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- Type tables double-spaced on pages separate from the text.
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- Each column should have a short or abbreviated heading.
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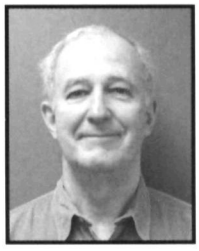

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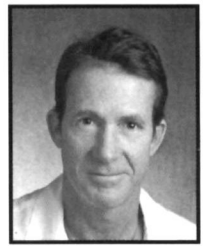

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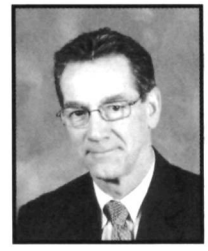

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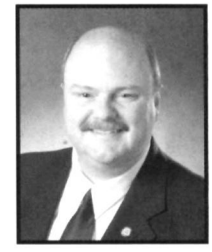

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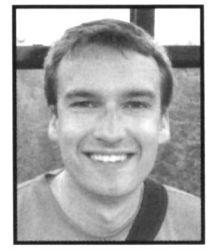

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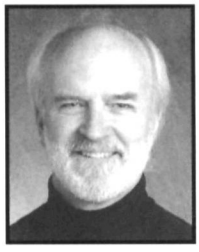

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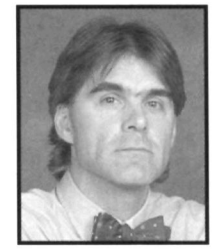

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Pr VIMPAT™
lacosamide

Prescribing Summary

Patient Selection Criteria

THERAPEUTIC CLASSIFICATION: Antiepileptic Agent

INDICATIONS AND CLINICAL USE

Adults (≥18 years of age) VIMPAT (lacosamide) is indicated as adjunctive therapy in the management of partial-onset seizures in adult patients with epilepsy who are not satisfactorily controlled with conventional therapy. VIMPAT (lacosamide) solution for injection for intravenous use is an alternative when oral administration is temporarily not feasible. **Geriatrics (≥65 years of age)** The clinical experience with VIMPAT in elderly patients with epilepsy is limited (n=18). Caution should be exercised during dose titration and age-associated decreased renal clearance should be considered in elderly patients (see **WARNINGS AND PRECAUTIONS, Special Populations, Geriatrics, DOSAGE AND ADMINISTRATION** and **ACTION AND CLINICAL PHARMACOLOGY, Special Populations and Conditions, Geriatrics**). **Pediatrics (<18 years of age)** The safety and efficacy of VIMPAT in pediatric patients (<18 years of age) have not been established and its use in this patient population is not indicated (see **WARNINGS AND PRECAUTIONS, Special Populations, Pediatrics**). Only ten pediatric patients (16 to 17 years of age) participated in controlled trials of partial-onset seizures.

CONTRAINDICATIONS

- Patients who are hypersensitive to the active substance or to any of the excipients. For a complete listing, see the **DOSAGE FORMS, COMPOSITION AND PACKAGING** section of the product monograph.
- Patients with a history of, or presence of, second-or third-degree atrioventricular (AV) block.
- Patients with hypersensitivity to peanuts or soya should not take VIMPAT (lacosamide) film-coated tablets.

Safety Information

WARNINGS AND PRECAUTIONS

General Withdrawal of Antiepileptic Drugs (AEDs) As with all AEDs, VIMPAT (lacosamide) should be withdrawn gradually (over a minimum of 1 week) to minimize the potential of increased seizure frequency. (see **DOSAGE AND ADMINISTRATION, Recommended Dose and Dosage Adjustment**). **Cardiac Conduction PR Interval Prolongation** VIMPAT should be used with caution in patients with known conduction problems (e.g. marked first-degree atrioventricular (AV) block, sick sinus syndrome without pacemaker), or with severe cardiac disease such as myocardial ischemia or heart failure. In such patients, obtaining an ECG before beginning VIMPAT, and after VIMPAT is titrated to steady-state, is recommended. Caution should be exercised when VIMPAT is given with other drugs that prolong the PR interval (e.g. carbamazepine, pregabalin, lamotrigine or beta-blockers), as further PR prolongation is possible (see **DRUG INTERACTIONS**). In clinical trials of healthy subjects and patients with epilepsy, VIMPAT treatment was associated with PR interval prolongation in a dose-dependent manner (see **ACTION AND CLINICAL PHARMACOLOGY, Pharmacodynamics**). Patients with significant electrocardiographic (ECG) abnormalities were systematically excluded from these trials. The mean PR interval increase (at t_{max}) in a clinical pharmacology ECG trial of healthy subjects was 13.6ms for the 400 mg/day VIMPAT group, 18.2ms for the 800 mg/day VIMPAT group, and 6.3ms for the placebo group. The mean increase in PR interval at the end of 12 weeks maintenance treatment for patients with partial-onset seizures who participated in the controlled trials was 1.4ms, 4.4ms, and 6.6ms for the VIMPAT 200, 400, and 600 mg/day groups, respectively, and -0.3ms for the placebo group. The mean maximum increase in PR interval in these controlled trials was 12.7ms, 14.3ms, and 15.7ms in the VIMPAT 200, 400, and 600 mg/day groups and 11.2ms in the placebo group. Among patients who participated in these controlled trials, asymptomatic first-degree atrioventricular (AV) block was detected on ECG and reported as an adverse reaction for 0.4% (4/944 patients) in the VIMPAT group and 0% (0/364 patients) in the placebo group (see **ADVERSE REACTIONS**). VIMPAT administration may predispose to atrial arrhythmias (atrial fibrillation or flutter), especially in patients with diabetic neuropathy and/or cardiovascular disease.

Atrial Fibrillation and Atrial Flutter In the short-term investigational trials of VIMPAT in epilepsy patients, there were no cases of atrial fibrillation or flutter. In patients with diabetic neuropathy, 0.6% of patients treated with VIMPAT experienced an adverse reaction of atrial fibrillation or atrial flutter, compared to 0% of placebo-treated patients. VIMPAT administration may predispose to atrial arrhythmias (atrial fibrillation or flutter), especially in patients with diabetic neuropathy and/or cardiovascular disease. Patients should be made aware of the symptoms of atrial fibrillation and flutter (e.g. palpitations, rapid pulse, shortness of breath) and told to contact their physician should any of these symptoms occur.

Syncope In the short-term controlled trials of VIMPAT in epilepsy patients with no significant system illnesses, there was no increase in syncope compared to placebo. In the short-term controlled trials of VIMPAT in patients with diabetic neuropathy, 1.0% of patients who were treated with VIMPAT reported an adverse reaction of syncope or loss of consciousness, compared to 0% of placebo-treated patients with diabetic neuropathy. Most of the cases of syncope were observed in patients receiving doses above 400 mg/day. The cause of syncope was not determined in most cases. However, several were associated with either changes in orthostatic blood pressure, atrial flutter/fibrillation (and associated tachycardia), or bradycardia (see **ADVERSE REACTIONS, Intravenous Adverse Reactions**). **Carcinogenesis and Mutagenesis** see **Product Monograph Part II: TOXICOLOGY, Carcinogenicity and Mutagenicity** for discussion on animal data.

Hypersensitivity Multiorgan hypersensitivity reactions (also known as Drug Rash with Eosinophilia and Systemic Symptoms, or DRESS), Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) have been reported with other anticonvulsants. Typically, although not exclusively, DRESS presents with fever and rash associated with other organ system involvement, that may or may not include eosinophilia, hepatitis, nephritis, lymphadenopathy, and/or myocarditis. Because these disorders are variable in their expression, other organ system signs and symptoms not noted here may also occur. If any of these hypersensitivity reactions are suspected, VIMPAT should be discontinued and alternative treatment started.

Neurologic Dizziness and Ataxia Treatment with VIMPAT has been associated with dizziness and ataxia which could increase the occurrence of accidental injury or falls. In controlled clinical trials, dizziness was experienced by 25% of patients with partial-onset seizures taking 1 to 3 concomitant AEDs randomized to the recommended doses (200 to 400 mg/day) of VIMPAT (compared with 8% of placebo patients) and was the adverse event most frequently leading to discontinuation (3%). Ataxia was experienced by 6% of patients randomized to the recommended doses (200 to 400 mg/day) of VIMPAT (compared to 2% of placebo patients) (see **ADVERSE REACTIONS, Clinical Trial Adverse Drug Reactions**). There was a substantial increase in the frequency of occurrence of these events when patients received VIMPAT doses greater than 400 mg/day. Accordingly, patients should be advised not to drive a car or to operate other complex machinery or perform hazardous tasks until they are familiar with the effects of VIMPAT on their ability to perform such activities (see **Part III: CONSUMER INFORMATION**).

Ophthalmological Effects In controlled trials in patients with partial-onset seizures, VIMPAT treatment was associated with vision-related adverse events such as blurred vision (VIMPAT, 8%; placebo, 3%) and diplopia (VIMPAT, 11%; placebo, 2%). Three percent of patients randomized to VIMPAT discontinued treatment due to vision-related adverse events (primarily diplopia) (see **ADVERSE REACTIONS**). Patients should be informed that if visual disturbances occur, they should notify their physician promptly. If visual disturbance persists, further assessment, including dose reduction and possible discontinuation of VIMPAT, should be considered. More frequent assessments should be considered for patients with known vision-related issues or those who are already routinely monitored for ocular conditions.

Psychiatric Suicidal Ideation and Behavior Suicidal ideation and behaviour have been reported in patients treated with antiepileptic agents in several indications. All patients treated with antiepileptic drugs, irrespective of indication, should be monitored for signs of suicidal ideation and behaviour and appropriate treatment should be considered. Patients (and caregivers of patients) should be advised to seek medical advice should signs of suicidal ideation or behaviour emerge. An FDA meta-analysis of randomized placebo controlled trials, in which antiepileptic drugs were used for various indications, has shown a small increased risk of suicidal ideation and behaviour in patients treated with these drugs. The mechanism of this risk is not known. There were 43892 patients treated in the placebo controlled clinical trials that were included in the meta-analysis. Approximately 75% of patients in these clinical trials were treated for indications other than epilepsy and, for the majority of non-epilepsy indications the treatment (antiepileptic drug or placebo) was administered as monotherapy. Patients with epilepsy represented approximately 25% of the total number of patients treated in the placebo controlled clinical trials and, for the majority of epilepsy patients, treatment (antiepileptic drug or placebo) was administered as adjunct to other antiepileptic agents (i.e., patients in both treatment arms were being treated with one or more antiepileptic drug). Therefore, the small increased risk of suicidal ideation and behaviour reported from the meta-analysis (0.43% for patients on antiepileptic drugs compared to 0.24% for patients on placebo) is based largely on patients that received monotherapy treatment (antiepileptic drug or placebo) for non-epilepsy indications. The study design does not allow an estimation of the risk of suicidal ideation and behaviour for patients with epilepsy that are taking antiepileptic drugs, due both to this population being the minority in the study, and the drug-placebo comparison in this population being confounded by the presence of adjunct antiepileptic drug treatment in both arms.

Special Populations Women of Childbearing Potential / Contraception: There was no clinically relevant interaction between lacosamide and oral contraceptives (ethinylestradiol and levonorgestrel) in clinical studies (see **DRUG INTERACTIONS, Drug-Drug Interactions, Oral Contraceptives**). **Pregnant Women:** There are no studies with lacosamide in pregnant women. Studies in animals did not indicate any teratogenic effects in rats or rabbits, but embyrotoxicity was observed in rats and rabbits at maternal toxic doses (see **TOXICOLOGY, Reproduction Studies**). Since the potential risk for humans is unknown, VIMPAT should not be used during pregnancy unless the benefit to the mother clearly outweighs the potential risk to the foetus. If women decide to become pregnant while taking VIMPAT, the use of this product should be carefully re-evaluated. **Pregnancy Registry:** Physicians are advised to recommend that pregnant patients taking VIMPAT enroll in the North American Antiepileptic Drug Pregnancy Registry. This can be done by calling the toll free number 1-888-233-2334, and must be done by patients themselves. Information on the registry can also be found at the following website: http://www.aedpregnancyregistry.org/ **Nursing Women:** It is unknown whether lacosamide is excreted in human breast milk. Animal studies have shown excretion of lacosamide in breast milk. Because many drugs are excreted into human milk, a decision should be made whether to discontinue nursing or to discontinue lacosamide, taking into account the importance of the drug to the mother. **Fertility:** No adverse effects on male or female fertility or reproduction were observed in rats at doses producing plasma exposures (AUC) up to approximately 2 times the plasma AUC in humans at the maximum recommended human dose (MRHD) of 400 mg/day. **Geriatrics (≥65 years of age):** The experience with VIMPAT in elderly patients with epilepsy is limited (n=18). Although no dose reduction is necessary in elderly patients, caution should be exercised during dose titration and age-associated decreased renal clearance with an increase in AUC levels should be considered in elderly patients (see **DOSAGE AND ADMINISTRATION** and **ACTION AND CLINICAL PHARMACOLOGY, Special Populations and Conditions, Geriatrics**). **Pediatrics (<18 years of age):** VIMPAT is not indicated for use in pediatrics (<18 years of age) as there is insufficient data on safety and efficacy of the drug in this population (see **INDICATIONS and DOSAGE AND ADMINISTRATION**). **Monitoring and Laboratory Tests** see **WARNINGS AND PRECAUTIONS, Cardiac Conduction.**

ADVERSE REACTIONS

Adverse Drug Reaction Overview In controlled clinical trials in patients with partial-onset seizures, 924 patients received VIMPAT (lacosamide). Some of the most frequently reported adverse reactions in controlled clinical trials with lacosamide treatment were dizziness, nausea, and vision-related events (e.g. diplopia, blurred vision). They were dose-related and usually mild to moderate in intensity.

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Clinical Trial Adverse Drug Reactions *Because clinical trials are conducted under very specific conditions, the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse drug reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.*

Table 1 gives the incidence of treatment-emergent adverse events that occurred in ≥1% of adult patients with partial-onset seizures in the total VIMPAT group (N=944) and for which the frequency was greater than placebo, in controlled clinical trials. The majority of adverse events were reported with a maximum intensity of 'mild' or 'moderate'.

Table 1: Treatment-Emergent Adverse Event Incidence in Double-Blind, *Placebo-Controlled Partial-Onset Seizure Trials (Events* ≥1% of Patients in the total VIMPAT group and More Frequent Than in the Placebo Group).

MedDRA System Organ Class/ Preferred Term	Placebo N=364 %	200 mg/day N=270 %	400 mg/day N=471 %	600 mg/day N=203 %
Ear and labyrinth disorders				
Vertigo	1	5	3	4
Tinnitus	1	0	2	2
Eye disorders				
Diplopia	2	6	10	16
Vision blurred	3	2	9	16
Conjunctivitis	<1	2	<1	0
Gastrointestinal disorders				
Nausea	4	7	11	17
Vomiting	3	6	9	16
Diarrhoea	3	3	5	4
Constipation	1	1	2	4
Flatulence	0	3	2	1
Dyspepsia	1	1	2	2
Toothache	1	2	2	1
Dry Mouth	1	1	1	2
Hypoaesthesia oral	0	0	1	1
General disorders and administration site conditions				
Fatigue	6	7	7	15
Gait disturbance	<1	<1	2	4
Asthenia	1	2	2	4
Irritability	1	1	2	2
Chest pain	1	2	1	2
Pyrexia	1	2	1	1
Feeling drunk	0	0	1	3
Oedema peripheral	0	1	<1	2
Feeling abnormal	<1	0	1	2
Infections and infestations				
Nasopharyngitis	6	6	8	4
Bronchitis	0	2	1	1
Rhinitis	<1	<1	1	1
Ear infection	<1	1	1	0
Cystitis	<1	1	<1	1
Gastroenteritis	0	1	<1	0
Injury, poisoning and procedural complications				
Skin laceration	2	2	3	3
Fall	<1	1	2	1
Head injury	<1	2	1	1
Joint sprain	0	1	1	2
Investigations				
Positive rombergism	0	1	1	2
Gamma-glutamyltransferase increased	<1	2	<1	1
White blood cell count decreased	<1	0	<1	2
Metabolism and nutrition disorders				
Decreased appetite	<1	<1	2	3
Hypercholesterolaemia	<1	1	1	1
Musculoskeletal and connective tissue disorders				
Muscle spasms	<1	1	1	2
Neck pain	<1	1	1	1
Nervous system disorders				
Dizziness	*8*	*16*	*30*	*53*
Headache	9	11	14	12
Ataxia	2	4	7	15
Somnolence	5	5	8	8
Tremor	4	4	6	12
Nystagmus	4	2	5	10
Balance disorder	0	1	5	6
Memory impairment	2	1	2	6
Cognitive disorder	<1	<1	2	2
Hypoaesthesia	1	2	2	2
Dysarthria	<1	<1	1	3
Disturbance in attention	1	0	1	2
Psychiatric disorders				
Depression	1	2	2	2
Insomnia	1	2	2	1
Confusional state	1	0	2	3
Mood altered	<1	1	1	2
Respiratory, thoracic and mediastinal disorders				
Dyspnoea	<1	0	1	1
Epistaxis	0	1	1	0
Skin and subcutaneous tissue disorders				
Pruritus	1	3	2	3
Hyperhidrosis	<1	0	1	2

Table 2: Incidence of Most Common Dose-Related Treatment-Emergent Adverse Events in Double-Blind, Placebo-Controlled Partial-Onset Seizure Trials (Events ≥1% of Patients in the total VIMPAT group and More Frequent Than in the Placebo Group).

MedDRA Preferred Term	Placebo N=364 %	200 mg/day N=270 %	400 mg/day N=471 %	600 mg/day N=203 %
Diplopia	2	6	10	16
Vision blurred	3	2	9	16
Nausea	4	7	11	17
Vomiting	3	6	9	16
Dizziness	8	16	30	53
Ataxia	2	4	7	15
Tremor	4	4	6	12
Nystagmus	4	2	5	10

For more detail on adverse events reported during clinical trials, see **ADVERSE REACTIONS** in the full product monograph.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- **Report online at www.healthcanada.gc.ca/medeffect**
- **Call toll-free at 1-866-234-2345**
- **Complete a Canada Vigilance Reporting Form and:**
  - **Fax toll-free to 1-866-678-6789, or**
  - **Mail to: Canada Vigilance Program**
    Health Canada
    Postal Locator 0701D
    Ottawa, ON K1A 0K9

Administration

DOSAGE AND ADMINISTRATION

General Considerations

VIMPAT (lacosamide) may be taken with or without food.

Film-coated tablets On the first day of treatment the patient starts with VIMPAT 50 mg tablets twice a day. During the second week, the patient takes VIMPAT 100 mg tablets twice a day. Depending on response and tolerability, VIMPAT 150 mg tablets may be taken twice a day during the third week and VIMPAT 200 mg tablets twice a day during the fourth week.

Solution for injection The solution for injection is infused over a period of 30 to 60 minutes twice daily. VIMPAT solution for injection can be administered intravenously (i.v.) without further dilution. Conversion to or from oral and i.v. administration can be done directly without titration. The total daily dose and twice daily administration should be maintained. There is experience with twice daily infusions of VIMPAT up to 5 days (N=53).

Compatibility and Stability VIMPAT solution for injection can be administered intravenously without further dilution or may be mixed with diluents. VIMPAT solution for injection was found to be physically compatible and chemically stable when mixed with the following diluents for at least 24 hours and stored in glass or polyvinyl chloride (PVC) bags at room temperature 15-30°C. Diluents: Sodium Chloride Injection 0.9% (w/v), Dextrose Injection 5% (w/v), Lactated Ringer's Injection. The stability of VIMPAT solution for injection in other infusion solutions has not been evaluated. Product with particulate matter or discoloration should not be used. Any unused portion of VIMPAT solution for injection should be discarded. Do not use if solution shows haziness, particulate matter, discoloration or leakage.

Recommended Dose and Dosage Adjustment

Adults The recommended starting dose for VIMPAT is 50 mg twice a day, with or without food, which should be increased to an initial therapeutic dose of 100 mg twice a day after one week. Depending on patient response and tolerability, the maintenance dose can be further increased by 50 mg twice a day every week, to a maximum recommended daily dose of 400 mg (200 mg twice a day). Doses above 400 mg/day do not confer additional benefit, are associated with more severe and substantially higher frequency of adverse reactions and are not recommended. In accordance with current clinical practice, if VIMPAT has to be discontinued, it is recommended this be done gradually (e.g. taper the daily dose by 200 mg/week). VIMPAT therapy can be initiated with either oral or intravenous (i.v.) administration.

Patients with Renal Impairment No dose adjustment is necessary in patients with mild or moderate renal impairment (creatinine clearance (CL_{CR}) >30 mL/min). A maximum dose of 300 mg/day is recommended for patients with severe renal impairment (CL_{CR} ≤30 mL/min) and in patients with end-stage renal disease. In all patients with any degree of renal impairment, the dose titration should be performed with caution (see **ACTION AND CLINICAL PHARMACOLOGY, Special Populations and Conditions, Renal Impairment**). Following a 4-hour hemodialysis treatment, AUC of VIMPAT was reduced by approximately 50%. Thus, dosage supplementation of up to 50% following hemodialysis may be considered. Treatment of patients with end-stage renal disease should be made with caution as there is limited clinical experience in subjects (N=8) and no experience in patients, and there is accumulation of a metabolite (with no known pharmacological activity).

Patients with Hepatic Impairment The dose titration should be performed with caution in patients with mild to moderate hepatic impairment. A maximum dose of 300 mg/day is recommended for patients with mild or moderate hepatic impairment. The pharmacokinetics of VIMPAT have not been evaluated in severe hepatic impairment. VIMPAT is not recommended in patients with severe hepatic impairment (see **ACTION AND CLINICAL PHARMACOLOGY, Special Populations and Conditions, Hepatic Impairment**). **Geriatrics (≥65 years of age)** Clinical experience with VIMPAT in elderly patients with epilepsy is limited (n=18). Although no dose reduction is necessary in elderly patients, caution should be exercised during dose titration and age-associated decreased renal clearance with an increase in AUC levels should be considered in elderly patients (see **ACTION AND CLINICAL PHARMACOLOGY, Special Populations and Conditions, Geriatrics**).

Pediatrics (<18 years of age) The safety and effectiveness of VIMPAT in pediatric patients <18 years has not been established, and therefore its use in this patient population is not indicated (see **INDICATIONS and WARNINGS AND PRECAUTIONS, Special Populations, Pediatrics**).

Missed Dose If the patient misses a dose by a few hours, they *should be instructed to take VIMPAT as soon as they remember.* If it is close to their next dose, they should be instructed to take their medication at the next regular time. Patients should not take two doses at the same time.

SUPPLEMENTAL PRODUCT INFORMATION

STORAGE AND STABILITY

Store at room temperature (15 – 30°C).

Product Monograph available on request.

UCB Canada Inc.
Oakville, Ontario
L6H 5R7

PAAB

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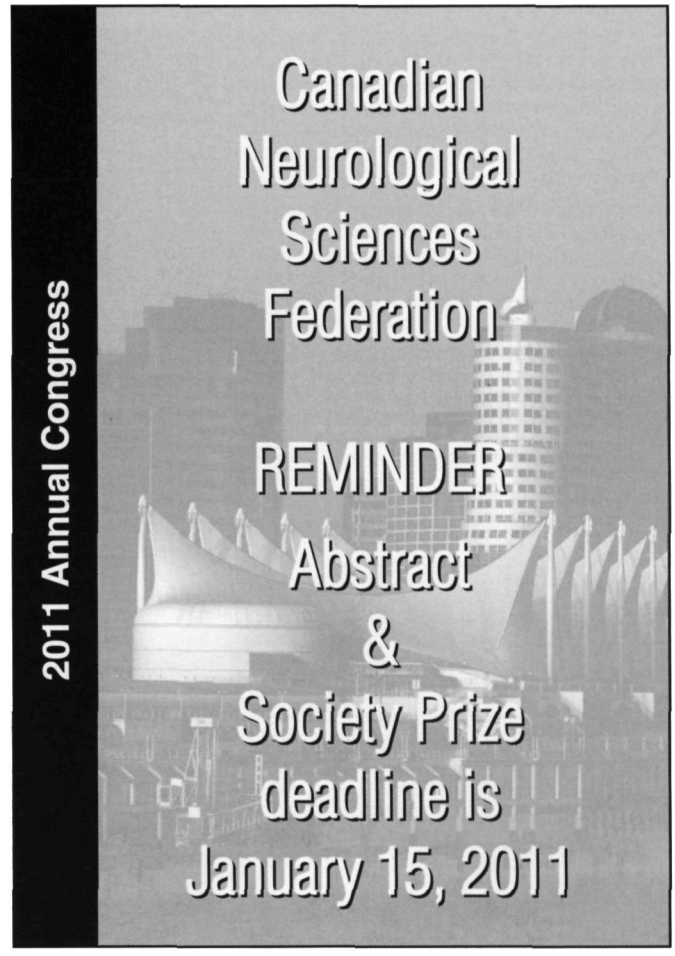
See our AD on A-4, A-5



NOTES

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AZILECT®

(rasagiline mesylate tablets)

PRESCRIBING SUMMARY

Patient Selection Criteria

THERAPEUTIC CLASSIFICATION: Antiparkinson Agent

INDICATIONS AND CLINICAL USE

AZILECT (rasagiline mesylate tablets) is indicated for the treatment of the signs and symptoms of idiopathic Parkinson's disease as initial monotherapy and as adjunct therapy to levodopa.

The effectiveness of AZILECT was demonstrated in patients with early Parkinson's disease who were receiving AZILECT as monotherapy and who were not receiving any concomitant dopaminergic therapy. The effectiveness of AZILECT as adjunct therapy was demonstrated in patients with Parkinson's disease who were treated with levodopa.

CONTRAINDICATIONS

Meperidine and Other Analgesics: AZILECT is contraindicated for use with meperidine. Serious reactions have been precipitated with concomitant use of meperidine (e.g., Demerol and other trade names) and MAO inhibitors, including selective MAO-B inhibitors. These reactions have been characterized by coma, severe hypertension or hypotension, severe respiratory depression, convulsions, malignant hyperpyrexia, excitation, peripheral vascular collapse and death. At least 14 days should elapse between discontinuation of AZILECT and initiation of treatment with meperidine.

For similar reasons, AZILECT should not be administered with the analgesic agents tramadol, methadone, and propoxyphene.

Other Drugs: AZILECT should not be used with the antitussive agent dextromethorphan. The combination of MAO inhibitors and dextromethorphan has been reported to cause brief episodes of psychosis or bizarre behavior. AZILECT is also contraindicated for use with St. John's wort, and cyclobenzaprine (a tricyclic muscle relaxant).

Sympathomimetic Amines: Like other MAOIs, AZILECT is contraindicated for use with sympathomimetic amines, including amphetamines as well as cold products and weight-reducing preparations that contain vasoconstrictors (e.g., pseudoephedrine, phenylephrine and ephedrine). Severe hypertensive reactions have followed the administration of sympathomimetics and non-selective MAO inhibitors. At least one case of hypertensive crisis has been reported in a patient taking the recommended doses of a selective MAO-B inhibitor and a sympathomimetic medication (ephedrine).

Antidepressants: AZILECT should not be administered concomitantly with antidepressants. Serotonin Syndrome has been observed following concomitant use of these medications both with selective and non-selective MAOI inhibitors. At least 14 days should elapse between discontinuation of AZILECT and initiation of treatment with a tricyclic, tetracyclic, SSRI, or SNRI antidepressant. Similarly, at least 14 days should elapse after discontinuing treatment with a tricyclic, tetracyclic, SSRI, or SNRI antidepressant before starting AZILECT. Because of the long half-lives of fluoxetine and its active metabolite, at least five weeks (perhaps longer, especially if fluoxetine has been prescribed chronically and/or at higher doses) should elapse between discontinuation of fluoxetine and initiation of AZILECT (see WARNINGS).

MAO inhibitors: AZILECT should not be administered along with other MAO inhibitors because of the increased risk of non-selective MAO inhibition that may lead to a hypertensive crisis. At least 14 days should elapse between discontinuation of AZILECT and initiation of treatment with MAO inhibitors.

Surgery: As with other MAOIs, patients taking AZILECT should not undergo elective surgery requiring general anesthesia. Also, they should not be given local anesthesia containing cocaine or sympathomimetic vasoconstrictors. AZILECT should be discontinued at least 14 days prior to elective surgery. If surgery is necessary sooner, benzodiazepines, mivacurium, fentanyl, morphine, and codeine may be used cautiously.

Pheochromocytoma: As with other MAOIs, AZILECT is contraindicated in patients with pheochromocytoma.

Safety Information

WARNINGS

Serotonin Syndrome: Severe CNS toxicity associated with hyperpyrexia and death has been reported with the combination of tricyclic or tetracyclic antidepressants, non-selective MAOIs (NARDIL, PARNATE), including the reversible MAOI moclobemide, and a selective MAO-B inhibitor, selegiline. These adverse events have included behavioral and mental status changes, diaphoresis, muscular rigidity, hypertension, syncope and death.

Serious, sometimes fatal, reactions with signs and symptoms including hyperthermia, rigidity, myoclonus, autonomic instability with rapid vital sign fluctuations, and mental status changes progressing to extreme agitation, delirium, and coma have been reported in patients receiving a combination of selective serotonin reuptake inhibitors (SSRIs), including fluoxetine (PROZAC), fluvoxamine (LUVOX) sertraline (ZOLOFT), and paroxetine (PAXIL), non-selective MAOIs, including the reversible MAOI moclobemide, or the selective MAO-B inhibitor selegiline. Similar reactions have been reported with serotonin-norepinephrine reuptake inhibitors (SNRIs). In the post-marketing period, non-fatal cases of serotonin syndrome have been reported in patients treated with antidepressants concomitantly with AZILECT.

At least 14 days should elapse between discontinuation of AZILECT and initiation of treatment with a tricyclic, tetracyclic, SSRI, or SNRI antidepressant. Similarly, at least 14 days should elapse after discontinuing treatment with a tricyclic, tetracyclic, SSRI, or SNRI antidepressant before starting AZILECT. Because of the long half-lives of fluoxetine and its active metabolite, at least five weeks (perhaps longer, especially if fluoxetine has been prescribed chronically and/or at higher doses) should elapse between discontinuation of fluoxetine and initiation of AZILECT (see CONTRAINDICATIONS).

Ciprofloxacin and Other CYP1A2 Inhibitors: Rasagiline plasma concentrations may increase up to 2-fold in patients using concomitant ciprofloxacin and other CYP1A2 inhibitors (see DOSAGE AND ADMINISTRATION, *Patients Taking Ciprofloxacin and Other CYP1A2 Inhibitors*).

Hepatic Insufficiency: AZILECT plasma concentration may increase in patients with mild (up to 2-fold, Child-Pugh score 5-6), moderate (up to 7-fold, Child-Pugh score 7-9), and severe hepatic (Child-Pugh score 10-15) impairment. Patients with mild hepatic impairment should be given the dose of 0.5 mg/day. AZILECT should not be used in patients with moderate or severe hepatic impairment.

PRECAUTIONS

General

Tyramine/rasagiline interaction: Rasagiline should not be used at daily doses exceeding the maximum recommended (1 mg/day) because of the risks associated with nonselective inhibition of MAO. Adequate studies above this dose have not been conducted. Therefore, if rasagiline is to be used without restrictions being placed on diet and concomitant drug use, it is critical to adhere to this maximum dose.

Melanoma: Epidemiological studies have shown that patients with Parkinson's disease have a higher risk (2- to approximately 6-fold higher) of developing melanoma than the general population. Whether the increased risk observed was due to Parkinson's disease or other factors, such as drugs used to treat Parkinson's disease, is unclear.

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For the reasons stated above, patients and providers are advised to monitor for melanomas frequently and on a regular basis. Ideally, periodic skin examinations should be performed by appropriately qualified individuals (e.g., dermatologists).

Dyskinesia Due to Levodopa Treatment: When used as an adjunct to levodopa AZILECT may potentiate dopaminergic side effects and exacerbate pre-existing dyskinesia (treatment-emergent dyskinesia occurred in about 18% of patients treated with 0.5 mg or 1 mg rasagiline as an adjunct to levodopa and 10% of patients who received placebo as an adjunct to levodopa). Decreasing the dose of levodopa may ameliorate this side effect.

Postural Hypotension: When used as monotherapy, postural hypotension was reported in approximately 3% of patients treated with 1 mg rasagiline and 5% of patients treated with placebo. In the monotherapy trial, postural hypotension did not lead to drug discontinuation and premature withdrawal in the rasagiline-treated patients or the placebo-treated patients.

When used as an adjunct to levodopa, postural hypotension was reported in approximately 6% of patients treated with 0.5 mg rasagiline, 9% of patients treated with 1 mg rasagiline and 3% of patients treated with placebo. Postural hypotension led to drug discontinuation and premature withdrawal from clinical trials in one (0.7%) patient treated with rasagiline 1 mg/day, no patients treated with rasagiline 0.5 mg/day and no placebo-treated patients.

Clinical trial data suggest that postural hypotension occurs most frequently in the first two months of rasagiline treatment and tends to decrease over time.

Hallucinations: In the monotherapy study, hallucinations were reported as an adverse event in 1.3% of patients treated with 1 mg rasagiline and in 0.7% of patients treated with placebo. In the monotherapy trial, hallucinations led to drug discontinuation and premature withdrawal from clinical trials in 1.3% of the 1 mg rasagiline-treated patients and in none of the placebo-treated patients.

When used as an adjunct to levodopa, hallucinations were reported as an adverse event in approximately 5% of patients treated with 0.5 mg/day, 4% of patients treated with 1 mg/day rasagiline and 3% of patients treated with placebo. Hallucinations led to drug discontinuation and premature withdrawal from clinical trials in about 1% of patients treated with 0.5 mg/day or 1 mg/day and none of the placebo-treated patients.

Information for Patients

Patients receiving AZILECT should be given the following instructions by the physician:

- The risk of exceeding the recommended daily dose (1 mg/day) should be explained. The explanation should describe the signs and symptoms associated with MAOI induced hypertensive reactions. Patients should be urged to immediately report any severe headache or other atypical or unusual symptoms not previously experienced.
- Patients should be cautioned of the possibility of developing hallucinations and instructed to report them to their health care provider promptly should they develop.
- Patients should be advised to inform their physician if they are taking, or planning to take, any prescription or over-the-counter drugs especially with antidepressants and over-the-counter cold medications since there is a potential for interaction with AZILECT. Patients should not use meperidine with AZILECT.
- Patients taking AZILECT as adjunct to levodopa should be advised there is the possibility of increased dyskinesia and postural hypotension.
- Patients are advised to monitor for melanomas frequently and on a regular basis. Ideally, periodic skin examinations should be performed by appropriately qualified individuals (e.g. dermatologists).
- Patients should be instructed to take AZILECT as prescribed. If a dose is missed the next dose should be taken at the usual time on the following day. The patient should not double-up the dose of AZILECT.

Drug Interactions

Meperidine: Serious, sometimes fatal, reactions have been precipitated with concomitant use of meperidine (e.g., Demerol and other trade names) and MAO inhibitors, including selective MAO-B inhibitors (see CONTRAINDICATIONS).

Dextromethorphan: The concomitant use of AZILECT and dextromethorphan was not allowed in clinical studies. The combination of MAO inhibitors and dextromethorphan has been reported to cause brief episodes of psychosis or bizarre behavior. Therefore, in view of AZILECT's MAO-inhibitory activity, dextromethorphan should not be used concomitantly with AZILECT (see CONTRAINDICATIONS).

Sympathomimetic medications: The concomitant use of AZILECT and sympathomimetic medications was not allowed in clinical studies. Severe hypertensive reactions have followed the administration of sympathomimetics and non-selective MAO inhibitors. One case of hypertensive crisis has been reported in a patient taking the recommended doses of a selective MAO-B inhibitor and a sympathomimetic medication (ephedrine). Therefore, in view of AZILECT's MAO-inhibitory activity, AZILECT should not be used concomitantly with sympathomimetics, including nasal and oral decongestants and cold remedies (see CONTRAINDICATIONS).

MAO inhibitors: AZILECT should not be administered along with other MAO inhibitors, including reversible MAOI (moclobemide) and selective MAO-B inhibitors (selegiline) because of the increased risk of non-selective MAO inhibition that may lead to a hypertensive crisis (see CONTRAINDICATIONS).

Selective serotonin reuptake inhibitors (SSRIs), Serotonin norepinephrine reuptake inhibitors (SNRIs), tricyclic and tetracyclic antidepressants: Concomitant use of SSRI, SNRI, tricyclic, and tetracyclic antidepressants with AZILECT is contraindicated (see CONTRAINDICATIONS).

Levodopa/carbidopa: (see PRECAUTIONS, General, *Dyskinesias Due to Levodopa Treatment*).

Ciprofloxacin and Other CYP1A2 Inhibitors: Rasagiline plasma concentrations may increase up to 2-fold in patients using concomitant ciprofloxacin and other CYP1A2 inhibitors. This could result in increased adverse events (see WARNINGS, *Ciprofloxacin and Other CYP1A2 Inhibitors*).

Theophylline: Co-administration of rasagiline 1 mg/day and theophylline, a substrate of CYP1A2, up to 500 mg twice daily to healthy subjects (n=24), did not affect the pharmacokinetics of either drug.

Laboratory Tests

No specific laboratory tests are necessary for the management of patients on AZILECT.

Use in Pregnancy

Reproductive studies conducted with rasagiline in animals did not reveal any negative effect at doses much higher than those used in the clinical studies. However, there are no adequate and well-controlled studies of rasagiline in pregnant women. Because animal reproduction studies are not always predictive of human response, AZILECT should be used during pregnancy only if clearly needed.

Nursing Mothers

Experimental data indicated that rasagiline inhibits prolactin secretion and, thus, may inhibit lactation. It is not known whether rasagiline is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when AZILECT is administered to a nursing woman.

Use in Children

The safety and effectiveness of AZILECT in patients below 18 years of age have not been established.

Use in the Elderly

Approximately half of patients in clinical trials were 65 years and over. There were no significant differences in the safety profile of the geriatric and non-geriatric patients.

Renal Insufficiency: Conclusive data are not available for renally-impaired patients. As unconjugated rasagiline is not excreted by the kidney, rasagiline can be given at usual doses in patients with mild renal impairment. Due to the absence of adequate safety data, rasagiline should not be administered to patients with moderate to severe renal impairment.

ADVERSE REACTIONS

During the clinical development of AZILECT (rasagiline mesylate tablets), 1361 Parkinson's disease patients received AZILECT as initial monotherapy, or as adjunct therapy to levodopa. As these two populations differ, not only in the adjunct use of levodopa during AZILECT treatment, but also in the severity and duration of their disease, they may have differential risks for various adverse events. Therefore, most of the adverse events data in this section are presented separately for each population.

Monotherapy

Adverse events leading to discontinuation in controlled clinical studies:

In the double-blind, placebo-controlled trials conducted in patients receiving AZILECT as monotherapy, approximately 5% of the 149 patients treated with rasagiline discontinued treatment due to adverse events compared to 2% of the 151 patients who received placebo.

The only adverse event that led to the discontinuation of more than one patient was hallucinations.

Adverse event incidence in controlled clinical studies:

The most commonly observed adverse events that occurred in ≥5% of patients receiving AZILECT 1 mg as monotherapy (n=149) participating in the double-blind, placebo-controlled trial and that were at least 1.5 times the incidence in the placebo group (n=151), were: flu syndrome, arthralgia, depression, dyspepsia and fall.

Adjunct therapy

Adverse events leading to discontinuation in controlled clinical studies:

In a double-blind, placebo-controlled trial (PRESTO) conducted in patients treated with AZILECT as adjunct to levodopa therapy, approximately 9% of the 164 patients treated with AZILECT 0.5 mg/day and 7% of the 149 patients treated with AZILECT 1 mg/day discontinued treatment due to adverse events compared to 6% of the 159 patients who received placebo. The AEs that led to discontinuation of more than one rasagiline-treated patient were diarrhea, weight loss, hallucination, and rash. Adverse event reporting was considered more reliable for PRESTO than for the second controlled trial (LARGO); therefore only the adverse event data from PRESTO are presented in this section of labelling.

Adverse event incidence in controlled clinical studies:

The most commonly observed adverse events that occurred in ≥5% of patients receiving AZILECT 1 mg (n=149) as adjunct to levodopa therapy participating in the double-blind, placebo-controlled trial (PRESTO) and that were at least 1.5 times the incidence in the placebo group (n=159) in descending order of difference in incidence were dyskinesia, accidental injury, weight loss, postural hypotension, vomiting, anorexia, arthralgia, abdominal pain, nausea, constipation, dry mouth, rash, ecchymosis, somnolence and paresthesia.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
  - Fax toll-free to 1-866-678-6789
  - Mail to: Canada Vigilance Program
    Health Canada
    Postal Locator 0701C
    Ottawa, ON K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available in the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

Administration

DOSAGE AND ADMINISTRATION

Dosing Considerations:

The recommended and maximum dose in both monotherapy and adjunct therapy is 1 mg once daily.

AZILECT can be taken with or without food.

There is no evidence that additional benefit will be obtained from the administration of doses higher than that recommended. Furthermore, higher doses will likely result in a loss of selectivity of rasagiline towards MAO-B with an increase in the inhibition of MAO-A. There is an increased risk of adverse reactions with higher doses as well as an increased risk of hypertensive episode ("cheese reaction").

Monotherapy

The recommended AZILECT dose for the treatment of Parkinson's disease patients is 1 mg administered once daily.

Adjunctive Therapy

The dosage of AZILECT shown to be effective in controlled clinical trials for adjunct therapy was 0.5 – 1 mg once daily. The recommended initial dose is 0.5 mg administered once daily. If a sufficient clinical response is not achieved, the dose may be increased to 1 mg administered once daily.

Change of levodopa dose in adjunct therapy: When AZILECT is used in combination with levodopa a reduction of the levodopa dosage may be considered based upon individual response. During the controlled trials of AZILECT as adjunct therapy to levodopa, levodopa dosage was reduced in some patients. In clinical studies, dosage reduction of levodopa was allowed within the first 6 weeks if dopaminergic side effects, including dyskinesia and hallucinations, emerged. In the PRESTO study levodopa dosage reduction occurred in 8% of patients in the placebo group and in 16% and 17% of patients in the 0.5 mg/day and 1 mg/day rasagiline groups, respectively. In those patients who had levodopa dosage reduced, the dose was reduced on average by about 7%, 9%, and 13% in the placebo, 0.5 mg/day, and 1 mg/day groups, respectively. In the LARGO study levodopa dosage reduction occurred in 6% of patients in the placebo group and in 9% in the rasagiline 1 mg/day group. In patients who had their levodopa dosage reduced, the dose was reduced on average by about 13% and 11% in the placebo and the rasagiline groups, respectively.

Patients with Hepatic Impairment: AZILECT plasma concentration will increase in patients with hepatic impairment. Patients with mild hepatic impairment should use AZILECT 0.5 mg daily of AZILECT. AZILECT should not be used in patients with moderate to severe hepatic impairment (see WARNINGS, *Hepatic Insufficiency).*

Patients with Renal Impairment: Conclusive data are not available for renally-impaired patients. As unconjugated rasagiline is not excreted by the kidney, rasagiline can be given at usual doses in patients with mild renal impairment. Due to the absence of adequate safety data, rasagiline should not be administered to patients with moderate to severe renal impairment.

Patients Taking Ciprofloxacin and Other CYP1A2 Inhibitors: Rasagiline plasma concentrations are expected to double in patients taking concomitant ciprofloxacin and other CYP1A2 inhibitors. Therefore, patients taking concomitant ciprofloxacin or other CYP1A2 inhibitors should use 0.5 mg daily of AZILECT (see WARNINGS, *Ciprofloxacin and Other CYP1A2 Inhibitors).*

Supplemental Product Information

ADVERSE REACTIONS

Monotherapy

Table 1 lists treatment-emergent adverse events that occurred in ≥2% of patients receiving AZILECT as monotherapy participating in the double-blind, placebo-controlled trial and were numerically more frequent than in the placebo group.

Table 1. Treatment-Emergent* Adverse Events in AZILECT 1 mg-Treated Monotherapy Patients

Placebo-Controlled Studies Without Levodopa Treatment	AZILECT 1 mg (n=149) % of patients	Placebo (n=151) % of patients
Headache	14	12
Arthralgia	7	4
Dyspepsia	7	4
Depression	5	2
Fall	5	3
Flu syndrome	5	1
Conjunctivitis	3	1
Fever	3	1
Gastroenteritis	3	1
Rhinitis	3	1
Arthritis	2	1
Ecchymosis	2	0
Malaise	2	0
Neck Pain	2	0
Paresthesia	2	1
Vertigo	2	1

*Incidence ≥2% in AZILECT 1 mg group and numerically more frequent than in placebo group.

Other events of potential clinical importance reported by 1% or more of Parkinson's disease patients receiving AZILECT as monotherapy, and at least as frequent as in the placebo group, in descending order of frequency, include: dizziness, diarrhea, chest pain, albuminuria, allergic reaction, alopecia, angina pectoris, anorexia, asthma, hallucinations, impotence, leukopenia, libido decreased, liver function tests abnormal, skin carcinoma, syncope, vesiculobullous rash, vomiting.

There were no significant differences in the safety profile based on age or gender.

Adjunct therapy

Table 2 lists treatment-emergent adverse events that occurred in ≥2% of patients treated with AZILECT 1 mg/day as adjunct to levodopa therapy participating in the double-blind, placebo-controlled trial (PRESTO) and that were numerically more frequent than the placebo group. The table also shows the rates for the 0.5 mg group in PRESTO.

Table 2. Incidence of Treatment-Emergent* Adverse Events in Patients Receiving AZILECT as Adjunct to Levodopa Therapy in PRESTO

	AZILECT 1 mg + Levodopa (n=149) % of patients	AZILECT 0.5 mg + Levodopa (n=164) % of patients	Placebo + Levodopa (n=159) % of patients
Dyskinesia	18	18	10
Accidental injury	12	8	5
Nausea	12	10	8
Headache	11	8	10
Fall	11	12	8
Weight loss	9	2	3
Constipation	9	4	5
Postural hypotension	9	6	3
Arthralgia	8	6	4
Vomiting	7	4	1
Dry mouth	6	2	3
Rash	6	3	3
Somnolence	6	4	4
Abdominal pain	5	2	1
Anorexia	5	2	1
Diarrhea	5	7	4
Ecchymosis	5	2	3
Dyspepsia	5	4	4
Paresthesia	5	2	3
Abnormal dreams	4	1	1
Hallucinations	4	5	3
Ataxia	3	6	1
Dyspnea	3	5	2
Infection	3	2	2
Neck pain	3	1	1
Sweating	3	2	1
Tenosynovitis	3	1	0
Dystonia	3	2	1
Gingivitis	2	1	1
Hemorrhage	2	1	1
Hernia	2	1	1
Myasthenia	2	2	1

*Incidence ≥2% in AZILECT 1 mg group and numerically more frequent than in placebo group.

Several of the more common adverse events seemed dose-related, including weight loss, postural hypotension, and dry mouth.

Other events of potential clinical importance reported in PRESTO by 1% or more of patients treated with rasagiline 1 mg/day as adjunct to levodopa therapy and at least as frequent as in the placebo group, in descending order of frequency, include: skin carcinoma, anemia, albuminuria, amnesia, arthritis, bursitis, cerebrovascular accident, confusion, dysphagia, epistaxis, leg cramps, pruritus, skin ulcer.

There were no significant differences in the safety profile based on age or gender.

Other Adverse Events Observed During All Phase II/III Clinical Trials

Rasagiline was administered to approximately 1361 patients during all PD phase II/III clinical trials. About 771 patients received rasagiline for at least one year, approximately 361 patients received rasagiline for at least two years and 245 patients received rasagiline for more than three years, with 138 patients treated for more than five years. The long-term safety profile was similar to that observed with shorter duration exposure.

The frequencies listed below represent the proportion of the 1361 individuals exposed to rasagiline who experienced events of the type cited.

All events that occurred at least twice (or once for serious or potentially serious events) except those already listed above, trivial events, terms too vague to be meaningful, adverse events with no plausible relation to treatment and events that would be expected in patients of the age studied were reported without regard to determination of a causal relationship to rasagiline.

Events are further classified within body system categories and enumerated in order of decreasing frequency using the following definitions: frequent adverse events are defined as those occurring in at least 1/100 patients, infrequent adverse events are defined as those occurring in less than 1/100 to at least 1/1000 patients and rare adverse events are defined as those occurring in fewer than 1/1000 patients.

Body as a whole: *Frequent:* asthenia; *Infrequent:* chills, face edema, flank pain, photosensitivity reaction.

Cardiovascular system: *Frequent:* bundle branch block; *Infrequent:* deep thrombophlebitis, heart failure, migraine, myocardial infarct, phlebitis, ventricular tachycardia; *Rare:* arterial thrombosis, atrial arrhythmia, AV block complete, AV block second degree, bigeminy, cerebral hemorrhage, cerebral ischemia, ventricular fibrillation.

Digestive system: *Frequent:* gastrointestinal hemorrhage; *Infrequent:* colitis, esophageal ulcer, esophagitis, fecal incontinence, intestinal obstruction, mouth ulceration, stomach ulcer, stomatitis, tongue edema; *Rare:* hematemesis, hemorrhagic gastritis, intestinal perforation, intestinal stenosis, jaundice, large intestine perforation, megacolon, melena.

Hemic and Lymphatic systems: *Infrequent:* macrocytic anemia; *Rare:* purpura, thrombocythemia.

Metabolic and Nutritional disorders: *Infrequent:* hypocalcemia.

Musculoskeletal system: *Infrequent:* bone necrosis, muscle atrophy; *Rare:* arthrosis.

Nervous system: *Frequent:* abnormal gait, anxiety, hyperkinesia, hypertonia, neuropathy, tremor; *Infrequent:* agitation, aphasia, circumoral paresthesia, convulsion, delusions, dementia, dysarthria, dysautonomia, dysesthesia, emotional lability, facial paralysis, foot drop, hemiplegia, hypesthesia, incoordination, manic reaction, myoclonus, neuritis, neurosis, paranoid reaction, personality disorder, psychosis, wrist drop; *Rare:* apathy, delirium, hostility, manic depressive reaction, myelitis, neuralgia, psychotic depression, stupor.

Respiratory system: *Frequent:* cough increased; *Infrequent:* apnea, emphysema, laryngismus, pleural effusion, pneumothorax; *Rare:* interstitial pneumonia, larynx edema, lung fibrosis.

Skin and Appendages: *Infrequent:* eczema, urticaria; *Rare:* exfoliative dermatitis, leukoderma.

Special senses: *Infrequent:* blepharitis, deafness, diplopia, eye hemorrhage, eye pain, glaucoma, keratitis, ptosis, retinal degeneration, taste perversion, visual field defect; *Rare:* blindness, parosmia, photophobia, retinal detachment, retinal hemorrhage, strabismus, taste loss, vestibular disorder.

Urogenital system: *Frequent:* hematuria, urinary incontinence; *Infrequent:* acute kidney failure, dysmenorrhea, dysuria, kidney calculus, nocturia, polyuria, scrotal edema, sexual function abnormal, urinary retention, urination impaired, vaginal hemorrhage, vaginal moniliasis, vaginitis; *Rare:* abnormal ejaculation, amenorrhea, anuria, epididymitis, gynecomastia, hydroureter, leukorrhea, priapism.

Postmarketing Experience

The following adverse events have been identified during postapproval use of AZILECT. Because these events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Nervous system: serotonin syndrome characterized by agitation, confusion, rigidity, pyrexia, and myoclonus have been reported by patients treated with antidepressants concomitantly with AZILECT

Cardiovascular system: Cases of elevated blood pressure, including rare cases of hypertensive crisis, associated with ingestion of unknown amounts of tyramine-rich foods; one report of elevated blood pressure in a patient using the ophthalmic vasoconstrictor tetrahydrozoline hydrochloride

SYMPTOMS AND TREATMENT OF OVERDOSAGE

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

Symptoms

Symptoms reported following overdose of AZILECT in doses ranging from 3 mg to 100 mg include dysphoria, hypomania, hypertensive crisis, and serotonin syndrome.

The following description of presenting symptoms and clinical course is based upon overdose descriptions of non-selective MAO inhibitors.

Characteristically, signs and symptoms of non-selective MAOI overdose may not appear immediately. Delays of up to 12 hours between ingestion of drug and the appearance of signs may occur. Importantly, the peak intensity of the syndrome may not be reached for upwards of a day following the overdose. Death has been reported following overdosage. Therefore, immediate hospitalization, with continuous patient observation and monitoring for a period of at least two days following the ingestion of such drugs in overdose, is strongly recommended.

The clinical picture of MAOI overdose varies considerably; its severity may be a function of the amount of drug consumed. The central nervous and cardiovascular systems are prominently involved.

Signs and symptoms of overdosage may include, alone or in combination, any of the following: drowsiness, dizziness, faintness, irritability, hyperactivity, agitation, severe headache, hallucinations, trismus, opisthotonos, convulsions, and coma; rapid and irregular pulse, hypertension, hypotension and vascular collapse; precordial pain, respiratory depression and failure, hyperpyrexia, diaphoresis, and cool, clammy skin.

Treatment

There is no specific antidote for rasagiline overdose. The following suggestions are offered based upon the assumption that rasagiline overdose may be modeled after non-selective MAO inhibitor poisoning. Treatment of overdose with non-selective MAO inhibitors is symptomatic and supportive. Respiration should be supported by appropriate measures, including management of the airway, use of supplemental oxygen, and mechanical ventilatory assistance, as required. Body temperature should be monitored closely. Intensive management of hyperpyrexia may be required. Maintenance of fluid and electrolyte balance is essential.

Based on product monograph dated June 7, 2010.

Product Monograph available on request.

℞ AZILECT®

(rasagiline mesylate tablets)

See our AD on OBC

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PrLYRICA® PREGABALIN

PRESCRIBING SUMMARY

PATIENT SELECTION CRITERIA

THERAPEUTIC CLASSIFICATION
Analgesic Agent

INDICATIONS AND CLINICAL USE
LYRICA (pregabalin) is indicated for the management of neuropathic pain associated with diabetic peripheral neuropathy, postherpetic neuralgia and spinal cord injury. LYRICA is indicated for the management of pain associated with fibromyalgia. The efficacy of LYRICA in the management of pain associated with fibromyalgia for up to 6 months was demonstrated in a placebo-controlled trial in patients who had initially responded to LYRICA during a 6-week open-label phase.

Use in Special Populations
Geriatrics (>65 years of age): Pregabalin oral clearance tended to decrease with increasing age. This decrease in pregabalin oral clearance is consistent with age-related decreases in creatinine clearance. Reduction of pregabalin dose may be required in patients who have age-related compromised renal function (see *WARNINGS AND PRECAUTIONS, Geriatrics* [*>65 years of age*]).

Pediatrics (<18 years of age): The safety and efficacy of pregabalin in pediatric patients (<18 years of age) have not been established.

Renal: There have been reports of patients, with or without previous history, experiencing renal failure while receiving pregabalin alone or in combination with other medications. Discontinuation of pregab alin showed reversibility of this event in some cases (see Product Monograph, *WARNINGS AND PRECAUTIONS; ADVERSE REACTIONS, Post-Marketing Adverse Drug Reactions; and DOSAGE AND ADMINISTRATION*). Because pregabalin is eliminated primarily by renal excretion, the dose of pregabalin should be adjusted as noted for elderly patients or those with renal impairment (see Product Monograph, *ACTION AND CLINICAL PHARMACOLOGY* and *DOSAGE AND ADMINISTRATION*).

Pregnant Women: There are no adequate and well-controlled studies in pregnant women. Pregabalin should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Labour and Delivery: The effects of pregabalin on labour and delivery in pregnant women are unknown.

Nursing Women: It is not known if pregabalin is excreted in human breast milk; however, it is present in the milk of rats. Because of the potential for adverse reactions in nursing infants from pregabalin, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

CONTRAINDICATIONS
Patients who are hypersensitive to pregabalin or to any ingredient in the formulation or component of the container.

SAFETY INFORMATION

WARNINGS AND PRECAUTIONS
Angioedema: There have been post-marketing reports of angioedema in patients, some without reported previous history/episode(s), during initial/acute and chronic treatment with LYRICA. Specific symptoms included swelling of the face, mouth (tongue, lips, and gums), neck, throat, and larynx/upper airway. There have been reports of life-threatening angioedema with respiratory compromise requiring emergency treatment. Some of these patients did not have reported previous history/episode(s) of angioedema. LYRICA should be immediately discontinued in patients with these symptoms. During the pre-marketing assessment of pregabalin in clinical trials, angioedema was reported as a rare reaction (see Product Monograph, *ADVERSE REACTIONS,* Less Common Clinical Trial Adverse Reactions and Post-Marketing Adverse Drug Reactions). Caution should be exercised when prescribing LYRICA to patients with previous history/episode(s) of angioedema and related events. In addition, patients who are taking other drugs associated with angioedema (eg, ACE-inhibitors) may be at increased risk of developing this condition.

Hypersensitivity: There have been post-marketing reports of hypersensitivity reactions (e.g. skin redness, blisters, hives, rash, dyspnea, and wheezing). Pregabalin should be discontinued immediately if such symptoms occur (see Product Monograph, Post-Marketing Adverse Drug Reactions).

Renal Failure: In both clinical trials of various indications and post-marketing database, there are reports of patients, with or without previous history, experiencing renal failure while receiving pregabalin alone or in combination with other medications. Discontinuation of pregabalin should be considered as it has shown reversibility of this event in some cases. Caution is advised when prescribing pregabalin to the elderly or those with any degree of renal impairment (see Product Monograph, Special Populations, *Renal;* Abrupt or Rapid Discontinuation; *ADVERSE REACTIONS,* Post-Marketing Adverse Drug Reactions; and *DOSAGE AND ADMINISTRATION*).

Tumorigenic Potential: In standard preclinical in vivo lifetime carcinogenicity studies of pregabalin, a high incidence of hemangiosarcoma was identified in two different strains of mice. The clinical significance of this finding is uncertain. Clinical experience during pregabalin's premarketing development provides no direct means to assess its potential for inducing tumors in humans.

Ophthalmological Effects: In controlled studies, pregabalin treatment was associated with vision-related adverse events such as blurred vision (amblyopia) (6% pregabalin and 2% placebo) and diplopia (2% pregabalin and 0.5% placebo). Approximately 1% of pregabalin-treated patients discontinued treatment due to vision-related adverse events (primarily blurred vision). Of the patients who did not withdraw, the blurred vision resolved with continued dosing in approximately half of the cases (see Product Monograph, *Post-Marketing Adverse Drug Reactions*).

Patients should be informed that if changes in vision occur, they should notify their physician.

Peripheral Edema: LYRICA may cause peripheral edema. In controlled peripheral neuropathic pain and fibromyalgia clinical trials, pregabalin treatment caused peripheral edema in 9% of patients compared with 3% of patients in the placebo group. In these studies, 0.7% of pregabalin patients and 0.3% of placebo patients withdrew due to peripheral edema (see Product Monograph, *ADVERSE REACTIONS, Peripheral Edema*).

In controlled clinical trials of up to 13 weeks in duration of patients without clinically significant heart or peripheral vascular disease, there was no apparent association between peripheral edema and cardiovascular complications such as hypertension or congestive heart failure. In the same trials, peripheral edema was not associated with laboratory changes suggestive of deterioration in renal or hepatic function.

Higher frequencies of weight gain and peripheral edema were observed in patients taking both LYRICA and a thiazolidinedione antidiabetic agent compared to patients taking either drug alone. As the thiazolidinedione class of antidiabetic drugs can cause weight gain and/or fluid retention, possibly exacerbating or leading to heart failure, care should be taken when co-administering LYRICA and these agents.

Congestive Heart Failure: In controlled clinical studies, events of congestive heart failure were reported at an infrequent rate (between 0.1% and 1%; see Product Monograph, *ADVERSE REACTIONS,* Less Common Clinical Trial Adverse Reactions).

There have been post-marketing reports of congestive heart failure in some patients receiving pregabalin (see Product Monograph, *ADVERSE REACTIONS*, Post-marketing Adverse Drug Reactions). Although this adverse reaction has mostly been observed in elderly cardiovascular-compromised patients during pregabalin treatment for a neuropathic pain indication, some cases have occurred in patients without reported edema or previous history of cardiovascular disease. Pregabalin should be used with caution in these patients. Discontinuation of pregabalin may resolve the reaction.

Gastrointestinal: There have been post-marketing reports of events related to reduced lower gastrointestinal tract function (eg. intestinal obstruction, paralytic ileus, and constipation) in patients, some without reported previous history/episode(s), during initial/acute and chronic treatment with LYRICA, primarily in combination with other medications that have the potential to produce constipation. Some of these events were considered serious and required hospitalization. In a number of instances, patients were taking opioid analgesics including tramadol.

Caution should be exercised when LYRICA and opioid analgesics are used in combination, and measures to prevent constipation may be considered, especially in female patients and elderly as they may be at increased risk of experiencing lower gastrointestinal-related events (see Product Monograph, *ADVERSE REACTIONS*, Post-Marketing Adverse Drug Reactions).

Weight Gain: LYRICA may cause weight gain. In pregabalin-controlled peripheral neuropathic pain and fibromyalgia clinical trials with durations of up to 14 weeks, a gain of 7% or more over baseline weight was observed in 8% of pregabalin-treated patients and 3% of placebo-treated patients. Few patients treated with pregabalin (0.6%) withdrew from controlled trials due to weight gain (see Product Monograph, *ADVERSE REACTIONS*, Weight Gain).

Pregabalin-associated weight gain was related to dose and duration of exposure. Pregabalin-associated weight gain did not appear to be associated with baseline BMI, gender, or age. Weight gain was not limited to patients with edema and was not necessarily due to edema-related events (see Product Monograph, *WARNINGS AND PRECAUTIONS*, Peripheral Edema).

Although weight gain was not associated with clinically important changes in blood pressure in short-term controlled studies, the long-term cardiovascular effects of pregabalin-associated weight gain are unknown.

While the effects of pregabalin-associated weight gain on glycemic control have not been systematically assessed, in controlled and longer-term open-label clinical trials with diabetic patients, pregabalin treatment did not appear to be associated with loss of glycemic control (as measured by HbA_{1c}).

Dizziness and Somnolence: LYRICA may cause dizziness and somnolence. In controlled studies, pregabalin caused dizziness in 32% of patients compared to 8% in placebo. Somnolence was experienced by 17% and 4% of the patients treated with pregabalin and placebo, respectively. These events begin shortly after the initiation of therapy and generally occur more frequently at higher doses. In these studies, dizziness and somnolence led to withdrawal of 5% (placebo: 0.5%) and 3% (placebo: 0.1%) of the pregabalin-treated patients, respectively. For the remaining patients who experienced these events, dizziness and somnolence persisted until the last dose of pregabalin in 35% and 49% of the patients, respectively (see Product Monograph, *ADVERSE REACTIONS*, Tables 2, 4, and 11, and Post-Marketing Adverse Drug Reactions).

Abrupt or Rapid Discontinuation: Following abrupt or rapid discontinuation of pregabalin, some patients reported symptoms including insomnia, nausea, headache, anxiety, hyperhidrosis and diarrhea. Pregabalin should be tapered gradually over a minimum of one week rather than discontinued abruptly (see Product Monograph, *ADVERSE REACTIONS*, *Adverse Events Following Abrupt or Rapid Discontinuation*).

ADVERSE REACTIONS
Because clinical trials are conducted under very specific conditions, the adverse reaction rates observed in clinical trials may not reflect the rates observed in practice and should not be compared to the rates in clinical trials of another drug. Adverse drug reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.

Clinical Trial Adverse Drug Reactions
Most Common Adverse Events in All Pre-marketing Controlled Clinical Studies of Neuropathic Pain: The most commonly observed adverse events (≥5% and twice the rate of that seen in placebo) in pregabalin-treated patients were: dizziness, somnolence, peripheral edema, and dry mouth. Adverse events were usually mild to moderate in intensity.

Adverse Events from a Controlled Clinical Study in Neuropathic Pain Associated with Spinal Cord Injury: The most commonly observed treatment-related adverse events (≥5% and twice the rate of that seen in placebo) in pregabalin-treated patients were: somnolence, dizziness, asthenia, dry mouth, edema, myasthenia, constipation, thinking abnormal, amblyopia, and amnesia. Adverse events were usually mild to moderate in intensity.

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Most Common Adverse Events in Controlled Clinical Studies in Fibromyalgia: The most commonly observed treatment-related adverse events (≥5% and twice the rate of that seen in placebo) in pregabalin-treated patients were: dizziness (37.5%), somnolence (18.6%), weight gain (10.6%), dry mouth (7.9%), blurred vision (6.7%), peripheral edema (6.1%), constipation (5.8%), and disturbance in attention (5.3%). Adverse events were usually mild to moderate in intensity.

To monitor drug safety, Health Canada collects information on serious and unexpected effects of drugs. If you suspect a patient has had a serious or unexpected reaction to this drug, you may notify Health Canada by telephone: 1-866-234-2345.

ADMINISTRATION

DOSING CONSIDERATIONS

Patients with Impaired Renal Function

Pregabalin is primarily eliminated from the systemic circulation by renal excretion as unchanged drug. In some elderly patients and those with a medical history of significant renal insufficiency, daily dosages should be reduced accordingly (see Table in Supplemental Product Information).

Adults

Neuropathic pain associated with diabetic peripheral neuropathy and postherpetic neuralgia: The recommended starting dose for LYRICA is 150 mg/day, given in two or three divided doses (75 mg BID or 50 mg TID), with or without food in patients with a creatinine clearance rate of at least 60 mL/min. Efficacy of LYRICA has been demonstrated within the first week. Based on individual patient response and tolerability, the dose may be increased to 150 mg BID (300 mg/day) after one week.

For patients who experience significant and ongoing pain and can tolerate pregabalin 300 mg/day well, maximum daily dose of 600 mg (300 mg twice a day, BID) can be used. However, in clinical trials, LYRICA 600 mg/day did not provide additional significant efficacy and patients treated with this dose experienced markedly higher rates of adverse events and discontinued the trial more frequently (see Product Monograph, *ADVERSE REACTIONS*, Tables 1 and 5). Doses above 600 mg/day have not been studied and are not recommended.

Neuropathic pain associated with spinal cord injury: The recommended starting dose for LYRICA is 150 mg/day, given in two divided doses (75 mg BID), with or without food in patients with a creatinine clearance rate of at least 60 mL/min. Efficacy of LYRICA has been demonstrated within the first week. Based on individual patient response and tolerability, the dose may be increased to 150 mg BID (300 mg/day) after one week.

For patients who experience significant and ongoing pain and can tolerate pregabalin 300 mg/day well, a maximum daily dose of 600 mg (300 mg twice a day, BID) may be considered. Doses above 600 mg/day have not been studied and are not recommended.

Pain associated with fibromyalgia: The recommended dosage is 300 to 450 mg/day, given in two divided doses. The recommended starting dose for LYRICA is 150 mg/day, given in two divided doses (75 mg BID), with or without food in patients with a creatinine clearance rate of at least 60 mL/min. Based on individual response and tolerability, the dose may be increased to 150 mg BID (300 mg/day) after one week. Patients who do not experience sufficient benefit with 300 mg/day may be further increased to 225 mg BID (450 mg/day). In some patients, efficacy of LYRICA has been demonstrated within the first week.

For patients who experience significant and ongoing pain and can tolerate pregabalin 300 mg/day well, maximum daily dose of 600 mg (300 mg twice a day, BID) can be used. However, in clinical trials of fibromyalgia, LYRICA 600 mg/day did not provide additional significant efficacy and patients treated with this dose experienced significantly higher rates of adverse events and discontinued the trial more frequently (see Product Monograph, *ADVERSE REACTIONS*, Tables 7 and 10). In view of the dose-related adverse events, the decision to treat patients with doses above 450 mg/day should be based on clinical judgment of the treating physician. Doses above 600 mg/day have not been studied and are not recommended.

ADMINISTRATION

LYRICA is given orally with or without food.

STUDY REFERENCES

References:

1. LYRICA Product Monograph, Pfizer Canada Inc., June 21, 2010.
2. Moulin DE *et al.* Pharmacological management of chronic neuropathic pain – consensus statement and guidelines from the Canadian Pain Society. *Pain Res Manage 2007*;12:13-21.
3. Arnold LM *et al.* A 14-week, randomized, double-blinded, placebo-controlled monotherapy trial of pregabalin in patients with fibromyalgia. *J Pain* 2008;9:792-805.

   14-week, randomized, double-blind, multiple-dose, placebo-controlled, multicentre study. 745 patients who had moderate-to-severe pain, i.e. mean baseline score (mean of the last 7 daily diary pain scores prior to study medication) of ≥4, and a diagnosis of fibromyalgia based on the ACR criteria. This study used an enriched population as placebo responders (≥30% reduction in mean pain scores) during the one-week run-in phase were discontinued and did not enter the double-blind phase. 1.6% of patients screened (n=19/1,195) were reported to be placebo responders. Patients were randomized to LYRICA 300 mg/day (n=183), 450 mg/day (n=190), 600 mg/day (n=188), or placebo (n=184). Patients were allowed to take acetaminophen up to 4 g/day as needed for pain relief. The number of completers was: LYRICA 300 mg/day (n=123), 450 mg/day (n=125), 600 mg/day (n=113), or placebo (n=125). The primary endpoint was the reduction in endpoint mean pain scores. Pain scores rated on 11-point numerical scale from 0 (no pain) to 10 (worst possible pain) during the past 24 hours. Mean baseline pain scores were 6.7 for LYRICA 300 mg/day, 6.7 for 450 mg/day, 6.8 for 600 mg/day, and 6.6 for placebo.
4. Crofford LJ *et al.* Fibromyalgia relapse evaluation and efficacy for durability of meaningful relief (FREEDOM): a 6-month, double-blind, placebo-controlled trial with pregabalin. *Pain* 2008;136:419-31.

   26-week, long-term relapse observation study. Patients who met the ACR criteria for fibromyalgia and who had a score of ≥40 on the pain Visual Analog Scale (VAS) were eligible to enter a 6-week, open-label, dose-optimization phase. During this phase, patients were titrated up to a total daily dose of 300 mg, 450 mg, or 600 mg. 566 LYRICA responders were randomized in the double-blind phase to either their optimized LYRICA dose (n=279) or to placebo (n=287). 38% of LYRICA responders completed 26 weeks of treatment vs 19% on placebo. The primary endpoint was time to loss of therapeutic response. Loss of therapeutic response was defined as having either a <30% reduction in pain VAS score, or worsening of symptoms necessitating alternate treatment. Responders were defined as having a ≥50% reduction in pain on the VAS and self-rating on the Patient Global Impression of Change scale of "much improved" or "very much improved".
5. Freynhagen R *et al.* Efficacy of pregabalin in neuropathic pain evaluated in a 12-week, randomised, double-blind, multicentre, placebo-controlled trial of flexible- and fixed-dose regimens. *Pain* 2005;115:254-63.

   In a 12-week, multicentre, randomized, double-blind, placebo-controlled study, 338 patients with either DPN (n=249) or PHN (n=89) were randomized to receive BID flexible-dose pregabalin (150-600 mg/day), fixed-dose pregabalin (600 mg/day) or placebo. In the flexible-dose arm, dose could be adjusted up or down over the first four weeks based on patients' individual response and tolerability. The primary efficacy measurement was mean pain score at endpoint, derived from ratings recorded by patients in a daily diary on an 11-point numerical pain rating scale (0=no pain, 10=worst possible pain). A significant difference in pain scores versus placebo was seen in the flexible dose range 150-600 mg/day ($p \leq 0.05$, weeks 2-3 and $p \leq 0.01$, weeks 4-12), and the fixed dose of 600 mg/day ($p \leq 0.05$, week 1 and $p \leq 0.01$, weeks 2-12).
6. Mease PJ *et al.* A randomized, double-blind, placebo-controlled, phase III trial of pregabalin in the treatment of patients with fibromyalgia. *J Rheumatol* 2008;35:502-14.

   Multicentre, double-blind, 13-week, randomized trial. 748 patients who met the ACR criteria for fibromyalgia and who had an average mean pain score of ≥4 on an 11-point numeric rating scale (NRS) during the baseline assessment were randomized to LYRICA 300 mg/day (n=185), 450 mg/day (n=183), 600 mg/day (n=190), or placebo (n=190). Patients were allowed to take acetaminophen up to 4 g/day as needed for pain relief. The number of completers was: LYRICA 300 mg/day (n=123), 450 mg/day (n=121), 600 mg/day (n=111), or placebo (n=130). The primary endpoint was the reduction in endpoint mean pain scores (mean of the last 7 daily pain scores while on study medication). Pain-related sleep difficulties were assessed using the Medical Outcomes Study-Sleep Scale (MOS-SS), a scale that runs from 0-100. Mean baseline MOS-SS score for overall sleep problem index was 65.0.

SUPPLEMENTAL PRODUCT INFORMATION

Warnings and Precaution

See the Product Monograph for further information on the following: tumorigenic potential, ophthalmological effects, peripheral edema, congestive heart failure, weight gain, dizziness and somnolence, sexual function/reproduction, and special populations.

Drug Interactions

Overview: Since pregabalin is predominately excreted unchanged in the urine, undergoes negligible metabolism in humans (≤2% of a dose recovered in urine as metabolites), does not inhibit drug metabolism in vitro, and is not bound to plasma proteins, LYRICA (pregabalin) is unlikely to produce, or be subject to, pharmacokinetic interactions.

Drug Abuse and Dependence/Liability: Pregabalin is not known to be active at receptor sites associated with drugs of abuse. As with any CNS active drug, physicians should carefully evaluate patients for history of drug abuse and observe them for signs of LYRICA misuse or abuse (e.g., development of tolerance, dose escalation, drug-seeking behaviour).

ADMINISTRATION

Dosage Adjustment Based on Renal Function: Dosing adjustment should be based on creatinine clearance (Cl_{cr}), as indicated in Table 1.

Pregabalin is effectively removed from plasma by hemodialysis. Over a 4-hour hemodialysis treatment, plasma pregabalin concentrations are reduced by approximately 50%. For patients receiving hemodialysis, pregabalin daily dose should be adjusted based on renal function. In addition to the daily dose adjustment, a supplemental dose should be given immediately following every 4-hour hemodialysis treatment (see Table below).

Table 1. Pregabalin Dosage Adjustment Based on Renal Function

Creatinine Clearance (Cl_{cr}) (mL/min)	Total Pregabalin Daily Dose (mg/day)[a] Recommended Dose Escalation*				Dose Regimen
	Starting dose	up to		Maximum daily dose	
≥60	150	300	450	600	BID or TID
30-60	75	150	225	300	BID or TID
15-30	25-50	75	100-150	150	QD or BID
<15	25	25-50	50-75	75	QD
Supplementary dosage following hemodialysis (mg)[b]					
Patients on the 25 mg QD regimen: take one supplemental dose of 25 mg or 50 mg					
Patients on the 25-50 mg QD regimen: take one supplemental dose of 50 mg or 75 mg					
Patients on the 50-75 mg QD regimen: take one supplemental dose of 75 mg or 100 mg					
Patients on the 75 mg QD regimen: take one supplemental dose of 100 mg or 150 mg					

TID = Three divided doses; BID = Two divided doses; QD = Single daily dose.
* Based on individual patient response and tolerability.
[a] Total daily dose (mg/day) should be divided as indicated by dose regimen to provide mg/dose.
[b] Supplementary dose is a single additional dose.

Overdosage

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

Signs, Symptoms and Laboratory Findings of Acute Overdosage in Humans: The highest known dose of pregabalin received in the clinical development program in which there was no fatal outcome was 15,000 mg in 1 patient. The types of adverse events experienced by patients who received an overdose were not clinically different from other patients receiving recommended doses of pregabalin. In post-marketing experience, fatal outcomes in cases in which pregabalin has been taken in combination with other medications have been reported with a pregabalin overdose as low as 800 mg in a day. In none of these cases has pregabalin been established as the cause of death or in pregabalin monotherapy. The lowest fatal dose with pregabalin alone has not yet been identified.

The most commonly reported adverse events observed when pregabalin was taken in overdose (dose range from 800 mg/day up to 11,500 mg as a single dose) included affective disorder, somnolence, confusional state, depression, agitation, and restlessness.

Treatment or Management of Overdose: There is no specific antidote for overdose with pregabalin. If indicated, elimination of unabsorbed drug may be attempted by emesis or gastric lavage; usual precautions should be observed to maintain the airway. General supportive care of the patient is indicated including monitoring of vital signs and observation of the clinical status of the patient. A Certified Poison Control Center should be contacted for up-to-date information on the management of overdose with pregabalin.

Hemodialysis: Standard hemodialysis procedures result in significant clearance of pregabalin (approximately 50% in 4 hours) and should be considered in cases of overdose. Although hemodialysis has not been performed in the few known cases of overdose, it may be indicated by the patient's clinical state or in patients with significant renal impairment.

Availability of Dosage Forms

LYRICA is available in dosage strengths of 25 mg, 50 mg, 75 mg, 100 mg*, 150 mg, 200 mg*, 225 mg, and 300 mg capsules.

* Not commercially available in Canada

For a copy of the Product Monograph or full Prescribing Information, please contact: Pfizer Canada Medical Information at 1-800-463-6001 or visit www.pfizer.ca.

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2011 Congress-at-a-Glance

wednesday june 15	07:00 - 08:45	Continental Breakfast
	09:00 - 17:15	Neurology Resident Review – Multiple Sclerosis ***Chair TBA***
	09:00 - 17:15	Neurosurgery Resident Review – Peripheral Nerve Surgery ***Rajiv Midha, Shobhan Vachhrajani & Ryojo Akagami***
	09:00 - 17:15	ALS ***Charles Krieger***
	09:00 - 12:15	Stroke ***Chair TBA***
	09:00 - 12:15	Dementia ***Ging-Yuek Robin Hsiung***
	12:30 - 13:45	Lunch & Poster Viewing
	12:30 - 13:45	Co-developed Industry Symposium (Stroke)
	12:30 - 13:45	Co-developed Industry Symposium (Headache)
	14:00 - 17:15	Headache ***Gordon Mackie***
	14:00 - 17:15	Neurocritical Care ***Draga Jichici & Jeanne Teitelbaum***
	14:00 - 17:15	Functional Neurosurgery ***Christopher Honey***
	17:15 – 19:30	Exhibitors Reception
thursday june 16	07:00 - 08:15	Continental Breakfast
	08:30 - 09:15	Distinguished Guest Lecture – ***Henry Barnett***
	09:30 - 17:00	Child Neurology Day – Tibbles Lecture: ***Ingrid Scheffer***
	09:30 - 12:30	CNS / CSCN Plenary & Chair's Select Abstracts - Gloor Lecture: ***Angela Vincent,*** Richardson Lecture: ***Judy Illes***
	09:30 - 12:30	CNSS Plenary & Chair's Select Abstracts - Penfield Lecture: ***William Couldwell,*** CNSS Society Lecture: ***Allan Taylor***
	12:45 - 14:00	Lunch, Exhibit & Poster Viewing
	12:45 - 14:00	Co-developed Industry Symposium (Epilepsy)
	12:45 - 14:00	Co-developed Industry Symposium (Neuropathic Pain)
	14:15 - 17:30	Multiple Sclerosis ***Chair TBA***
	14:15 - 17:30	Neurovascular & Interventional Neuroradiology ***Gary Redekop***
	14:15 - 17:30	EEG ***Seyed Mirsattari***
	14:15 - 17:30	Spine ***Eric Massicotte***
	18:00 - 20:00	Movement Disorders SIG ***Silke Cresswell***
	18:00 - 20:00	Headache SIG ***Gordon Robinson***
	18:00 - 20:00	Neuromuscular Diseases SIG ***Kristine Chapman***
	18:00 - 20:00	Epilepsy Video SIG ***Richard McLachlan***
friday june 17	07:00 - 08:15	Continental Breakfast
	08:30 - 11:15	Platform Sessions
	11:30 - 13:15	Grand Rounds
	13:15 - 15:00	Lunch, Exhibit & Poster Author Stand-by Tours
	13:15 - 15:00	Digital Poster and Exhibit Viewing
	13:15 - 14:45	Scotiabank Wills & Estates Planning Seminar
	15:00 - 18:15	Epilepsy ***Nizam Ahmed***
	15:00 - 18:15	Neuro-oncology ***David Eisenstat***
	15:00 - 18:15	Neuro-ophthalmology ***William Fletcher***
	15:00 - 18:15	Advances in Neurobiology ***Zelma Kiss & Peter Smith***
	15:00 - 18:15	Neuromuscular Diseases ***Mike Nicolle***
	15:00 - 18:15	Advances in Neurosurgery ***Brian Toyota***
	19:00 - 24:00	Presidents' Social Event

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The Neurological Sciences Foundation of Canada Inc.

The Neurological Sciences Foundation of Canada (NSFC) is a charitable organization. The NSFC's work is entirely dependent on donations and raises money annually in support of activities and initiatives of importance to neurologists, neurosurgeons and the neurological community.

Since 2007 the NSFC has **distributed over $238,000 in grants** to fund numerous organizations and other learning activities including, but not limited to:

- the CNSF Congress to help defray the costs of the Distinguished Guest Lecture and Opening Plenary sessions
- the Canadian Association of Neuroscience Nurses
- the Canadian Association of Electroneurophysiology Technologists
- the Association of Electromyography Technologists of Canada
- the Canada Cuba Project, through the recently formed CNSF International Development Committee
- Think First
- the Canadian Movement Disorders Group and the CNSF… for Neurology and Neurosurgery Resident Education, through the Don Paty Fund

WE NEED YOUR SUPPORT! Without your support, funding to the specific organizations and projects and new initiatives may not occur.

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The Neurological Sciences Foundation of Canada Inc.
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Calgary, Alberta T2H 2K6
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Yes, I wish to help advance the objectives of the NSFC and the Neurological Community.

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