

Doctor, soldier, *tinkerer*

Military surgeon Dr. Dennis Filips had a simple idea for closing life-threatening wounds. Now his clamp device is winning innovation awards and is almost ready for the marketplace

BY VANESSA SANTILLI



Photos: Larry Wong/Edmonton Journal 2012

While training medics before they'd be sent overseas to Afghanistan, retired combat trauma surgeon Dr. Dennis Filips had a revelation. After watching his trainees struggle immensely to stop bleeding, he came up with the idea for a device that would close life-threatening wounds within seconds.

"Often, quite a few minutes would go by before they'd even have the opportunity to stop the bleeding," Dr. Filips told the *Medical Post* on the phone from Luxor, Egypt, where he was promoting the ITClamp (Innovative Trauma Care clamp).

The clamp is a small, handheld device resembling a hair clip that can be applied to an open injury. It stops bleeding within seconds, simply by applying it to the wound and squeezing it shut, explained Dr. Filips explained.

For these efforts, in April his firm Innovative Trauma Care Inc. was the grand prize winner of the TEC Edmonton VenturePrize, a business competition where new companies submit their business models and talk to a panel of experts about their plans' viability. The company, founded in 2010, took home \$90,000 that will go toward the launch of the ITClamp, which should take place later this year. This is the company's first product.

Also in April, Dr. Filips won the top innovator award at the Life Science and Healthcare Ventures Summit in New York, which venture capital funds host.

Born in Edmonton, Dr. Filips served in the military for 20 years before retiring. "I was overseas for five operational tours: three in Afghanistan, one in Bosnia and one in the Golan Heights."

Military service is something that has always been honoured in his family, he says.

"My wife is still active in the Canadian Forces and is serving as the commanding officer of 1 Service Battalion, with more than 1,100 troops under

her command." His father-in-law was a career infantry officer.

Skills gained during his time abroad have been transferable into his new venture, he says. "Serving in the military has given me a sense of commitment and discipline and helped me to develop leadership skills that are directly relevant to team-building in the corporate environment."

Dr. Filips says he's always been a tinkerer, creating or modifying tools to fit a particular need.

"I was moved to start the company because I could not easily convince anyone to take hold of the idea and run with it," he says, adding that he felt the only way

to do this properly would be to surround himself with people who had the necessary business skills to develop and commercialize the idea.

Co-founder and chief operating officer Ian Atkinson has known Dr. Filips for more than 30 years. He calls his friend "a natural" when it comes to the more technical aspects of the product.

"But he's also extremely confident when it comes to the leading of the company and the leading of the business side of this. As a teammate, he's phenomenal."

Atkinson says he thinks their new product is going to have an impact on how traumas are handled. "I honestly believe this is going to be a bit of a game-changer," he said.

Dr. Filips kept up his surgical skills until last January, but has now taken a temporary leave from clinical practice to focus entirely on the company.

Until this year, "my partner and I had funded the company ourselves to the tune of \$400,000 in cash, plus we have gone without salaries to keep the costs down. Funding to date has been from friends and family and 'angel investors,' with almost \$1 million raised since January.



Dr. Dennis Filips (left) and his longtime friend Ian Atkinson developed the ITClamp (above) to close life-threatening, open wounds quickly in the field.

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they were doing, had arranged an appointment with an oncologist in Toronto so they could get a second opinion on Mary's chemo. The second opinion concurred with the first; they were disappointed there was no cure, but comforted to know they could stay at home and get top-of-the-line care. "I don't know how you did it, Agnes," the husband said, "but thank you. Thank you."

And there it was: Agnes is always there. She's there when a dog bites someone's kid, she's there when someone's steeling herself to hear about a wor-

risome test result, she's there when the love of someone's life is dying. She's a bit like family.

We often talk about the health-care team in terms of doctors and nurses plus allied health-care folks. But if I didn't understand it before, I do now: Agnes is the first person our patients look for when they come needing care. And in that, she gives more than she'll ever receive.

Monica Kidd is a family doctor and assistant professor of medicine at Memorial University of Newfoundland in St. John's, N.L.



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—Dr. Dennis Filips

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In total, the team is looking to raise another \$9 million to \$10 million in the next

year, he says.

And although the idea for the device sprang from the high-stress combat zone, it can

also be used to help patients in everyday situations.

In terms of practicality, the ITClamp doesn't require a lot of training, says Dr. Filips, and could be used in an ER setting

"By having a device like this, we can have a nurse or nursing student or a medical student go around and close off wounds while all of the other life-saving procedures are being done."

Hemorrhaging

One of the clamp's most impressive functions is that it will provide patients with temporary stabilization of external bleeding, addressing massive hemorrhaging—which is a leading cause of death in traumatic injury.

"In the trauma room . . . you wind up getting blood all over the place as patients bleed externally while life-saving operations are going on, just because there hasn't been time to close off all these wounds," said Filips. "And they wind up losing . . . a few litres of blood over a few hours before there's time" to close them.

The clamp is easy to carry due to its small size, says Atkinson. "It weighs an ounce so it can be carried in a pocket, it can be carried in a med bag. It's not something that requires a huge amount of space for a soldier to carry or police officers to put in their first-aid kits."

The cost estimate of the ITClamp is \$65, which should be within a few dollars of the final price, says Dr. Filips.

"I'm hoping that by being able to incorporate the skill of surgeons into this device, we can decrease blood loss and increase survival by putting it into the hands of people with minimal training—whether it be a paramedic, soldier or even your average person."

Some of the markets Dr. Filips and Atkinson hope to tap into include EMS providers, emergency room physicians and military units in North America, Europe, Australia and New Zealand.

This is the first device the company has developed, but stay tuned as there's more on the way, notes Dr. Filips.

"We have ideas to expand the functioning of this device, so this will be a technology platform," he says. "We also have plans to come out with other life-saving devices that address airway and breathing issues." MP

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 ($\geq 5\%$ 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.

Most Common Adverse Events in Controlled Clinical Studies in Fibromyalgia: The most commonly observed treatment-related adverse events ($\geq 5\%$ 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:

- LYRICA Product Monograph. Pfizer Canada Inc., June 21, 2010.
- 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.
- Arnold LM et al. A 14-week, randomized, double-blind, 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 ($\geq 30\%$ 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.
- 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 ≥ 4 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 $\geq 50\%$ reduction in pain on the VAS and self-rating on the Patient Global Impression of Change scale of "much improved" or "very much improved".
- Freynhagen R et al. Efficacy of pregabalin in neuropathic pain evaluated in a 12-week, randomized, 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 ($p < 0.05$, weeks 2-3 and $p < 0.01$, weeks 4-12), and the fixed dose of 600 mg/day ($p < 0.05$, week 1 and $p < 0.01$, weeks 2-12).
- 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.

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 ($\approx 2\%$ 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_c), 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 _c) (mL/min)	Total Pregabalin Daily Dose (mg/day)*				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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