PRESS RELEASE

Health Canada approves XERMELO™ (telotristat ethyl) for the treatment of adult patients suffering from refractory carcinoid syndrome diarrhea[1]

XERMELO™ is a first-in-class treatment option for patients whose refractory carcinoid syndrome diarrhea is inadequately controlled with somatostatin analogue (SSA) therapy alone[2]

Mississauga, ON, October 16, 2018 - Ipsen Biopharmaceuticals Canada Inc. announced today Health Canada's approval of XERMELO™ (telotristat ethyl) for the treatment of refractory carcinoid syndrome (CS) diarrhea, in combination with somatostatin analogue (SSA) therapy, in patients inadequately controlled by SSA therapy alone.[3]

XERMELO™ is a novel, orally administered, inhibitor of the enzyme tryptophan hydroxylase and is designed to reduce the production of serotonin.[4] The approval was based on the positive results of the TELESTAR pivotal trial and the TELECAST trial, two phase 3, randomized, placebo-controlled, 12-week trials where the efficacy and the safety of XERMELO™ were demonstrated in carcinoid syndrome patients. Both trials reported statistically significant reductions of bowel movement (BM) frequency compared with placebo and change in u5-HIAA from baseline.[5]

"Carcinoid syndrome symptoms, especially the diarrhea, can be devastating for those affected. The approval of XERMELO™ is a great development for our NET patients whose symptoms aren't controlled by SSA alone – it can bring back their quality of life," says Dr. Simron Singh, Medical Oncologist and Co-Founder, Susan Leslie NETs Clinic at Odette Cancer Centre, Sunnybrook Health Sciences Centre in Toronto. "This is an exciting new treatment for those patients whose carcinoid syndrome is not adequately controlled with existing SSA therapy alone."

Neuroendocrine tumours (NETs) are rare tumours that grow in the neuroendocrine system of the body.[6] This system is responsible for the production of hormones which are released into the bloodstream, therefore the presence of NETs can disrupt the hormone balance within the body, for example NETs can trigger an over-production of serotonin.[7] When serotonin is present in large amounts within the body, it can disrupt a number of bodily processes causing diarrhea, flushing, wheezing and cardiac damage.[8] Carcinoid syndrome is the terminology used to classify this collection of symptoms.[9] Carcinoid syndrome is incurable in over 95 per cent of patients.[10] The disease can cause a range of symptoms with one of the most common being diarrhea, which affects 75 per cent of patients.[11] Diarrhea can negatively affect a patient's emotional, social and physical well-being with over 10 per cent of patients having seven or more BM a day.[12]

"Carcinoid syndrome diarrhea, can be extremely debilitating, significantly affecting a patient's quality of life – and many find it to be the most difficult syndrome related symptom to control," says Jacqueline Herman, President and Director of Treatment Access & Health Policy of

CNETS Canada (Carcinoid-Neuroendocrine Tumour Society). “In many cases the severity is bad enough that patients aren’t able to hold down a job or lead a normal life, so having a new treatment option that helps manage this symptom will be transformational for these patients.”

“Ipsen is committed to further establishing our company as the leader in NETs. We continue to develop new, innovative therapies for difficult-to-treat diseases and for patients faced with limited options,” says Ed Dybka, General Manager for Ipsen Biopharmaceuticals Canada, Inc. “Health Canada’s approval of XERMELO™ adds to our portfolio of oncology products that treat carcinoid syndrome and is a further demonstration of our, and our partner Lexicon Pharmaceuticals’, commitment to bringing new treatments to Canada and to improving patients’ lives.”

About the TELESTAR and TELECAST Trials

The TELESTAR trial evaluated 136 adult patients who were randomized to receive treatment with XERMELO™ 250 mg, telotristat ethyl 500 mg or placebo three times daily. All patients had well-differentiated metastatic neuroendocrine tumours and carcinoid syndrome, were on SSA therapy and had ≥4 BMs per day. The primary endpoint was demonstrated by a significant reduction in BM frequency (-1.4/per day for XERMELO ™ 250 mg vs -0.6/per day for placebo) averaged over the 12-weeks in both doses studied ($p<0.001$).

In the TELESTAR trial, the proportion of patients who achieved a durable response was two-fold higher in the XERMELO™ 250 mg group than those in the placebo group (44.4% vs. 20.0%). Durable response was defined as at least a 30 per cent reduction in daily BM over at least half the days of the 12-week treatment period.[13]

The TELECAST trial had a similar study design to the TELESTAR trial and evaluated 76 patients who had well-differentiated metastatic neuroendocrine tumours with carcinoid syndrome. Most patients (92.1%) had fewer than 4 BM per day, and all except 9 were treated with SSA therapy. A statistically significant improvement in the change in u5-HIAA at Week 12 compared to baseline was demonstrated and the estimated treatment difference was -54.0% (95% CL: -85.0, -25.1; $p<0.001$).

During both studies, patients were allowed to use rescue medication, i.e., short-acting SSA therapy and anti-diarrheals for symptomatic relief.

The most frequently reported adverse events (AEs) were gastrointestinal disorders, including nausea and abdominal pain. Gastrointestinal disorders accounted for discontinuation in 10.0 per cent of patients treated with XERMELO™ 250 mg tid over 12 weeks and 7.0 per cent with placebo.

About Ipsen

Ipsen Biopharmaceuticals Canada Inc., the Canadian affiliate of Ipsen, is headquartered in Mississauga, Ontario with established operations since October 2015. For more information on Ipsen Biopharmaceuticals Canada Inc. visit www.ipsen.ca. Ipsen is a global specialty-driven biopharmaceutical group focused on innovation and specialty care. The group develops and commercializes innovative medicines in three key therapeutic areas – Oncology, Neuroscience and Rare Diseases. Its commitment to Oncology is exemplified through its growing portfolio of key therapies for prostate cancer, neuroendocrine tumors, renal cell carcinoma and pancreatic cancer. Ipsen’s R&D is focused on its innovative and differentiated technological platforms located in the heart of the leading biotechnological and life sciences hubs (Paris-Saclay, France; Oxford, UK; Cambridge, US). The Group has about 5,400 employees worldwide. Ipsen is listed in Paris (Euronext: IPN) and in the United States through a Sponsored Level I American

Depositary Receipt program (ADR: IPSEY). For more information on Ipsen, visit www.ipsen.com.

About Ipsen in Oncology
Ipsen Canada has built an oncology portfolio that focuses on fighting cancers with high unmet medical needs such as kidney cancer, neuroendocrine tumours and other niche oncology diseases including carcinoid syndrome. Ipsen has also fortified scientific partnerships with top researchers, trusted academic institutions and leading pharmaceutical and biotech companies with the goal of developing effective and innovative therapeutic solutions that improve treatment outcomes for patients and support healthcare professionals in their daily practice.

About the Lexicon and Ipsen Collaboration
On October 22, 2014, Ipsen and Lexicon Pharmaceuticals entered into a license agreement for the commercialization of XERMELO® (telotristat ethyl). Under the agreement, Lexicon granted Ipsen an exclusive license to commercialize XERMELO® in all territories excluding the United States and Japan, where Lexicon retains commercialization rights. XERMELO® was approved by the U.S. Food and Drug Administration on February 28, 2017 and by the European Commission on September 19, 2017.

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[1] XERMELO™ Product Monograph. Ipsen Biopharmaceuticals Canada Inc. October 11, 2018
[2] XERMELO™ Product Monograph. Ipsen Biopharmaceuticals Canada Inc. October 11, 2018
[3] XERMELO™ Product Monograph. Ipsen Biopharmaceuticals Canada Inc. October 11, 2018
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