CANADIAN NEUROLOGICAL SCIENCES FEDERATION
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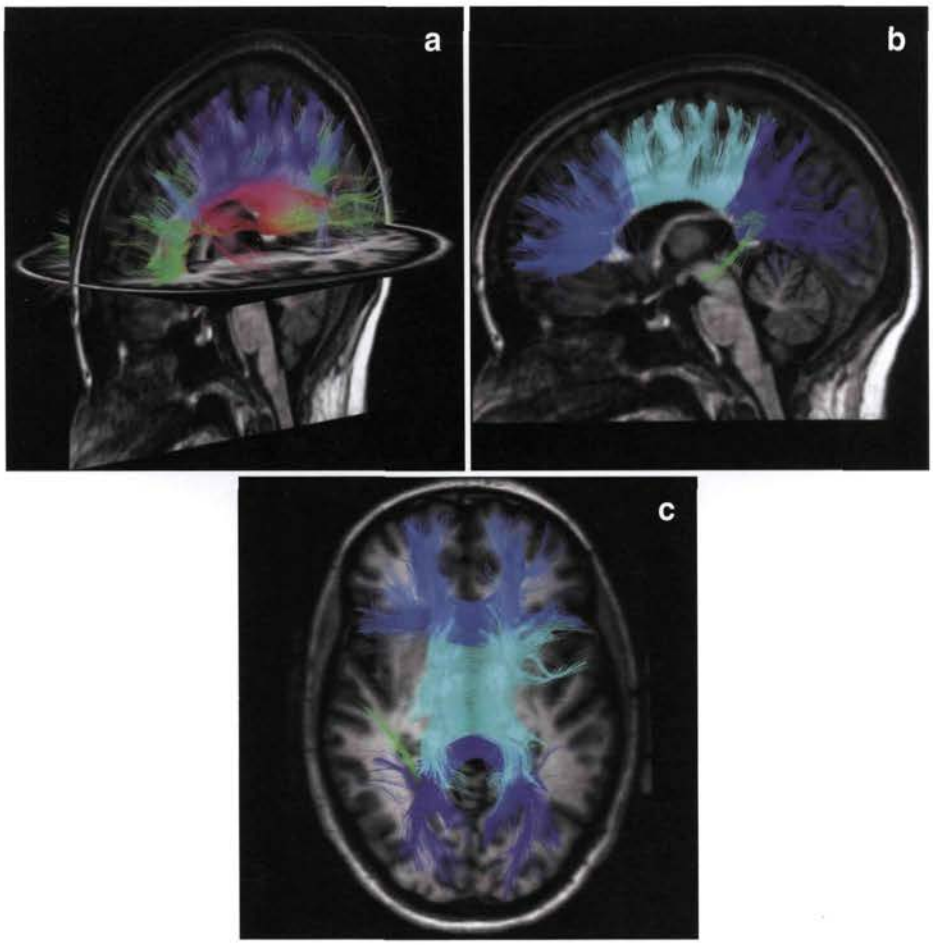

Tractography in the Study of the Human Brain: A Neurosurgical Perspective

David Fortin, Camille Aubin-Lemay, Arnaud Boré, Gabriel Girard, Jean-Christophe Houde, Kevin Whittingstall, Maxime Descoteaux

Original Article - Can J Neurol Sci. 2012; 39: 747-756

(a) The corpus callosum in a standard directional color-coded view. (b) The corpus callosum in side (c) and top view, using a color segmentation for the genu, body and splenium, as well as the tapetum fibers (green).

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COPAXONE®

PATIENT EXPERIENCE DATA

15 YEARS

USE IN CLINICAL PRACTICE IN CANADA[1]

OVER 1 MILLION

PATIENT-YEARS OF EXPERIENCE WORLDWIDE[2]

COPAXONE® is indicated for the treatment of ambulatory patients with Relapsing Remitting Multiple Sclerosis (RRMS) to decrease the frequency of clinical exacerbations; to reduce the number and volume of active brain lesions identified on Magnetic Resonance Imaging (MRI).

COPAXONE® is indicated for the treatment of patients who have experienced a single demyelinating event, accompanied by abnormal MRI scans, and are considered to be at risk of developing Clinically Definite MS (CDMS), after alternative diagnoses are excluded: to delay the onset of definite MS; to decrease the number and volume of active brain lesions and overall disease burden (as identified by MRI scans).

The safety and efficacy of COPAXONE® in chronic progressive MS have not been established. In placebo-controlled clinical trials, the most commonly observed adverse events associated with the use of COPAXONE® occurring at an incidence of at least 10% and at least 1.5 times higher than in placebo treated patients were: injection site reactions, vasodilatation, rash, dyspnea and chest pain.

References: 1. Health Canada. COPAXONE Notice of Compliance. Accessed online at http://webprod3.hc-sc.gc.ca/noc-ac/info.do?lang=eng&no=3831 2. Data on file. Periodic Safety Update Report (PSUR), Global Drug Safety & Pharmacovigilance, Teva Pharmaceutical Limited, January 12, 2012.

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For brief prescribing information see pages A-25, A-26

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FACED WITH PAIN*

IN HER STRUGGLE WITH FIBROMYALGIA

*Fictitious patient. May not be representative of all fibromyalgia cases.

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First treatment indicated in Canada for adults for the management of pain associated with **fibromyalgia**[1]

Pregabalin: first-line treatment for chronic **neuropathic pain**[2]

DEMONSTRATED SIGNIFICANT RELIEF IN PAIN AND PAIN-RELATED SLEEP DIFFICULTIES IN FIBROMYALGIA[1]

Demonstrated powerful, rapid and sustained pain relief[1,3-5]

In fibromyalgia:

- In a 14 week study, LYRICA demonstrated significant pain reduction as early as week 1 ($p<0.05$ for all doses). Mean changes in pain scores at the end of the study for LYRICA-treated patients were significantly greater versus placebo (300 mg/day, n=183: -1.75, $p=0.0009$; 450 mg/day, n=190: -2.03, $p<0.0001$; 600 mg/day, n=188: -2.05, $p<0.0001$; placebo, n=184: -1.04)[3]
- In another study of 26 weeks' duration of patients who initially responded to LYRICA during a 6-week, open-label phase, 68% of those who continued on their optimized dose (n=279) maintained a treatment response versus 39% of those on placebo (n=287). The time to loss of therapeutic response was longer in the LYRICA group ($p<0.0001$)[4]

Also in neuropathic pain (NeP):

- Sustained pain relief (starting at week 2 for LYRICA 150-600 mg/day, n=141; $p<0.05$ vs placebo, n=65) was demonstrated throughout a 12 week study in patients with DPN or PHN[5]

Demonstrated effective in relieving pain-related sleep difficulties[1,6]

In fibromyalgia:

- In a 13 week study, LYRICA reduced overall MOS-Sleep Scale scores significantly more at the end of the study vs. placebo (300 mg/day -19.1, $p=0.0174$; 450 mg/day: -20.41, $p=0.0026$; 600 mg/day: -19.49, $p=0.0101$; placebo: -14.29)[6]

Also in NeP:

- LYRICA reduced sleep disturbances across several studies in DPN and PHN, of 8-12 weeks duration[1]

Flexible dosing across all indications[1†]

LYRICA (pregabalin) is indicated for the management of neuropathic pain associated with diabetic peripheral neuropathy (DPN), postherpetic neuralgia (PHN) and spinal cord injury in adults. LYRICA may be useful in the management of central neuropathic pain in adults. LYRICA is indicated for the management of pain associated with fibromyalgia in adults. 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.

LYRICA is contraindicated in patients who are hypersensitive to pregabalin or to any ingredient in the formulation or component of the container.

The most commonly observed adverse events (≥5% and twice the rate as that seen with placebo) in the recommended dose range of 150 mg/day to 600 mg/day in PHN and DPN patients were: dizziness (9.0-37.0%), somnolence (6.1-24.7%), peripheral edema (6.1-16.2%), and dry mouth (1.9-14.9%) and were dose related; in spinal cord injury patients: somnolence (41.4%), dizziness (24.3%), asthenia (15.7%), dry mouth (15.7%), edema (12.9%), constipation (12.9%), amnesia (10.0%), myasthenia (8.6%), amblyopia (8.6%), and thinking abnormal (8.6%); in fibromyalgia patients: dizziness (37.5%), somnolence (18.6%), weight gain (10.6%), dry mouth (7.9%), blurred vision (6.7%), and peripheral edema (6.1%). In LYRICA-treated fibromyalgia patients, the most commonly observed dose-related adverse events were: dizziness (22.7-46.5%), somnolence (12.9-20.7%), weight gain (7.6-13.7%), peripheral edema (5.3-10.8%). The most commonly observed adverse events in the PHN, DPN, spinal cord injury and fibromyalgia patients were usually mild to moderate in intensity. Discontinuation rates due to adverse events for LYRICA and placebo, respectively, were 9% and 4% in DPN, 14% and 7% in PHN, 21% and 13% in spinal cord injury, and 20% and 11% in fibromyalgia. There was a dose-dependent increase in rate of discontinuation due to adverse events in fibromyalgia.

There have been post-marketing reports of angioedema in patients, some without reported previous history/episodes, including life-threatening angioedema with respiratory compromise. Caution should be exercised in patients with previous history/episodes of angioedema and in patients who are taking other drugs associated with angioedema.

In clinical trials and in post-marketing experience, there have been reports of patients, with or without previous history, experiencing renal failure alone or in combination with other medications. Caution is advised when prescribing to the elderly or those with any degree of renal impairment.

There have been post-marketing reports of events related to reduced lower gastrointestinal tract function (e.g., 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.

Dosage reduction is required in patients with renal impairment (creatinine clearance <60 mL/min) and in some elderly patients as LYRICA is primarily eliminated by renal excretion.

Please see Prescribing Information for complete Warnings and Precautions, Adverse Reactions, Dosage and Administration and patient selection criteria.

† Please consult Prescribing Information for complete Dosage and Administration instructions.

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Pr LYRICA® PREGABALIN

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See prescribing information and study parameters on pages A-15, A-16

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Deadline for Applications: December 15, 2012

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VIMPAT® (lacosamide) is indicated as adjunctive therapy in the management of partial-onset seizures in adult patients with epilepsy (≥18 years of age) who are not satisfactorily controlled with conventional therapy. The clinical experience with VIMPAT® in elderly patients with epilepsy (≥65 years of age) is limited. Caution should be exercised during dose titration and age-associated decreased renal clearance should be considered in elderly patients. 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.

VIMPAT® is contraindicated in patients who are hypersensitive to the active substance or to any of the excipients and in patients with a history of, or presence of, second- or third-degree atrioventricular (AV) block.

Second degree or higher AV block has been reported in post-marketing experience. Patients should be made aware of the symptoms of second-degree or higher AV block (e.g. slow or irregular pulse, feeling of lightheadedness and fainting), and told to contact their physician should any of these symptoms occur. VIMPAT® should be used with caution in patients with known conduction problems (e.g. marked first-degree AV block, sick sinus syndrome without pacemaker), or with a history of 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 especially be exerted when treating elderly patients as they may be at increased risk of cardiac disorder or when VIMPAT® is given with other drugs that prolong the PR interval (e.g. carbamazepine, pregabalin, lamotrigine, beta-blockers, and class I antiarrhythmic drugs), as further PR prolongation is possible. In clinical trials of healthy subjects and patients with epilepsy, VIMPAT® treatment was associated with PR interval prolongation in a dose-dependent manner. 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 or irregular pulse, shortness of breath) and told to contact their physician should any of these symptoms occur. Atrial fibrillation and flutter have been reported in open-label epilepsy trials and in postmarketing experience.

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 anticonvulsants. If any of these hypersensitivity reactions are suspected, VIMPAT® should be discontinued and alternative treatment started.

Treatment with VIMPAT® has been associated with dizziness and ataxia, which could increase the occurrence of accidental injury or falls. 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.

In controlled trials in patients with partial-onset seizures, VIMPAT® treatment was associated with vision-related adverse events such as blurred vision and diplopia. Patients should be informed

ucb

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When seizure control is still an issue for your patient

Bring VIMPAT® into the picture

Efficacy in patients inadequately controlled on 1 to 3 AEDs*†[1]

- Significant median **36-39% reduction in seizure frequency** per 28 days from baseline to maintenance phase*[1]
  - VIMPAT® 400 mg/day vs. placebo: Ben-menachem, *et al.* (39% vs. 10%, $p \leq 0.01$); Chung, *et al.* (37.3% vs. 20.8%, $p \leq 0.01$); Halász, *et al.* (36.4% vs. 20.5%, $p \leq 0.05$)*[1]

Generally well tolerated when added to common concomitant therapy

- Some of the most frequently reported **adverse reactions** with VIMPAT® 400 mg/day were dizziness (30%), nausea (11%), and vision-related events, including diplopia (10%) and blurred vision (9%)

The recommended starting dose for VIMPAT® is 50 mg twice a day 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 of VIMPAT® can be increased by 50 mg twice daily every week, to a **maximum recommended dose of 400 mg/day**.[1]

Please consult product monograph for complete dosing and administration instructions.

POWER for added control.

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.

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.

There are no studies with VIMPAT® in pregnant women. 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. It is unknown whether VIMPAT® is excreted in human breast milk. Because many drugs are excreted into human milk, a decision should be made whether to discontinue nursing or to discontinue VIMPAT®, taking into account the importance of the drug to the mother.

As with all antiepileptic drugs, VIMPAT® should be withdrawn gradually (over a minimum of 1 week) to minimize the potential of increased seizure frequency.

In controlled clinical trials in patients with partial-onset seizures, some of the most frequently reported adverse reactions with VIMPAT® treatment were dizziness (16% and 30% for 200 mg and 400 mg treatment groups, respectively, vs. 8% placebo), nausea (7% and 11% vs. 4%), and vision related events [diplopia (6% and 10% vs. 2%) and blurred vision (2% and 9% vs. 3%)]. They were dose-related and usually mild to moderate in intensity. The adverse events most commonly leading to discontinuation were dizziness, coordination abnormal, vomiting, diplopia, nausea, vertigo, and vision blurred.

Please see the VIMPAT® Product Monograph for full prescribing information.

* 3 randomized, double-blind, placebo-controlled, multicentre trials studying VIMPAT® (lacosamide) as adjunctive therapy in adult patients with POS with or without secondary generalization. In the studies, patients were to have been taking a stable dosage regimen of one to three AEDs, with or without vagal nerve stimulation in the 4 weeks before enrollment and during the baseline period. Following the 8-week baseline phase, subjects were randomized and up-titrated by initiating treatment at 100 mg/day, and increased in weekly increments of 100 mg/day to the target dose. The titration phase lasted 4-6 weeks. Patients then entered a 12-week maintenance phase period.[2,3,4]

† AED=anti-epileptic drug

References: 1. VIMPAT® Product Monograph, UCB Canada Inc., October 6, 2011. 2. Ben-Menachem E, Biton V, Jatuzis D, *et al.* Efficacy and safety of oral lacosamide as adjunctive therapy in adults with partial-onset seizures. *Epilepsia* 2007; 48(7):1308-1317. 3. Chung S, Sperling MR, Biton V *et al.* Lacosamide as adjunctive therapy for partial onset seizures: A randomized controlled trial. *Epilepsia* 2010; 51(6):958-967. 4. Halász P, Kalviainen R, Mazurkiewicz-Beldzińska M, *et al.* Adjunctive lacosamide for partial-onset seizures: Efficacy and safety results from a randomized controlled trial. *Epilepsia* 2009; 50(3):443-453.

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See prescribing summary on page A-20 to A-23

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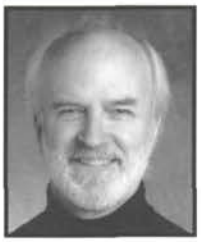

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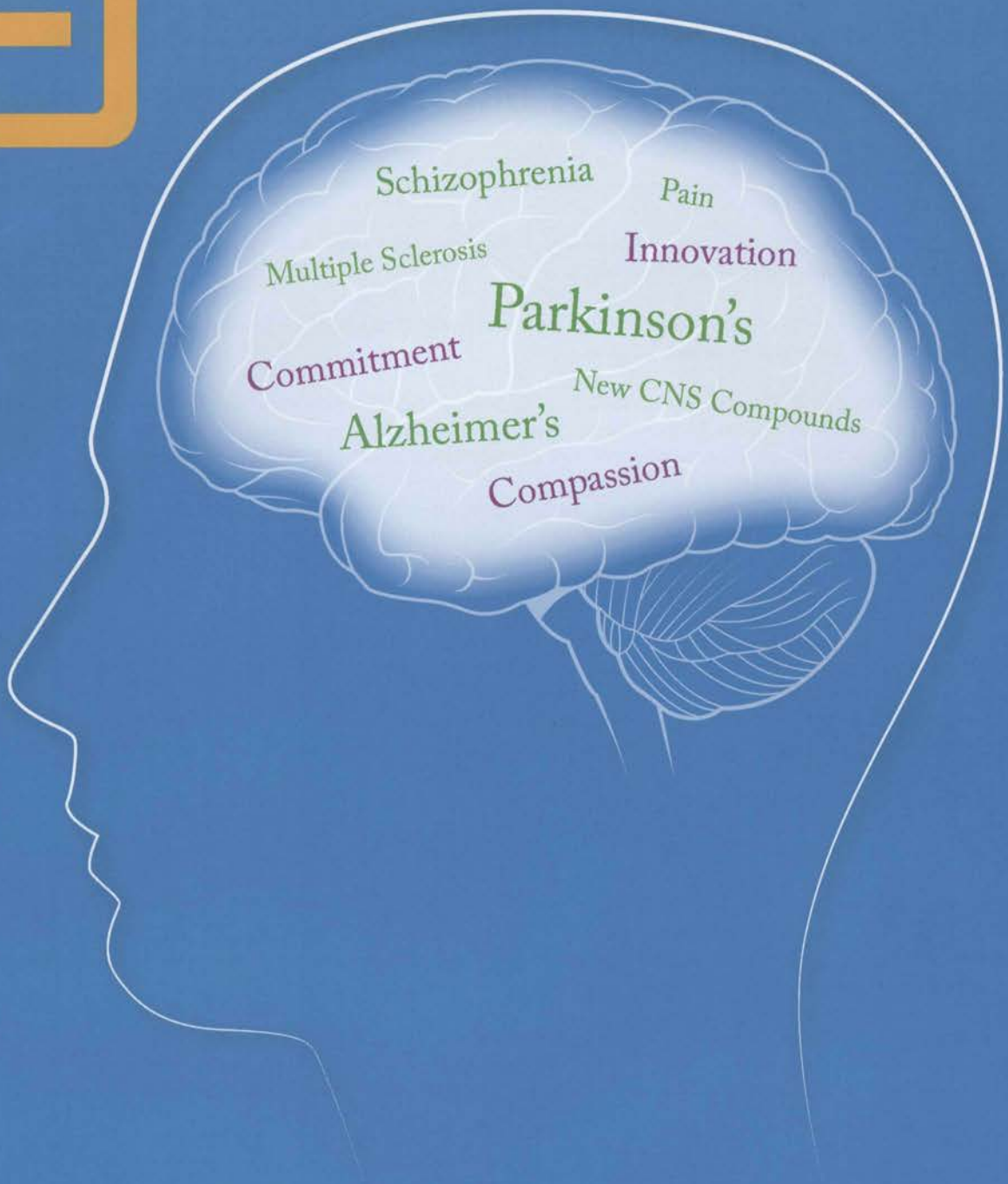

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Professionals Seek Efficiencies to Save Time, Money and Achieve Long-Term Financial Health

While they are known for their dedicated care for others, busy professionals often admit that it's hard to muster the same enthusiasm for attending to their own needs, including practice efficiency.

By taking time to find better ways to operate – including not-so-obvious financial efficiencies – you can save time and money and maximize your resources, to meet both long-term work and life goals.

"Like many business owners, professionals are often more passionate about the service they provide than about the day-to-day operations or financial details," observes John Roberts, Vice President, Small Business Banking, Scotiabank. "That means they need to be deliberate about finding time to review the financial management of their practice with a knowledgeable team of advisors."

For example, Roberts notes that you should review account arrangements with your financial institution, to ensure you are receiving available discounts that reflect your transaction volumes and patterns. Similarly, a professional should consider specialized banking technologies that can save time and reduce costs, ranging from automated, pre-authorized billing to merchant debit and credit services at a preferred rate.

Professionals should also examine their borrowing arrangements, including the use of a business credit card to separate personal from professional expenses and to earn rewards points or other relevant benefits.

Efficient borrowing also means having a cash flow plan - which may include an operating line of credit to manage fluctuating payables, receivables and inventory - and a capital plan, including term loans or lease financing to handle equipment or major purchases.

"It really is important to refresh your business plan periodically, including projections to recognize any cash flow highs and lows, and to anticipate your needs to fund growth in the business," notes Roberts, adding that Scotiabank offers a convenient cash flow projection tool at www.getgrowingforbusiness.com.

Roberts recommends that a professional should regularly meet their financial advisor – or set up a second opinion planning conversation with a small business advisor, especially if something changes in their business. He explains that, "Health care professionals tell patients to call if anything changes in their condition, and the same goes for your finances, whether it's growth in the practice, succession planning, or changing personal priorities, like saving for a child's education or their own retirement."

"Although professionals are extremely busy, a regular touch base with your financial advisor can save time and money and improve cash position," concludes Roberts. "With expert advice, you can focus on what you do best, while also achieving long-term financial health." Contact a Scotiabank small business advisor to arrange for a second opinion or to learn more about the Scotia Professional Plan and other services.

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