic Asthenisia:* As with other antipsychotic agents, uncommon cases of allelic asthenisia have been reported in patients treated with quetiapine. *Akinesia:* There have been common reports of akinesia in patients administered quetiapine. *Hypersensitivity:* Uncommon cases of hypersensitivity including angioedema have been reported. *QTc Changes:* In a 600 mg/day therapeutic study, 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 class of SEROQUEL. 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 9.8% 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 uncommon cases of abnormal dreams and nightmares in patients administered quetiapine. *Suicide-Related Events:* In three trials of patients with MDD the incidence of suicide-related events was 2.3% (5/144) for quetiapine and 1.3% (1/75) for placebo in patients 10-24 and 0.6% (11/1798) for quetiapine and 0.7% for placebo (7/1054) in patients >25 years of age. *Irritability:* There have been uncommon cases of irritability in patients administered quetiapine. *Increased Appetite:* There have been uncommon cases of increased appetite in patients administered quetiapine. *Abnormal Hematologic and Clinical Chemistry Findings:* As with other antipsychotics, uncommon cases of leucopenia and/or neutropenia have been observed in patients administered quetiapine. Uncommon cases of eosinophilia and thrombocytopenia (platelet count decreased, <100 x 10⁹/L on at least one occasion) have been observed. Based on clinical trial adverse event reports and 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 x 10⁹/L, the incidence of at least one occurrence of neutrophil count <1.5 x 10⁹/L was 1.5% in patients treated with SEROQUEL XR and 1.5% for SEROQUEL, compared to 0.8% in placebo-treated patients. In all placebo-controlled monotherapy clinical trials among patients with a baseline neutrophil count >1.5 x 10⁹/L, the incidence of at least one occurrence of neutrophil count <1.5 x 10⁹/L was 1.72% 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 x 10⁹/L, among patients with a baseline neutrophil count >1.5 x 10⁹/L, the incidence of at least one occurrence of neutrophil count <1.5 x 10⁹/L was 0.21% in patients treated with SEROQUEL and 0% in placebo-treated patients and the incidence of <1.5 - <1.0 x 10⁹/L was 0.15% 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 (ALT, AST or uncommon cases of >3× normal) 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. Sporadic 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 FSH were not observed and there was no indication that SEROQUEL causes clinically relevant hypothyroidism (see WARNINGS AND PRECAUTIONS, Endocrine and Metabolic). *Hyperglycemia:* Blood glucose increases in hyperglycemic levels (fasting blood glucose >7.0 mmol/L or a non-fasting blood glucose >11.1 mmol/L on at least one occasion) have been observed commonly (≥1% - <10%) with quetiapine in clinical trials. In short-term (12 weeks duration or less) placebo-controlled clinical trials (3542 treated with quetiapine and 1490 treated with placebo), the percent of patients who had a fasting blood glucose ≥7.0 mmol/L or a non-fasting blood glucose ≥11.1 mmol/L was 2.5% for quetiapine and 2.1% for placebo. In a 24-week trial (active-controlled), 115 patients treated with SEROQUEL) designed to maintain 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 Metabolic). *Cholesterol and Triglyceride Abnormalities:* Very common (≥10%) cases of elevations in serum triglyceride levels (>2.258 mmol/L on at least one occasion) and elevations in total cholesterol (unclear exactly 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, which was driven by increases in LDL cholesterol. The mean LDL level increased at Week 24 by 10% in patients administered SEROQUEL, which were 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-Marketing Adverse Drug Reactions:* During post-marketing experience, neutropenia 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 neutropenia and/or neutropenia include pre-existing low white cell count and history of drug-induced neutropenia 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 (≥0.01% - <0.1%) during the use of SEROQUEL, sometimes in patients with no reported history of hyperglycemia (see WARNINGS AND PRECAUTIONS, Endocrine and Metabolic). Angioedema 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 angioedema associated with SEROQUEL use, which is generally accepted to be an underestimate due to underreporting, does not exceed the background incidence rate estimates. Estimates of the background incidence rate (all causes) of severe life-threatening angioedema in the general population range between 80 and 310 cases per million person-years, and the incidence rate of drug-induced angioedema is assumed to be 14 cases per million person-years. In addition, the all-cause fatal anaphylaxis rate is reported to be one per million person-years while 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, pancytopenia 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. *Antipsychotics:* SEROQUEL did not induce the hepatic enzymes involved in the metabolism of antipsychotics. *Lorazepam:* SEROQUEL did not affect the steady-state 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 were seen, 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 enhanced 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 to 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 ascertaining 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, Risperidone and Risperidone:* Fluoxetine (60 mg daily), imipramine (75 mg bid), risperidone (7.5 mg bid) and risperidone (3 mg bid) did not significantly alter the steady-state pharmacokinetics of SEROQUEL. *In patients taking the following antihypertensives:* enalapril, lisinopril, clonidine, dehydralazine, methyldopa, prazosin, terazosin and remifentanil, 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 peak plasma concentrations of the antihypertensive. **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 overdoses, 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 9000 mg and has 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 patient 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.

AstraZeneca

Member

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 (26%), somnolence (24%), dizziness (14%) and fatigue (7%). *Elderly*: somnolence (33%), dry mouth (20%), headache (19%) and fatigue (6%).

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.

SeroquelXR.ca

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See prescribing summary on page