INTRODUCING

Pr myinfla™ ER

colchicine 0.5 mg
extended-release tablets

The first
0.5 mg colchicine
available in
Canada*

In adult patients with existing coronary artery disease

Add PrMYINFLA™ to standard therapies for reduction of atherothrombotic events

MYINFLA (colchicine extended-release tablets) is indicated for the reduction of atherothrombotic events in adult patients with existing coronary artery disease, in addition to standard therapies, including LDL-C-lowering and antithrombotic drug treatment.

LDL-C: low-density lipoprotein cholesterol
*Comparative clinical significance has not been established.

Coronary artery disease (CAD) in Canada

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The burden at a glance

According to data from 2012-2013:[1]

~ 2.4 million Canadian adults (8.1%) were living with CAD.
This number increased from 1.5 million in 2000-2001.

Between 2000-2001 and 2012-2013, the number of newly diagnosed people with CAD declined from 221,800 to 158,000.

See the Canadian Cardiovascular Society Guidelines for information on the diagnosis and management of CAD[2]

Efficacy data in the COLCOT trial

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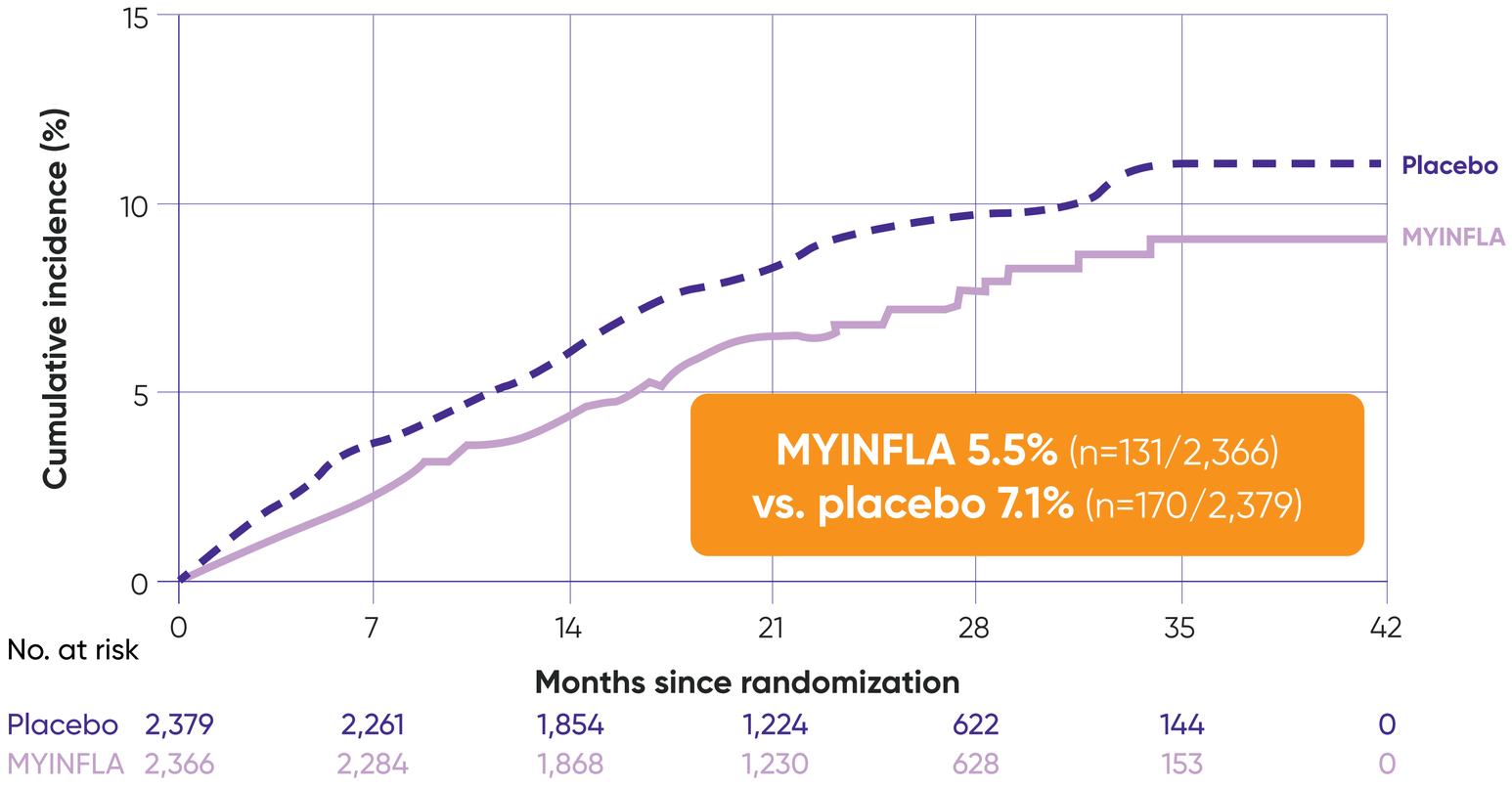
During the overall study period, MYINFLA reduced the risk of major cardiovascular events by 23% vs. placebo* (HR: 0.77 [95% CI: 0.61, 0.96]; *p*=0.02)

Primary endpoint
Time to the first event of cardiovascular mortality, resuscitated cardiac arrest, acute MI, stroke, or urgent hospitalization for angina requiring coronary revascularization (ITT population)



No. at risk

Placebo	2,379	2,261	1,854	1,224	622	144	0
MYINFLA	2,366	2,284	1,868	1,230	628	153	0

Adapted from Tardif et al.[3]

A subgroup analysis by gender, age, smoking status, history of diabetes, history of hypertension, prior MI, prior PCI or CABG, prior stroke or TIA, and baseline WBC count showed no significant interaction effects.

Primary endpoint occurred in:

- Patients > 65 years: 7.4% of MYINFLA patients vs. 9.4% of placebo patients (HR: 0.79 [95% CI: 0.55, 1.12]; *p*=0.20)
- Patients > 75 years: 11.2% of MYINFLA patients vs. 14.7% of placebo patients (HR: 0.76 [95% CI: 0.43, 1.34]; *p*=0.35)

COLCOT: Colchicine Cardiovascular Outcomes Trial; HR: hazard ratio; CI: confidence interval; MI: myocardial infarction; ITT: intent-to-treat; PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft surgery; TIA: transient ischemic attack; WBC: white blood cell; UHARCR: urgent hospitalization for angina requiring coronary revascularization
*COLCOT was a randomized, double-blind, multicentre, event-driven trial comparing MYINFLA (n=2,366) to placebo (n=2,379) in the secondary prevention of major cardiovascular events. Patients were eligible if they had experienced an MI within 30 days before enrolment, had completed any planned percutaneous revascularization procedures, and were treated according to national guidelines (intensive use of statins). The primary endpoint was the time from randomization to the first event of cardiovascular mortality, resuscitated cardiac arrest, acute MI, stroke, or UHARCR.

Efficacy data in the COLCOT trial

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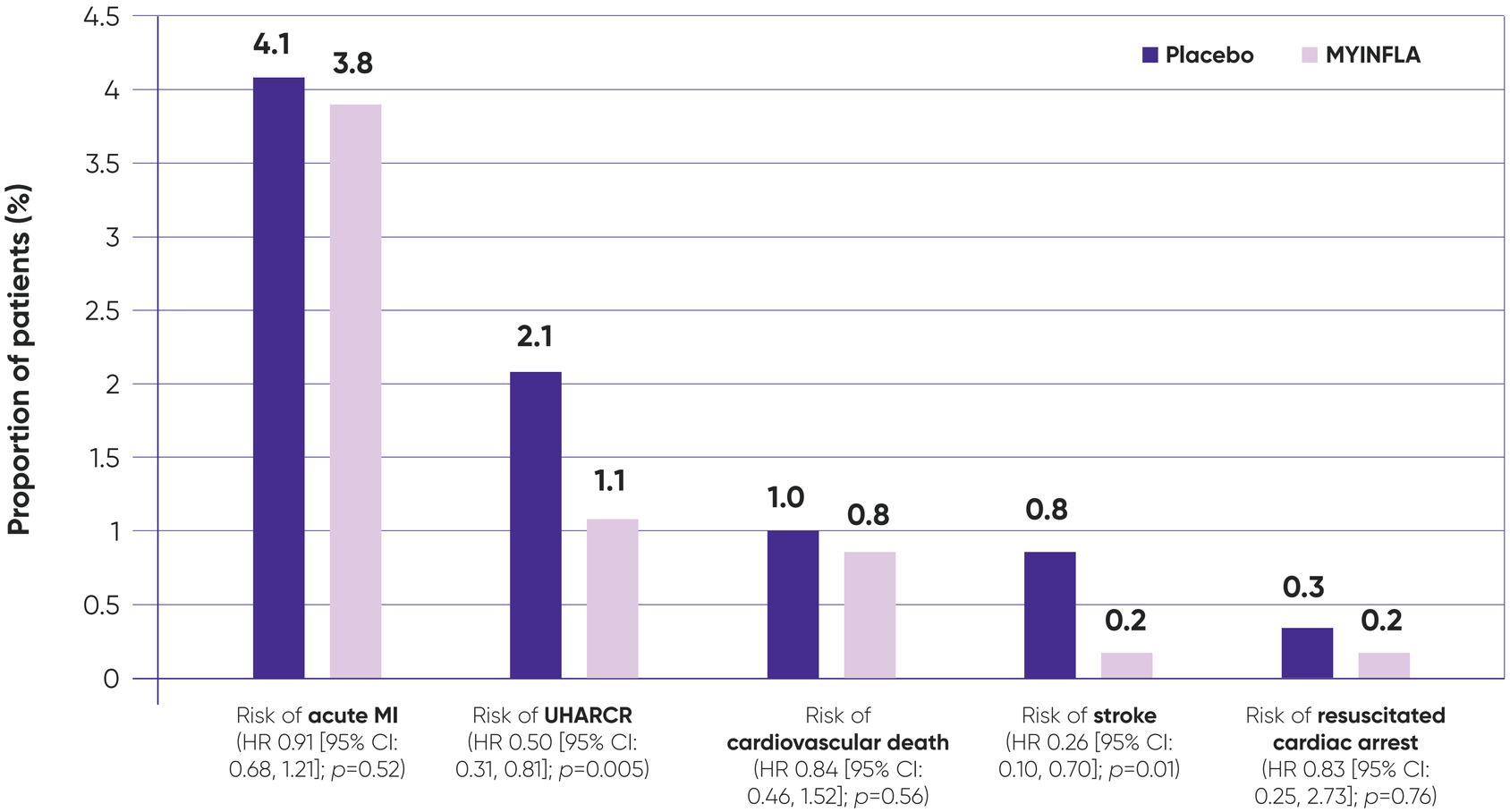
Component scores risk with MYINFLA vs. placebo*



Adapted from Product Monograph.[4]

34% significant reduction in the rate of total (first and recurrent) primary endpoint events with MYINFLA (n=154/2,366) vs. placebo (n=223/2,379) (0.66 [95% CI: 0.51, 0.86]; *p*=0.002) in the ITT study population.

*COLCOT was a randomized, double-blind, multicentre event-driven trial comparing MYINFLA (n=2,366) to placebo (n=2,379) in the secondary prevention of major cardiovascular events. Patients were eligible if they had experienced an MI within 30 days before enrolment, had completed any planned percutaneous revascularization procedures, and were treated according to national guidelines (intensive use of statins). The primary endpoint was the time from randomization to the first event of cardiovascular mortality, resuscitated cardiac arrest, acute MI, stroke, or UHARCR.

MYINFLA was generally well tolerated

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Related treatment-emergent adverse events (TEAEs) occurring in ≥ 1% of patients in the COLCOT trial (safety population)[4]

System organ class preferred term	MYINFLA N=2,330 n (%)	Placebo N=2,346 n (%)
Gastrointestinal disorders	267 (11.5)	255 (10.9)
Abdominal pain	17 (0.7)	24 (1.0)
Diarrhea	186 (8.0)	172 (7.3)
Nausea	28 (1.2)	15 (0.6)
Laboratory investigations*	66 (2.8)	72 (3.1)
Skin and subcutaneous tissue disorders†	34 (1.5)	26 (1.1)

16.0% of MYINFLA-treated patients reported related TEAEs vs. 15.8% of placebo-treated patients.

*No noteworthy imbalance of specific laboratory values observed across treatment groups.
†Includes alopecia 0.3%, allergic dermatitis 0.1%, erythema 0.1%, and pruritic rash 0.1% in colchicine-treated patients.

An anti-inflammatory agent

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Mechanism of action*

- Colchicine prevents the activation, degranulation, and migration of neutrophils due to the disruption of cytoskeletal functions through inhibition of β-tubulin polymerization into microtubules.
- Evidence suggests that colchicine may interfere with intracellular assembly of the inflammasome complex present in neutrophils and monocytes that mediate the activation of interleukin-1β.
- The mechanism of action is not completely understood.

Pharmacodynamics of MYINFLA

Pharmacodynamics of colchicine in prevention of atherothrombotic cardiovascular events is not completely understood.

Colchicine may **stabilize atherosclerotic plaques** and in animal models *in vivo* has been shown to exert the following:

- **Cardioprotective effects**
- **Anti-inflammatory effects**
- **Anti-atherosclerotic effects**

Favourable plaque-modifying effects of daily 0.5 mg colchicine therapy have been observed in patients with post-acute coronary syndrome.

- Independent of substantial low-density lipoprotein reduction or high-dose statin intensification

*Clinical significance has not been established.

Important Safety Information

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Clinical use:

- Not recommended for use in children
- Careful consideration in patients ≥ 65 years

Contraindications:

- Co-administration of strong P-glycoprotein (P-gp) inhibitors or strong CYP3A4 inhibitors
- Severe renal impairment (eGFR < 30 mL/min)
- Severe hepatic impairment
- Patients with existing blood dyscrasias

Relevant warnings and precautions:

- Toxicity including fatalities with co-administration of strong P-gp inhibitors and/or strong CYP3A4 inhibitors
- Caution in moderate renal and hepatic impairment
- Gastrointestinal disorders, e.g. diarrhea, nausea, vomiting, and abdominal pain or cramping
- Caution in patients with significant underlying gastrointestinal diseases
- Reports of myelosuppression, leucopenia, granulocytopenia, thrombocytopenia, pancytopenia, and aplastic anemia
- Reports of neuromuscular toxicity, and rhabdomyolysis with the concomitant use of atorvastatin, rosuvastatin, simvastatin, pravastatin, fluvastatin, lovastatin, gemfibrozil, fenofibrate, fenofibric acid, bezafibrate, or cyclosporine
- Not recommended in pregnant women
- Potential fertility risk
- Teratogenic risk
- Not recommended in breastfeeding women
- Monitoring: periodic blood tests are recommended

For more information:

Please consult the Product Monograph at https://pdf.hres.ca/dpd_pm/00062583.PDF for important information relating to adverse reactions, drug interactions, and dosing instructions that has not been discussed in this piece. The Product Monograph is also available by calling us at 1-888-550-6060.

eGFR: estimated glomerular filtration rate

NEW

In adult patients with existing CAD

Add MYINFLA to standard therapies for reduction of atherothrombotic events

Demonstrated 23% instantaneous risk reduction in major cardiovascular events in secondary prevention vs. placebo (primary composite endpoint) (HR: 0.77 [95% CI: 0.61, 0.96]; *p*=0.02) 5.5% vs. 7.1%

Generally well tolerated

- Safety of MYINFLA was evaluated in over 2,000 patients
  16.0% of MYINFLA-treated patients reported related TEAEs vs. 15.8% of placebo-treated patients

Convenient once-daily dosing

- 0.5 mg oral dosing, with or without food
- Avoid taking grapefruit or grapefruit juice with MYINFLA

MYINFLA: A convenient, low-dose add-on to standard therapies, including LDL-C-lowering and antithrombotic drug treatment

Made in Canada

1. Government of Canada. Report from the Canadian Chronic Disease Surveillance System: heart disease in Canada, 2018. Available from: https://www.canada.ca/en/public-health/services/publications/diseases-conditions/report-heart-disease-Canada-2018.html.
2. Mancini GB, Gosselin G, Chow B, et al. Canadian Cardiovascular Society guidelines for the diagnosis and management of stable ischemic heart disease. *Can J Cardiol*. 2014;30(8):837849.
3. Tardif JC, Kouz S, Waters DD, et al. Efficacy and safety of low-dose colchicine after myocardial infarction. *New Engl J Med*. 2019;381(26):24972505.
4. MYINFLA™ Product Monograph. Pendopharm, Division of Pharmascience Inc. August 20, 2021.

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