CANADA

PROVINCE OF QUEBEC
DISTRICT OF MONTREAL

NO: 500-06-000821-161

(Class Action)
SUPERIOR COURT

P. MARTEL

Petitioner

-vs.-

MERCK CANADA INC.
and
SCHERING-PLOUGH CANADA INC.
and
DAIICHI SANKYO COMPANY, LTD.

Respondents

AMENDED APPLICATION TO AUTHORIZE THE BRINGING OF A CLASS ACTION & TO APPOINT THE PETITIONER AS REPRESENTATIVE
(Art. 574 C.C.P and following)

TO THE HONOURABLE MR. JUSTICE GARY D.D. MORRISON OF THE SUPERIOR COURT, SITTING IN AND FOR THE DISTRICT OF MONTREAL, YOUR PETITIONER STATES AS FOLLOWS:

I. GENERAL PRESENTATION

A) The Action

1. Petitioner wishes to institute a class action on behalf of the following group, of which he is a member, namely:

    - all persons residing in Canada who were prescribed and have ingested the drug(s) OLMETEC® (Olmesartan Medoxomil) and/or OLMETEC PLUS® (Olmesartan Medoxomil and Hydrochlorothiazide) and their successors, assigns, family members, and dependants, or any other group to be determined by the Court;

    Alternately (or as a subclass)

    - all persons residing in Quebec who were prescribed and have ingested the drug(s) OLMETEC® (Olmesartan Medoxomil) and/or

OLMETEC PLUS® (Olmesartan Medoxomil and Hydrochlorothiazide) and their successors, assigns, family members, and dependants, or any other group to be determined by the Court;

2. "OLMETEC" is the brand name of the angiotensin II receptor blocker[1] drug Olmesartan Medoxomil, which is prescribed to patients in order to treat hypertension or mild to moderate high blood pressure and other medical conditions including renal disease;

3. "OLMETEC PLUS" is the brand name of the angiotensin II receptor blocker drug Olmesartan Medoxomil (as described above) in combination with Hydrochlorothiazide, which is a diuretic or "water pill" that helps control blood pressure by getting rid of excess salt and water;

4. Unless the context indicates otherwise, OLMETEC and OLMETEC PLUS will be collectively referred to as just OLMETEC;

5. Petitioner contends that Respondents represented to the medical and healthcare community, to Health Canada and to the Class Members that they researched, designed, developed, manufactured, and tested OLMETEC and that it had been found to be safe and/or effective for its intended use(s);

6. The Respondents concealed their knowledge and/or failed to warn the medical and healthcare community, Health Canada and (…) Class Members of the fact that the ingestion of OLMETEC increased the risk of developing multiple injuries, including, but not limited to:

    - Serious gastrointestinal injuries,
    - Olmesartan-Associated Enteropathy (OAE)[2],
    - Sprue-like enteropathy (<u>also known as olmesartan enteropathy in medical literature</u>),
    - Villous atrophy/blunting/damage,
    - Inflammation,
    - Nausea,
    - Vomiting,
    - Chronic diarrhea,
    - Malnutrition,
    - Dehydration,
    - Atrophy,
    - Kidney failure,

[1] Angiotensin II receptor blocker medicines are used to reduce blood pressure by blocking the actions of a chemical (angiotensin II) that causes blood vessels to constrict or tighten, thereby relaxing blood vessels.

[2] <u>Enteropathy is the preferred medical terminology for pathologic changes in the lining (mucosa) of the small intestine.</u>

- Weight loss,
- Abdominal and gastrointestinal pain,
- Colitis,
- Gastritis,
- Permanent injuries resulting from the above, and
- Death;

(the "Gastrointestinal Disorders")

7. The Respondents' liability rests on (i) defective design of OLMETEC, (ii) inadequate warning about the risk of developing Gastrointestinal Disorders, both pre- and post-sale, (iii) failure to notify of the full scope of risks known to be associated with and caused by OLMETEC, and (iv) safety misrepresentations;

8. The Respondents continue to manufacture, market, package, promote, advertise, distribute, label and/or sell OLMETEC throughout Canada, including within the province of Quebec, as safe and effective and with inadequate warnings as to its serious and adverse side effect of the Gastrointestinal Disorders which have severe and life-threatening complications which are permanent and lasting in nature and this has caused physical pain and mental anguish, including diminished enjoyment of life, as well as the need for lifelong medical treatment, monitoring and/or medications;

B) The Respondents

8. Respondent Merck Canada Inc. ("Merck") is a Canadian pharmaceutical corporation, with its head office in Kirkland, Quebec. Merck is and was at all relevant times involved in the research, design, development, formulation, manufacture, testing, marketing, packaging, promotion, advertising, distribution, labelling and/or sale of pharmaceutical products including OLMETEC. It is a subsidiary of Respondent Schering-Plough Canada Inc. that does business throughout Canada, including within the province of Quebec, as appears more fully from a copy of an extract from the *Registraire des enterprises*, produced herein as **Exhibit R-1**;

9. Respondent Merck is the sponsor or licensee for OLMETEC and OLMETEC PLUS in Canada and, is thus, responsible for its Product Monographs, which are the primary source of information for healthcare professionals and patients, setting out the uses, dosage, and risks associated with the drug;

10. Respondent Schering-Plough Canada Inc. ("Schering-Plough") is a Canadian pharmaceutical corporation, with its head office in Kirkland, Quebec. Schering-Plough is and was at all relevant times involved in the research, design, development, formulation, manufacture, testing, marketing, packaging, promotion, advertising, distribution, labelling and/or sale of pharmaceutical

products including OLMETEC. It is a parent company of Respondent Merck that does business throughout Canada, including within the province of Quebec, as appears more fully from a copy of an extract from the *Registraire des enterprises*, produced herein as **Exhibit R-2**;

11. Respondent Daiichi Sankyo Company, Ltd. ("Daiichi") is a global pharmaceutical corporation with its head office in Japan. Daiichi is and was at all relevant times involved in the research, design, development, formulation, manufacture, testing, marketing, packaging, promotion, advertising, distribution, labelling and/or sale of pharmaceutical products including OLMETEC. It is the owner of the following Canadian trade-marks: (word) OLMETEC (TMA613772), (design) OLMETEC PLUS (TMA704161), and (design) Man Design (TMA704669), as appears more fully from a copy of said trade-marks from the CIPO database, produced herein as **Exhibit R-3**;

12. Respondent Daiichi is the applicant and owner of the following Canadian patents: "COMPRESSED PREPARATION OF COMPOSITIONS COMPRISING OLMESARTAN MEDOXOMIL" (CA 2656181), "PULVERIZED CRYSTALS OF OLMESARTAN MEDOXOMIL" (CA 2681591), "METHOD FOR PRODUCING OMESARTAN MEDOXOMIL" (CA 2759163), "ACETONE SOLVATE CRYSTALS OF TRITYL OLMESARTAN MEDOXOMIL" (CA 2760031), as appears more fully from a copy of said patents from the CIPO database, produced herein as **Exhibit R-4**;

13. All Respondents have either directly or indirectly researched, designed, developed, formulated, manufactured, tested, marketed, packaged, promoted, advertised, distributed, labelled and/or sold OLMETEC to distributors and retailers for resale to hospitals, medical practitioners and to the general public throughout Canada, including within the Province of Quebec;

14. Given the close ties between the Respondents and considering the preceding, all Respondents are solidarily liable for the acts and omissions of the other;

C) The Situation

I. What is OLMETEC?

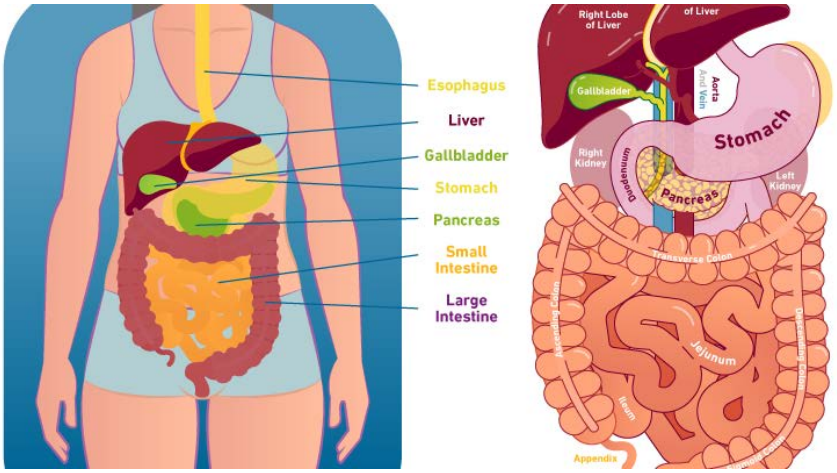
15. OLMETEC belongs to a group of medicines called angiotensin II receptor blockers ("ARB"s). Angiotensin II is a very potent chemical formed in the blood that causes muscles surrounding blood vessels to contract, thereby narrowing the vessels. This narrowing increases the pressure within the vessels and can cause high blood pressure (hypertension). Angiotensin II receptor blockers are medications that block the action of angiotensin II by preventing angiotensin II from binding to receptors on the muscles surrounding blood vessels. As a result, blood vessels enlarge (dilate) and blood pressure is reduced;

15.1 OLMETEC's mechanism of action for the treatment of hypertension is linked to the small intestine, the location for activation of the drug, with most absorption in the small intestine;

16. OLMETEC is an oral tablet prescription medication available in the 5 mg, 20 mg, and 40 mg dosages/strengths and OLMETEC PLUS is available in the 20 mg/12.5 mg, 40 mg/12.5 mg, and 40 mg/25 mg dosages/strengths;

17. OLMETEC and OLMETEC PLUS began being sold in Canada on December 22, 2008 as a prescription medication for the treatment of mild to moderate essential hypertension and as a prescription medication for the treatment of mild to moderate essential hypertension in patients for whom combination therapy is appropriate;

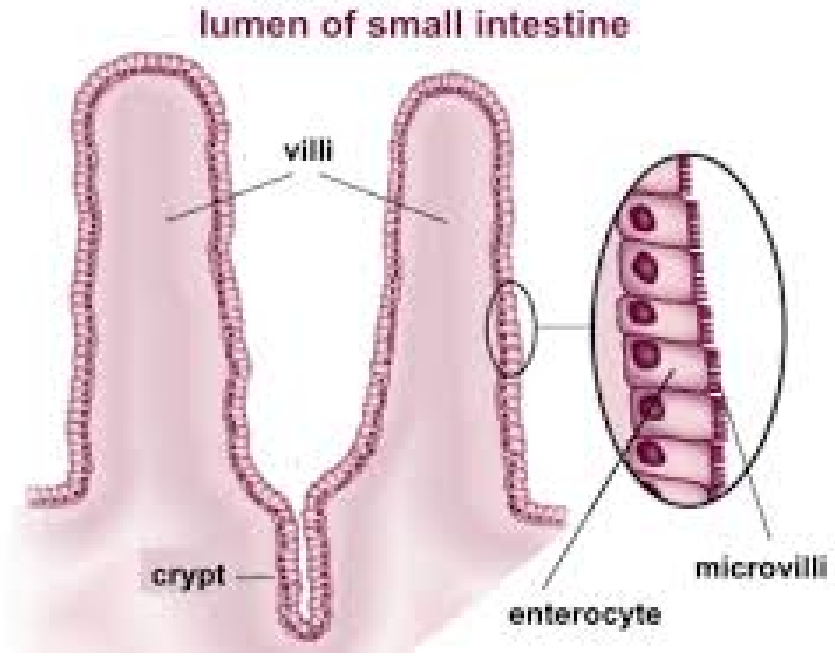
II. The Small Intestine

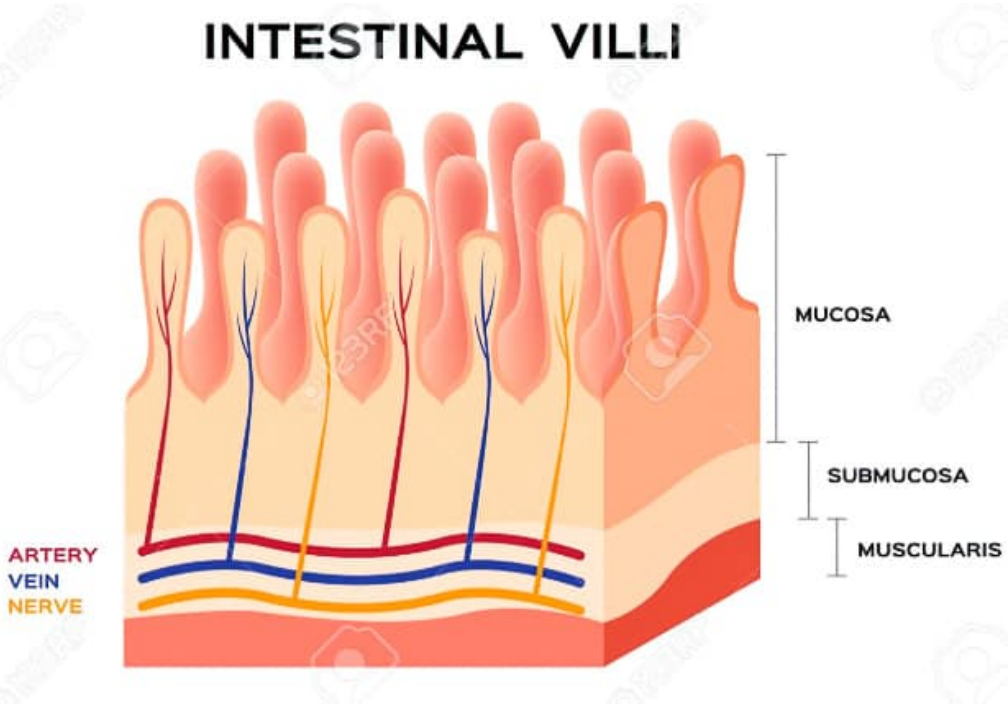


17.1 The small intestine functions as both an absorptive and a secretory organ, the whole as appears more fully from a copy of the Mayo Clinic article entitled "Not All That Flattens Villi Is Celiac Disease: A Review of Enteropathies" dated April 2018, produced herein as **Exhibit R-13**;

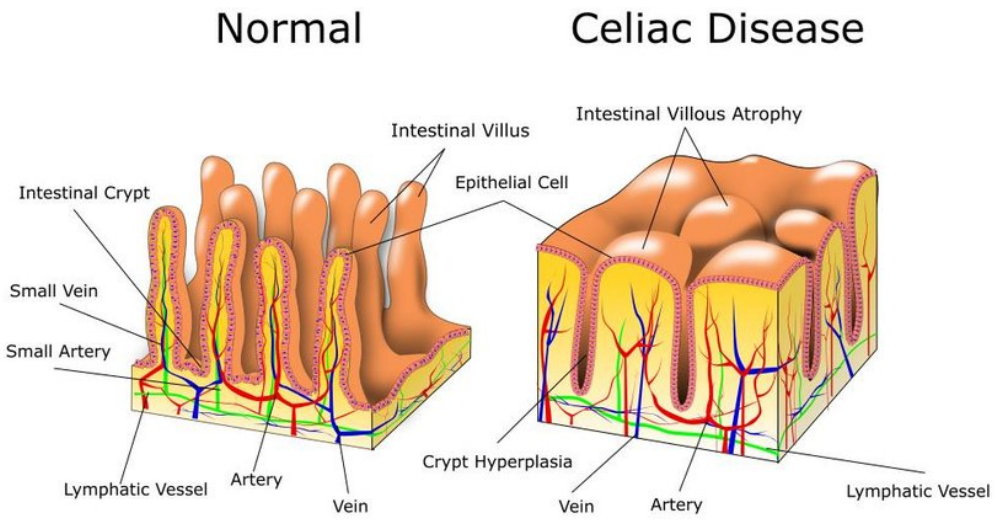
17.2 A healthy small intestine is lined with tiny finger-like projections called "villi". Villi dramatically increase the absorptive surface area of the small intestine and

produce many enzymes necessary for digestion. Between the villi are pit-like "crypts", which are responsible for regenerating damaged villi. In the normal intestine, the villi are approximately 4 times the length of the crypts;





17.3 As the intestine is damaged, the villi become shorter and the crypts become deeper as they hypertrophy to maintain sufficient villous structure. The healthy intestinal lining also contains all types of inflammatory cells at low numbers;



17.4 When damaged, both absorptive failure and secretion excess can occur. Features of clinically significant enteropathy include diarrhea and malabsorption;

17.5 More recently, olmesartan-associated enteropathy has been identified. It is typically classified by severe malabsorptive symptoms commonly leading to nutritional deficiencies and electrolyte abnormalities. Histologic features, including villous atrophy and a subepithelial collagenous layer consistent with collagenous sprue, can be found in the small bowel, gastric, and colonic mucosa. Diagnosis requires these histologic findings, negative celiac serology, lack of response to a gluten-free diet, and improvement after discontinuing OLMETEC. Treatment involves withdrawal of the drug, and in severe cases topical or systemic corticosteroids (Exhibit R-13);

17.6 The Gastrointestinal Disorders associated with OLMETEC can manifest after months or possibly even years, making the association with the drug all the more difficult to detect;

17.7 A person with Olmesartan enteropathy has their quality of life and social function significantly compromised by both chronic Gastrointestinal Disorders and by the burden of constant dietary restriction;

17.8 According to the Bucharest Consensus, the current medical treatment is to discontinue taking OLMETEC and clinical observation:

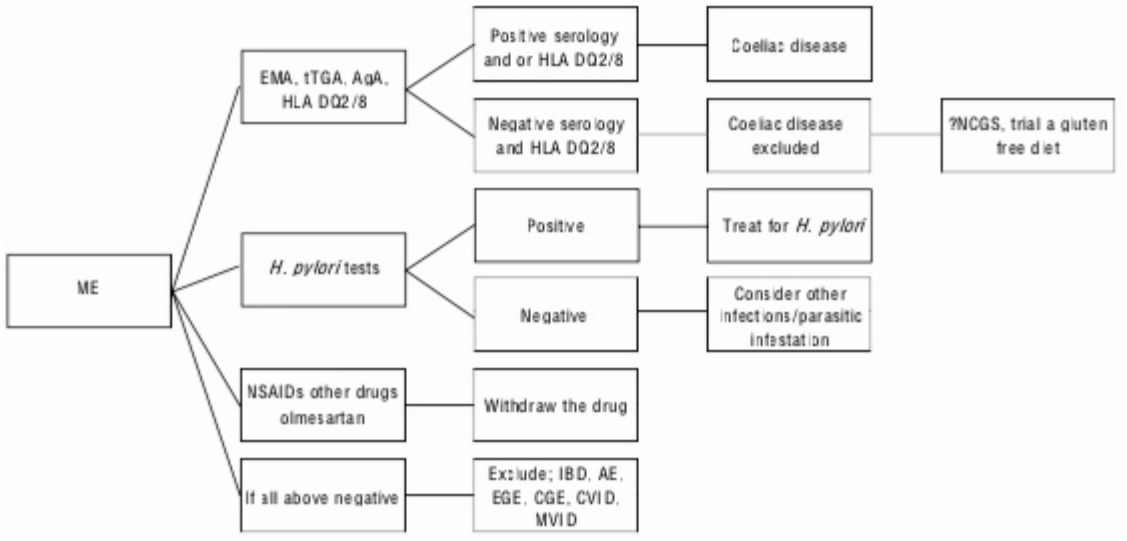


Figure 2 Algorithm for diagnosis the underlying condition behind microscopic enteritis.

The whole as appears more fully from a copy of the World Journal of Gastroenterology article entitled “Microscopic enteritis: Bucharest consensus” dated March 7, 2015, produced herein as **Exhibit R-14**;

III. The Scientific Studies Behind the Drugs

18. Since as early as 2012, there have been numerous studies published in medical journals that demonstrate that the ingestion of OLMETEC causes an increased risk of Gastrointestinal Disorders. In addition, the studies indicate that for patients experiencing the Gastrointestinal Disorders, the cessation of OLMETEC oftentimes alleviates these symptoms, as appears more fully from copies of the studies, produced herein *en liasse* as **Exhibit R-5**;

18.1 These studies include:

1) Alberto Rubio-Tapia, et al., “Severe Spruelike Enteropathy Associated With Olmesartan” (2012) 87:8 Mayo Clin. Proc. 732-738,

2) Stephanie E. Dreifuss, et al., “Spruelike Enteropathy Associated with Olmesartan: An Unusual Case of Severe Diarrhea” (2013) Case Reports in Gastrointestinal Medicine 1-3,

3) Marisa DeGaetani, et al., “Villous Atrophy and Negative Celiac Serology: A Diagnostic and Therapeutic Dilemma” (2013) 108 The American Journal of Gastroenterology 647-653,

4) Gioia Fiorucci, et al., “Severe spruelike enteropathy due to Olmesartan” (2014) 106:2 Rev Esp Enferm Dig 142-144,

5) Jennifer A Nielsen, Anita Steephen, & Matthew Lewin, “Angiotensin-II inhibitor (olmesartan)-induced collagenous sprue with resolution following discontinuation of drug” (2013) World J Gastroenterol 6928-6930,

6) Peter P Stanich, Martha Yearsley, & Marty M. Meyer, “Olmesartan-associated Sprue-like Enteropathy” (2013) 47:10 J Clin Gastroenterol 894-895,

7) Ali Safdar Khan, Shajan Peter, & C. Mel Wilcox, “Olmesartan-induced enteropathy resembling celiac disease” (2014) 46:1 Endoscopy E97-E98,

8) Megan E. Hartranft and Randolph E. Regal, ““Triple Phase” Budesonide Capsules for the Treatment of Olmesartan-Induced Enteropathy” (2014) 48:9 Annals of Pharmacotherapy 1234-1237,

9) Hélène Théophile, et al., “Five cases of sprue-like enteropathy in patients treated by olmesartan” (2014) 46 Digestive and Liver Disease 465-469,

10) Tran H. Tran and Hanlin Li, “Olmesartan and Drug-Induced Enteropathy” (2014) 39:1 Pharmacovigilance Forum 47-50,

11) Mahmoud Abdelghany, et al., “Olmesartan Associated Sprue-Like Enteropathy and Colon Perforation” (2014) Case Reports in Gastrointestinal Medicine 1-3,

12) G. Ianiro, et al., “Systematic review: sprue-like enteropathy associated with Olmesartan” (2014) 40 Aliment Pharmacol Ther 16-23,

13) L. Marthey, et al., “Olmesartan-associated enteropathy: results of a national survey” (2014) 40:9 Alimentary Pharmacology & Therapeutics 1103-1109,

14) Naresh Bhat, et al., “Olmesartan-related sprue-like enteropathy” (2014) 33:6 Indian J Gastroenterol 564-567,

15) Michele L. Sanford and Angela K. Nagel, “A Review of Current Evidence of Olmesartan Medoxomil Mimicking Symptoms of Celiac Disease” (2015) 28:2 Journal of Pharmacy Practice 189-192,

16) N. Heerasing, C. Hair, & S. Wallace, “Olmesartan-induced enteropathy” (2015) Internal Medicine Journal 117-118,

17) Mickael Basson, et al., “Severe intestinal malabsorption associated with olmesartan: a French nationwide observational cohort study” (2015) 65 Gut 1664–1669,

18) Marta Eusébio, et al., “Olmesartan-Induced Enteropathy: An Unusual Cause of Villous Atrophy” (2015) 23:2 GE Port J 91-95,

19) Eun-Young Karen Choi & Barbara J. McKenna, “Olmesartan-Associated Enteropathy: A Review of Clinical and Histologic Findings” (2015) 139 Arch Pathol Lab Med. 1242-1247,

20) Liliana Carneiro, et al., “Olmesartan-Induced Sprue Like Enteropathy” (2016) 23:2 GE Portuguese Journal of Gastroenterology 101-105,

21) Nina Burbure, et al., “Olmesartan-associated sprue-like enteropathy: A systematic review with emphasis on histopathology” (2016) 50 Human Pathology 127-134,

22) Isabel A. Hujoel & Alberto Rubio-Tapia, “Sprue-Like Enteropathy Associated With Olmesartan: A New Kid on the Enteropathy Block” (2016) 23:2 GE Portuguese Journal of Gastroenterology 61-65,

23) Raul Badillo & Massimo Raimondo, “Severe spruelike enteropathy associated with olmesartan observed by double-balloon enteroscopy” (2016) 83:1 Gastrointestinal Endoscopy 269-260,

24) Nassim Hammoudi, et al., “Olmesartan-induced enteropathy associated with cutaneous lesions” (2016) 4:4 Clinical Case Reports 379-382,

18.1 In addition, the following studies also demonstrate that the ingestion of OLMETEC causes an increased risk of the Gastrointestinal Disorders:

25) Eric V. Marietta, et al., “Drug-Induced Enteropathy” (2015) 33 Digestive Diseases 215-220, produced herein as **Exhibit R-15**,

26) Gianluca Ianiro, Antonio Gasbarrini & Giovanni Cammarota, “Olmesartan-associated sprue-like enteropathy: know your enemy” (2016) 51:7 Scand J Gastroenterol. 891, produced herein as **Exhibit R-16**,

27) Famularo G, Minisola G., “Relapsing Olmesartan-Associated Ileitis” (2016) 50:12 Ann Pharmacother 1070, produced herein as **Exhibit R-17**,

28) Michail Galanopoulos, et al., “Small bowel enteropathy associated with olmesartan medoxomil treatment” (2017) 30:1 Ann Gastroenterol 131-133, produced herein as **Exhibit R-18**,

29) Vivian S. Ebrahim, et al., “Olmesartan-associated enteropathy” (2017) 30:3 Proc (Bayl Univ Med Cent) 348-350, produced herein as **Exhibit R-19**,

30) Y.-H. Dong Y, et al., “Use of olmesartan and enteropathy outcomes: a multi-database study” (2018) 47:6 Aliment Pharmocol Ther. 792-800, produced herein as **Exhibit R-20**,

31) Eugenia N. Uche-Anya, et al., “Regional Patterns of Olmesartan Prescription and the Prevalence of Duodenal Villous Atrophy Throughout the United States” (2018) 16 Clinical Gastroenterology and Hepatology 584-585, produced herein as **Exhibit R-21**,

32) C. Melis, et al., “Sprue-like enteropathy, do not forget olmesartan!” (2018) 50:6 Dig Liver Dis. 621-624, produced herein as **Exhibit R-22**,

33) Kazunori Nagashima, Takehiko Katsurada, & Naoya Sakamoto, “A Case of Olmesartan-associated Sprue-like Enteropathy” (2018) 16 Clinical Gastroenterology and Hepatology xlv-xlvi, produced herein as **Exhibit R-23**,

34) MA Shahzad, et al., “Gastrointestinal: Olmesartan-induced enteropathy” (2018) 33:10 J Gastroenterol Hepatol 1691, produced herein as **Exhibit R-24**,

35) Nirmal K Onteddu, et al., “Olmesartan-induced enteropathy” (2018) BMJ Case Rep., produced herein as **Exhibit R-25**,

36) Lavanya Shenbagaraj & Gillian Swift, “Olmesartan-associated severe gastritis and enteropathy” (2018) 11:1 BMJ Case Rep., produced herein as **Exhibit R-26**,

37) Sripriya Gonakoti, Sanjiv Khullar, & Aarthi Rajkumar, “Olmesartan Associated Enteropathy: A Rare Underdiagnosed Cause of Diarrhea and Weight Loss” (2019) 20 Am J Case Rep 111-116, produced herein as **Exhibit R-27**,

38) A. Sadki, M., et al., « Traitement par olmésartan et entéropathie : à propos de deux cas et revue de la littérature » (2019) 40 La Revue de Médecine Interne 112-116, produced herein as **Exhibit R-28**,

39) Andromachi Makri, et al., “Significant Weight Loss In A Patient Taking Olmesartan: An Unusual Case Report” (2019) Curr Drug Saf., produced herein as **Exhibit R-29**,

40) Mónica Teixeira, et al., “Olmesartan-Associated Enteropathy: An Unexpected Cause of Chronic Diarrhoea” (2019) 6:4 Eur J Case Rep Intern Med., produced herein as **Exhibit R-30**;

41) Ayesha Kamal, et al., “Angiotensin II receptor blockers and gastrointestinal adverse events of resembling sprue-like enteropathy: a systematic review” (2019) 7:3 Gastroenterology Report 162-167, produced herein as **Exhibit R-31**;

42) Paulina Henry, et al., « Un cas inhabituel d’entéropathie secondaire à la prise d’olmesartan » (2019) 39: 3 Annales de Pathologie 237-240, produced herein as **Exhibit R-32**;

19. These studies indicate the importance of informing patients and healthcare professionals of these adverse side effects so that they may make informed decisions regarding this medication. In addition, should the patient have made an informed decision to take OLMETEC in spite of the serious risks, knowledge of these risks would have led to the cessation of its ingestion upon experiencing the Gastrointestinal Disorders as they would have been able to identify the reason for their existence;

20. The Respondents, in failing to advise doctors and patients of the increased risks associated with OLMETEC, effectively usurped their ability to make informed decisions regarding its use and removed their ability to limit and/or control the risk;

21. On November 26, 2009, less than a year after the approval and introduction of OLMETEC in Canada, the first Adverse Reaction was reported to Health Canada, whereby a 58-year-old male complained of diarrhea and nausea. After this, there were weekly and/or monthly reported adverse reactions reported until the present, with a total of 193 adverse events being reported to Health Canada, many of which complained about Gastrointestinal Disorders, as appears from a copy of Health Canada’s list of Adverse Reaction Reports through to October 2, 2015 and from October 3, 2015 to July 3, 2018, and from a copy of the actual reports, produced herein *en liasse* as **Exhibit R-6**;

22. On July 3, 2013, the United States Food and Drug Administration (“FDA”) issued a Drug Safety Communication warning that OLMETEC can cause intestinal problems known as sprue-like enteropathy. The FDA mandated changes to the label of these drugs to include this concern. Some of the findings of the FDA include, but are not limited to:

    (a) Symptoms of sprue-like enteropathy include severe, chronic diarrhea with substantial weight loss,

    (b) The enteropathy may develop months to years after starting OLMETEC, and sometimes require hospitalization,

(c) If patients taking OLMETEC develop these symptoms and no other cause is found, the drug should be discontinued, and therapy with another antihypertensive started;

(d) Discontinuation of OLMETEC has resulted in clinical improvement of sprue-like enteropathy symptoms in all patients, and

(e) Sprue-like enteropathy has not been detected with ARB drugs other than OLMETEC;

As appears more fully from a copy of the Drug Safety Communication, produced herein as **Exhibit R-7**;

23. Despite this mounting evidence and the growing number of adverse event reports, the Respondents have, to this day, failed to adequately and accurately inform consumers, healthcare professionals and the general public of the existence of a causal connection between the use of OLMETEC and Class Members injuries, including the Gastrointestinal Disorders;

IV. The Expert Reports

23.1 Five expert reports have been produced in the context of the U.S. litigation all of which confirm the causal connection between OLMETEC and the Gastrointestinal Disorders:

(1) Expert Report of Susan Huftless, PhD dated November 30, 2016, produced herein as **Exhibit R-33**;

(2) Expert Report of David A. Kessler, M.D. dated November 30, 2016, produced herein as **Exhibit R-34**;

(3) Expert Report of Benjamin Lebwohl, M.D. dated November 30, 2016, produced herein as **Exhibit R-35**;

(4) Expert Report of Daniel Leffler, M.D. dated November 24, 2016, produced herein as **Exhibit R-36**;

(5) Expert Report of Stephen M. Lagana, M.D. dated November 30, 2016, produced herein as **Exhibit R-37**;

23.2 Dr. Huftless' Expert Report (Exhibit R-33) examined the causal relationship between OLMETEC and enteropathy and confirmed that since 2006, there was evidence of a causal relationship between OLMETEC and enteropathy, the clinical trials were inadequately designed and conducted and insufficiently powered, best practices in pharmacovigilance required further investigation into the association, and that a search of the literature supports this causal relationship (there were 179 cases of OLMETEC-induced enteropathy by

November 30, 2016 with 80% of the cases having their symptoms gone after stopping to take OLMETEC);

23.3 Dr. Kessler's Expert Report (Exhibit R-34), in examining the allegations pertaining to OLMETEC and the U.S. FDA's regulatory process and standards, confirmed that "despite the fact that there was sound scientific evidence that met the FDA standard by the end of 2006, and certainly by 2007, in Daiichi Sankyo's possession, Daiichi Sankyo failed to act on it and inform doctors and patients";

23.4 Dr. Lebwohl's Expert Report (Exhibit R-35) examined the issue of whether OLMETEC causes the Gastrointestinal Disorders in a subset of users. In so doing, Dr. Lebwohl notes that "the pre-clinical and clinical testing that was performed was not adequately powered or designed to study gastrointestinal adverse effects. No specific test or study was perfomed prior to marketing Benicar to determine whether there was any effect on the gastrointestinal system, and there was no clinical or preclinical study performed to determine whether olmesartan caused any changes to the villi in the intestine, the small intestine". Dr. Lebwohl also confirms that it is "firmly established in the medical literature that a subset of patients utilizing [OLMETEC] develop a gastrointestinal syndrome characterized as sprue-like enteropathy, with related gastrointestinal side effects as a result of using this medication";

23.5 Dr. Leffler's Expert Report (Exhibit R-36) examined whether OLMETEC can cause inflammation and damage to the small intestine resulting in malabsorption, diarrhea, abdominal pain, weight loss, vomiting and related symptoms. Dr. Leffler discusses how the Gastrointestinal Disorders that patients experienced from taking OLMETEC were often misdiagnosed as one or a combination of celiac disease, refractory celiac disease, inflammatory bowel disease, various forms of colitis, autoimmune enteropathy or irritable bowel syndrome. Dr. Leffler opines that OLMETEC causes enteropathy with related gastrointestinal symptoms and malabsorption;

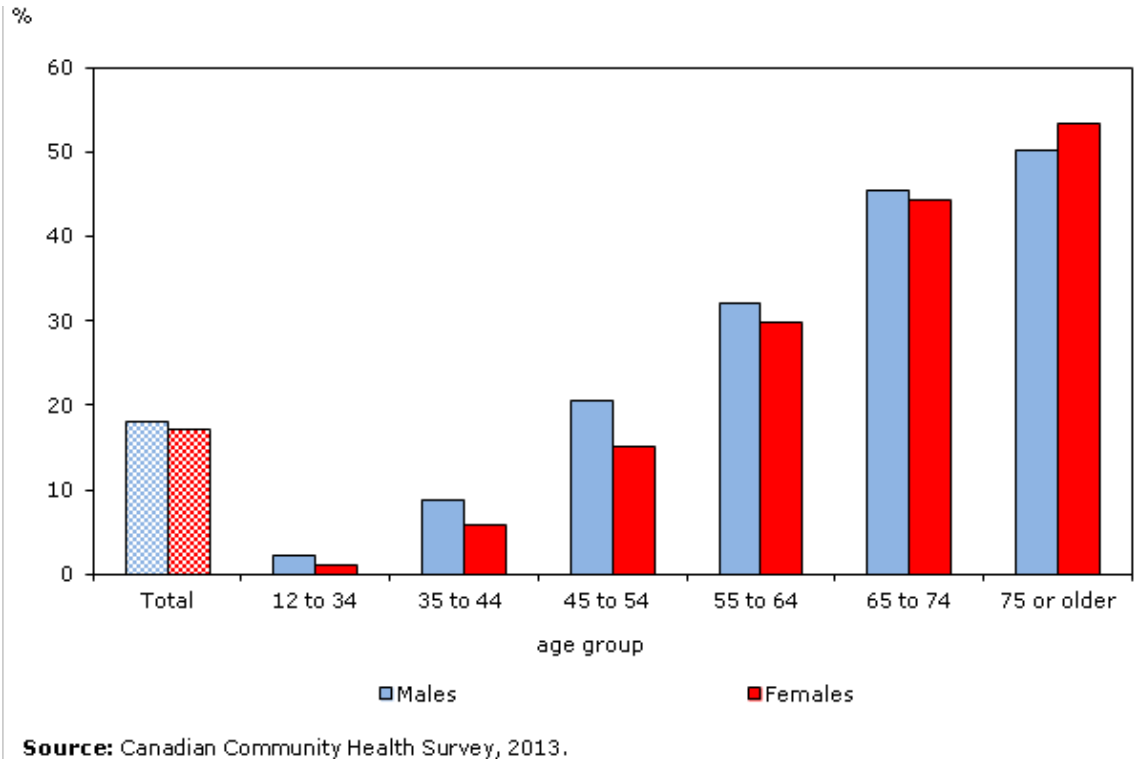
23.6 Dr. Lagana's Expert Report (Exhibit R-37) examined whether OLMETEC causes organic changes to the small intestine, including villous atrophy, and the condition now known as OAE, or Olmesartan enteropathy. In so doing, he concluded the following:

> "It is accepted in the medical community, including in the peer reviewed medical literature, without controversy, that some number of patients develops inflammation, villous atrophy, and other intestinal organic changes, and a spectrum of related gastrointestinal harm and symptoms including for example malabsorption, dehydration, chronic diarrhea, chronic vomiting, severe weight loss, abdominal pain, and nausea, as a result of the use of Olmesartan medoxomil…Based on my review of and familiarity with the peer reviewed medical literature, including

articles that I have co-authored, as well as my experience in a clinical and research setting, applying the scientifically accepted methods set forth above, there can be no reasonable dispute that this causality exists";

V. The Respondents' Practices

24. The Canadian market for hypertension treatment is immense. In 2013, 17.7% (5.3 million) of Canadians aged 12 and older reported being diagnosed with high blood pressure. The incidence of high blood pressure increases with age, with the highest rate of high blood pressure being the 75 and older age group, as appears more fully from a copy of the Statistics Canada publication entitled "High blood pressure, 2013", produced herein as **Exhibit R-8**;



Source: Canadian Community Health Survey, 2013.

25. The Respondents' drug, Olmesartan Medoxomil, was first introduced in the United States in 2002 and Respondent Daiichi (with other non-parties) engaged in an aggressive marketing campaign focussed on convincing physicians that it was the ARB with superior efficacy and more;

26. In 2006, the FDA found these efficacy and safety claims unsubstantiated and false or misleading as there was no evidence that that Olmesartan Medoxomil was superior to or safer than other ARBs. In addition, the FDA found that their marketing materials failed to include risk information necessary to qualify its safety and effectiveness claims. The FDA ordered Respondent Daiichi to

discontinue the use of approximately 50 promotional pieces and to disseminate corrective messages to physicians who received the materials;

27. On November 5, 2013, the FDA again found Respondent Daiichi's promotional material misleading, as appears more fully from a copy of the letter dated November 5, 2013, produced herein as **Exhibit R-9**;

28. On March 10, 2010, a former Daiichi sales representative brought suit against Respondent Daiichi alleging that they were using incentive programs to induce physicians to use its pharmaceuticals, including Olmesartan Medoxomil – the case settled five years later for over $39 million dollars to be paid to the U.S. government, as appears more fully from a copy of the Business Wire article dated January 9, 2015 and from a copy of the settlement agreement, produced herein *en liasse* as **Exhibit R-10**;

29. In spite of the strong indication that OLMETEC was causing Gastrointestinal Disorders, the Respondents failed to inform consumers, health care professionals, and the scientific community and they failed to perform further investigation into its safety;

30. This important information made its first appearance in the Product Monograph on November 5, 2013, years after the drugs had been introduced and years after the Respondents knew or should have known about the associated risks, as appears more fully from a copy of the Product Monograph for OLMETEC last revised on November 5, 2013, from a copy of the Product Monograph for OLMETEC PLUS last revised November 5, 2013, and from copies of eight previous Product Monographs, produced herein as **Exhibit R-11**;

30.2 The OLMETEC Product Monograph dated December 1, 2016 and the OLMETEC PLUS product monograph dated May 22, 2019 are produced herein *en liasse* as **Exhibit R-38**;

31. Even today, this disclosure is insufficient and many doctors are still unaware of the direct causal relationship between the use of OLMETEC and the development of Gastrointestinal Disorders;

32. There are feasible alternatives to OLMETEC in the form of angiotensin II receptor blockers for which there are no reported Gastrointestinal Disorders. OLMETEC suffers from a defective design, which was a substantial factor in causing the Plaintiff's and Class Members' injuries;

VI. The Respondents' Liability

33. Although OLMETEC is marketed, packaged, promoted, advertised, distributed, labelled and/or sold as a safe and effective prescription drug to reduce high

blood pressure, it has the serious side effect of the increased risk for Gastrointestinal Disorders;

33.1 Despite the vast amount of evidence that OLMETEC increases the risk of the Gastrointestinal Disorders, the Respondents have either failed to investigate or conduct any studies on the serious side effects of OLMETEC and/or failed to make public the results of any studies or investigations that they might have conducted;

34. A reasonably prudent drug researcher, designer, developer, formulator, manufacturer, tester, marketer, packager, promotor, advertiser, distributer, labeller and/or seller in the Respondents' position would have adequately warned both doctors and patients of the risks associated with the use of OLMETEC;

35. Despite a clear signal, the Respondents have failed to either alert the public and the scientific and medical community or to perform further investigation into the safety of OLMETEC;

36. The Respondents knew, or by the reasonable and careful employment of known scientific methods should have known, and, in the exercise of reasonable care toward patients who would be expected to ingest OLMETEC, should have known that:

    (a) Studies published in peer-reviewed scientific and medical literature found there may be an association between OLMETEC and Class Members' injuries;

    (b) These studies represent some of the best scientific evidence available for evaluating the association between OLMETEC and Class Members' injuries;

    (c) Physicians commonly prescribe OLMETEC as treatment for hypertension for prolonged periods of 6 months to 1 year or more;

    (d) Clinical trials for the OLMETEC only lasted up to 3 months in duration;

    (e) Olmesartan-Associated Enteropathy symptoms are typically and often experienced chronically over long periods of time; and

    (f) Clinical trials over periods greater than 3 months would have demonstrated the effects of longer-term cumulative exposure to OLMETEC;

37. The Respondents were negligent in the research, design, development, formulation, manufacture, testing, marketing, packaging, promotion, advertising, distribution, labelling and/or sale of OLMETEC in one or more of the following respects:

(a) They knew of should have known that OLMETEC increased the risk of the adverse side effect of Gastrointestinal Disorders while conferring no benefit over available feasible and safer alternatives that did not present the same risks and adverse effects;

(b) They failed to ensure that OLMETEC was not dangerous to consumers;

(c) They failed to conduct proper, adequate, appropriate and thorough pre-market and post-market testing to determine whether and to what extent the ingestion of OLMETEC poses serious health risks, including the Gastrointestinal Disorders;

(d) They failed to adequately test the product to ensure that they were acceptably safe and free from defects prior to placing it on the market;

(e) They failed to properly, adequately, appropriately, correctly, and timely warn the medical and health community, Health Canada, the Petitioner, Class Members, and the public in general of the significant and dangerous risks associated with OLMETEC and the severity thereof, both prior to releasing it into the Canadian marketplace and afterward (…);

(f) They failed to use care in researching, designing, developing and manufacturing their products so as to avoid posing unnecessary health risks to users of such products;

(g) They failed to conduct adequate pre-clinical and clinical testing, post-marketing surveillance and follow-up studies to determine the safety of the drug;

(h) They failed to advise the medical and scientific communities that the consumption of OLMETEC could result in severe and disabling side effects, including but not limited to, the Gastrointestinal Disorders;

(i) They misrepresented that OLMETEC was safe and that they were equivalent in safety as other forms of treatment for hypertension (…);

(j) They failed to provide adequate and timely warnings or sufficient indications about the increased potential health risks associated with the use of OLMETEC;

(k) They consistently under-reported, underestimated, withheld, and downplayed serious dangers of OLMETEC and misrepresented its efficacy and safety to the medical and health community, Health Canada, the Petitioner, Class Members, and the public in general (…);

(l) They failed to provide adequate updated and current information to Class Members and their physicians respecting the risks of OLMETEC as such information became available;

(m) They failed to provide prompt warnings of potential hazards of OLMETEC in the products' monograph and in the products' labelling;

(n) They failed to warn that Class Members and their physicians that the risks associated OLMETEC would exceed the risks of other available angiotensin II receptor blocker medications;

(o) After receiving actual or constructive notice of problems with OLMETEC, they failed to issue adequate warnings, to publicize the problem and otherwise act properly and in a timely manner to alert the public, the Class Members and their physicians of the drugs' inherent dangers;

(p) They failed to establish any adequate procedures to educate their sales representatives and prescribing physicians respecting the risks associated with the drug;

(q) They falsely stated and/or implied that OLMETEC was safe when they knew or ought to have known that this representation was false;

(r) They disregarded reports of Gastrointestinal Disorders among patients;

(s) They failed to accurately and promptly disclose to Health Canada information relating to Gastrointestinal Disorders associated with OLMETEC and to adequately modify the OLMETEC product monographs and product labelling accordingly and in a timely manner;

(t) They failed to monitor and to initiate a timely review, evaluation and investigation of reports of Gastrointestinal Disorders associated with OLMETEC in Canada (and around the world);

(u) They failed to properly investigate cases of Gastrointestinal Disorders caused by OLMETEC;

(v) <u>They failed to timely recall OLMETEC, publicize the problems and otherwise act properly and in a timely manner to alert the public of the inherent dangers associated therewith, including, the Gastrointestinal Disorders</u>;

(w) They deprived patients of a chance for safe, effective and/or successful alternative treatments; and

(x) In all circumstances of this case, they applied callous and reckless disregard for the health and safety of their consumers;

II. FACTS GIVING RISE TO AN INDIVIDUAL ACTION BY THE PETITIONER

38. On November 10, 2011 (…), Petitioner Martel was prescribed OLMETEC PLUS by his family physician in the 40 mg/ 25 mg dosage, which was intended to lower his high blood pressure;

39. Petitioner Martel filled his prescription at the Pharmaprix located at 1337 Boulevard Iberville, in Repentigny, Quebec and he took it as directed, namely, once daily in the mornings;

40. Within a few months' time, Petitioner Martel began to suffer from cramps in his lower abdomen about once a week and he would need to rush to the toilet shortly thereafter to relieve himself;

41. These symptoms increased in frequency being twice a week and then every few days;

42. During this time (whether or not he was experiencing cramping), his stools were exceedingly soft and often completely liquid (i.e. diarrhea);

43. In addition, he was unable to travel far distances in comfort as he could not predict when the abdominal cramping would begin and when he would need access to a toilet, which interfered with his profession as a travelling union representative;

44. Petitioner Martel (…) experienced chronic diarrhea, dehydration, weight loss, and abdominal and gastrointestinal pain for approximately 6 years;

45. At the advice of his family physician, Petitioner Martel went to see another doctor at the Centre Hospitalier Pierre-Le Gardeur in Terrebonne, Quebec on May 11, 2016 and on September 11, 2015, an abdominopelvic computed tomography[3] was performed. On February 4, 2016, (…) a colonoscopy was performed. It was (…) opined that there was nothing wrong with his digestive system;

46. Thereafter, Petitioner Martel conducted research online and discovered that OLMETEC can cause the symptoms that he was experiencing;

47. Petitioner Martel stopped taking OLMETEC PLUS around January 2016 and the Gastrointestinal Disorder symptoms disappeared within a few months;

[3] Computed tomography (CT) of the abdomen and pelvis is a diagnostic imaging test used to help detect diseases of the small bowel, colon and other internal organs and is often used to determine the cause of unexplained pain.

48. At no time was Petitioner Martel made aware of the risks of suffering from Gastrointestinal Disorders associated with taking OLMETEC PLUS;

49. Had the Respondents properly disclosed the risks associated with OLMETEC, Petitioner Martel would have avoided the risk of suffering Gastrointestinal Disorders by not using OLMETEC PLUS at all. Further, had Petitioner Martel been made aware of the risks of Gastrointestinal Disorders, he would not have had to suffer injury for 6 long years without any explanation of the cause, and instead would have simply discontinued his use of OLMETEC PLUS at the first sign of a Gastrointestinal Disorder;

50. Petitioner Martel is aware that several lawsuits were filed in the United States due to the defects associated with OLMETEC and due to the Respondents' conduct related thereto, as appears more fully from a copy of the In Re Benicar (Olmesartan) Products Liability Litigation Complaint Civil No. 15-2606, produced herein as **Exhibit R-12**;

51. As a result of the Respondents' conduct, Petitioner Martel suffered damages including, but not limited to physical and mental injuries, including pain, suffering, anxiety, fear, loss of quality and enjoyment of life, inflammation, chronic diarrhea, dehydration, weight loss, and abdominal and gastrointestinal pain, and the apportioned cost of the OLMETEC PLUS;

52. Petitioner's damages are a direct and proximate result of his use of the drug OLMETEC PLUS, Respondents' negligence and/or lack of adequate warnings, wrongful conduct, and the unreasonably dangerous and defective characteristics of the drug OLMETEC;

53. In consequence of the foregoing, Petitioner is justified in claiming damages;

III. FACTS GIVING RISE TO AN INDIVIDUAL ACTION BY EACH OF THE MEMBERS OF THE GROUP

54. Every member of the Class was prescribed and ingested the drug, OLMETEC or is the successor, family member, assign, and/or dependant of a person who was prescribed and/or ingested OLMETEC;

55. The Class Members' damages would not have occurred, but for the acts, omissions and/or negligence of the Respondents in failing to ensure that OLMETEC was safe to use, for failing to provide adequate warning of the unreasonable risks associated with using the drug, for false or misleading representations and for omitting to disclose important information to Class Members and to their physicians;

56. In consequence of the foregoing, each member of the Class is justified in claiming at least one or more of the following as damages:

a. Physical and mental injuries, including pain, suffering, anxiety, fear, loss of quality and enjoyment of life and increase risk of health problems;

b. Out-of-pocket expenses incurred or to be incurred, including those connected with hospital stays, medical treatment, life care, medications, medical monitoring services, and the diagnosis and treatment of OLMETEC side effect services;

c. Loss of income and loss of future income;

and

d. Punitive damages;

57. As a direct result of the Respondents' conduct, the users' family members and dependants have, had, and/or will suffer damages and loss including:

a. Out-of-pocket expenses, including paying or providing nursing, housekeeping and other services;

b. Loss of income and loss of future income; and

c. Loss of support, guidance, care, consortium, and companionship that they might reasonably have expected to receive if the injuries had not occurred;

58. All of these damages to the Class Members are a direct and proximate result of the use of OLMETEC and Respondents' conduct, negligence and reckless failure to adequately disclose necessary information and the risks associated with the drug;

IV. CONDITIONS REQUIRED TO INSTITUTE A CLASS ACTION

A) The composition of the class makes it difficult or impracticable to apply the rules for mandates to sue on behalf of others or for consolidation of proceedings

59. Petitioner is unaware of the specific number of persons who were prescribed and ingested OLMETEC, which information is confidential; however, it is safe to estimate that it is in the thousands. The Respondents, on the other hand, can establish this through their own business records;

60. Class Members are numerous and are scattered across the province and country;

61. In addition, given the costs and risks inherent in an action before the courts, many people will hesitate to institute an individual action against the Respondents. Even if the Class Members themselves could afford such individual litigation, it would place an unjustifiable burden on the courts. Furthermore, individual litigation of the factual and legal issues raised by the conduct of the Respondents would increase delay and expense to all parties and to the court system;

62. A multitude of actions instituted in different jurisdictions, both territorial (different provinces) and judicial districts (same province), risks having contradictory judgments on questions of fact and law that are similar or related to all members of the Class;

63. These facts demonstrate that it would be impractical, if not impossible, to contact each and every member of the Class to obtain mandates and to join them in one action;

63.1 In these circumstances, a class action is the only appropriate procedure for all of the members of the Class to effectively pursue their respective rights and have access to justice;

B) The claims of the members of the Class raise identical, similar or related issues of law or fact

64. Individual issues, if any, pale by comparison to the numerous common issues that will advance the litigation significantly;

65. The damages sustained by the Class Members flow, in each instance, from a common nucleus of operative facts, namely, Respondents' misconduct;

66. The claims of the Class Members raise identical, similar or related issues of fact or law as outlined hereinbelow;

67. The interests of justice favour that this application be granted in accordance with its conclusions;

V. NATURE OF THE ACTION AND CONCLUSIONS SOUGHT

68. The action that the Petitioner wishes to institute on behalf of the members of the class is an action in damages, injunctive relief, and declaratory judgment;

69. The conclusions that the Petitioner wishes to introduce by way of an application to institute proceedings appear hereinbelow.

A) The Petitioner requests that he be attributed the status of representative of the Class

70. Petitioner is a member of the Class;

71. Petitioner is ready and available to manage and direct the present action in the interest of the members of the Class that he wishes to represent and is determined to lead the present file to a final resolution of the matter, the whole for the benefit of the Class, as well as, to dedicate the time necessary for the present action before the Courts and the *Fonds d'aide aux actions collectives*, as the case may be, and to collaborate with his attorneys;

72. Petitioner has the capacity and interest to fairly, properly, and adequately protect and represent the interest of the members of the Class;

73. Petitioner has given the mandate to his attorneys to obtain all relevant information with respect to the present action and intends to keep informed of all developments;

74. Petitioner, with the assistance of his attorneys, is ready and available to dedicate the time necessary for this action and to collaborate with other members of the Class and to keep them informed;

75. Petitioner has given instructions to his attorneys to put information about this class action on its website and to collect the coordinates of those Class members that wish to be kept informed and participate in any resolution of the present matter, the whole as will be shown at the hearing, the whole as appears more fully from a copy of a redacted chart of potential Class Members who have inputted their information through the CLG website, produced herein as **Exhibit R-39**;

76. Petitioner is in good faith and has instituted this action for the sole goal of having his rights, as well as the rights of other Class members, recognized and protected so that they may be compensated for the damages that they have suffered as a consequence of the Respondents' conduct;

77. Petitioner understands the nature of the action;

78. Petitioner's interests are not antagonistic to those of other members of the Class;

79. Petitioner is prepared to be examined out-of-court on his allegations (as may be authorized by the Court) and to be present for Court hearings, as may be required and necessary;

80. Petitioner has spent time researching this issue on the internet and meeting with his attorneys to prepare this file. In so doing, he is convinced that the problem is widespread;

B) Petitioner suggests that this class action be exercised before the Superior Court of Justice in the district of Montreal

81. A great number of the members of the Class reside in the judicial district of Montreal and in the appeal district of Montreal;

82. The Petitioner's attorneys practice their profession in the judicial district of Montreal;

83. The Canadian Respondents' head offices are located in the judicial district of Montreal;

84. The present application is well founded in fact and in law.

FOR THESE REASONS, MAY IT PLEASE THE COURT:

GRANT the present application;

AUTHORIZE the bringing of a class action in the form of an application to institute proceedings in damages, injunctive relief, and declaratory relief;

APPOINT the Petitioner as representative of the persons included in the class herein described as:

- all persons residing in Canada who were prescribed and have ingested the drug(s) OLMETEC® (Olmesartan Medoxomil) and/or OLMETEC PLUS® (Olmesartan Medoxomil and Hydrochlorothiazide) and their successors, assigns, family members, and dependants, or any other group to be determined by the Court;

Alternately (or as a subclass)

- all persons residing in Quebec who were prescribed and have ingested the drug(s) OLMETEC® (Olmesartan Medoxomil) and/or OLMETEC PLUS® (Olmesartan Medoxomil and Hydrochlorothiazide) and their successors, assigns, family members, and dependants, or any other group to be determined by the Court;

IDENTIFY the principle issues of fact and law to be treated collectively as the following:

a) Does OLMETEC cause, exacerbate or contribute to an increased risk of dangerous side effects including:

- Serious gastrointestinal injuries
- Olmesartan-Associated Enteropathy (OAE)
- Sprue-like enteropathy
- Villous atrophy/blunting/damage
- Inflammation
- Nausea
- Vomiting
- Chronic diarrhea
- Malnutrition
- Dehydration
- Atrophy
- Kidney failure
- Weight loss
- Abdominal and gastrointestinal pain
- Colitis
- Gastritis
- Permanent injuries resulting from the above
- Death

(the "Gastrointestinal Disorders")?

b) Did the Respondents fail to adequately and properly test OLMETEC both before and/or after placing it on the market to ensure that it is safe?

c) Did the Respondents know or should have known about the risks associated with the use of OLMETEC?

d) Did the Respondents adequately and sufficiently advise/ warn Health Canada, Class members and/or their physicians about the health risks, including the Gastrointestinal Disorders, associated with the use of OLMETEC?

e) (…) Did the Defendants fail to notify Class Members of the full scope of risks known to be associated with and caused by OLMETEC, including the Gastrointestinal Disorders?

f) In the affirmative to any of the above questions, did Respondents conduct engage their solidary liability toward the members of the Class?

g) Are the Defendants liable to pay compensatory (…) damages to Class Members?

h) Are the Defendants liable to pay (…) aggravated or punitive damages and, if so, in what amount?

IDENTIFY the conclusions sought by the class action to be instituted as being the following:

GRANT the class action of the Plaintiff and each of the members of the class;

DECLARE that the Defendants failed to provide adequate warnings with regard to the dangerous side effects of OLMETEC;

RESERVE the right of each of the members of the class to claim future damages related to the use of OLMETEC;

DECLARE the Defendants solidarily liable for the damages suffered by the Petitioner and each of the members of the class;

CONDEMN the Defendants to pay to each member of the class a sum to be determined in compensation of the damages suffered, and ORDER collective recovery of these sums;

CONDEMN the Defendants to pay to each of the members of the class, punitive damages, and ORDER collective recovery of these sums;

CONDEMN the Defendants to pay interest and additional indemnity on the above sums according to law from the date of service of the motion to authorize a class action;

ORDER the Defendants to deposit in the office of this Court the totality of the sums which forms part of the collective recovery, with interest and costs;

ORDER that the claims of individual Class Members be the object of collective liquidation if the proof permits and alternately, by individual liquidation;

CONDEMN the Defendants to bear the costs of the present action including expert and notice fees;

RENDER any other order that this Honourable Court shall determine and that is in the interest of the members of the Class;

DECLARE that all members of the Class that have not requested their exclusion, be bound by any judgment to be rendered on the class action to be instituted in the manner provided for by the law;

FIX the delay of exclusion at thirty (30) days from the date of the publication of the notice to the members, date upon which the members of the Class that have not exercised their means of exclusion will be bound by any judgment to be rendered herein;

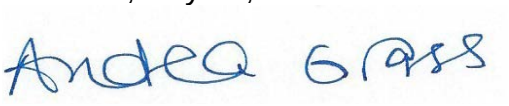
ORDER the publication of a notice to the members of the group in accordance with article 579 C.C.P. within sixty (60) days from the judgment to be rendered herein in The Globe and Mail, National Post, La Presse, the Gazette, the Toronto Star, and the Vancouver Sun;

ORDER that said notice be available on the Respondents' websites, Facebook page(s), and twitter accounts with a link stating "Notice to OLMETEC and OLMETEC PLUS users";

RENDER any other order that this Honourable Court shall determine is in the interest of the members of the Class;

THE WHOLE with costs, including all publication fees.

Montreal, July 23, 2019



_____

CONSUMER LAW GROUP INC.
Per: Me Andrea Grass
Attorneys for the Petitioner