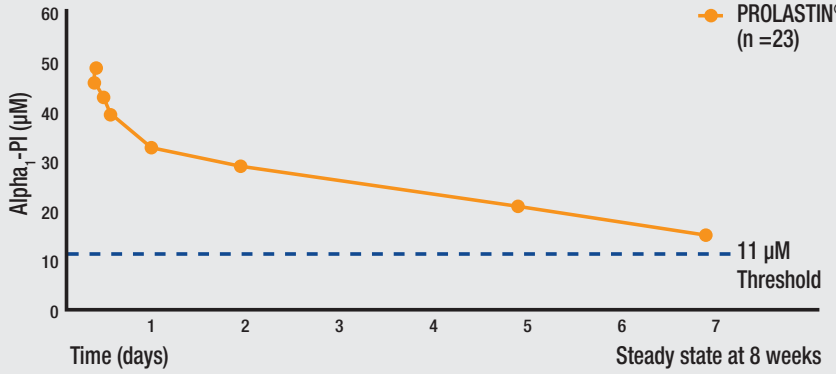
PROLASTIN® C
alpha$_1$-proteinase inhibitor (human)

The intended goal of augmentation therapy is to significantly raise AAT levels[1,2]

In clinical trials, PROLASTIN® -C was effective at raising AAT levels above the protective threshold[*, †, 1, 2]

Mean plasma AAT concentration vs time following treatment for PROLASTIN-C[3]



PROLASTIN-C significantly improved survival rates versus no augmentation therapy[2]

- Patients who received PROLASTIN-C had a 36% lower risk of death (P=0.02)[†, ‡, 4]

PROLASTIN-C is also associated with significantly slower lung function decline[2]

- Patients (FEV$_1$ 35-49%) receiving PROLASTIN-C had a 29% slower decline rate than those not on therapy (P=0.03)[†, ‡ ,4]

PROLASTIN-C has shown a trend toward preservation of lung density

- Patients treated with PROLASTIN-C had a trend of slower decline of Total Lung Capacity (TLC-adjusted PD15 {g/L}) compared to placebo (P=0.068)[†, §, 6]

* Levels > 11µm are estimated to be protective[3]

† These studies were undertaken with PROLASTIN, the previous brand name of PROLASTIN-C, which used a different manufacturing method, and was formulated to a concentration of 20 mg/mL (vs. 40 mg/mL for PROLASTIN-C). The two formulations of this product have been shown to be bioequivalent.[2,3]

‡ Based on open-label assessment of patient registry. Multivariate analysis of FEV$_1$ decline (mL/yr) by FEV$_1$ predicted and augmentation therapy status (n=1,048).

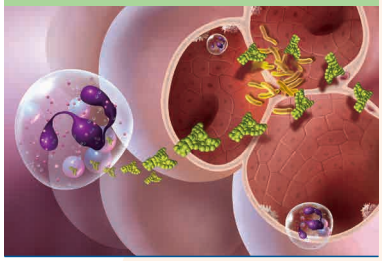
§ Randomized, double-blind placebo-controlled study of patients receiving weekly infusions of 60 mg/kg PROLASTIN® for up to 30 months. Primary endpoint was computed tomography (CT) lung density (n=77).

Alpha$_1$-antitrypsin (AAT) plays a critical role in protecting the lungs[5]

Lung damage is a result of both excess neutrophil elastase and insufficient AAT

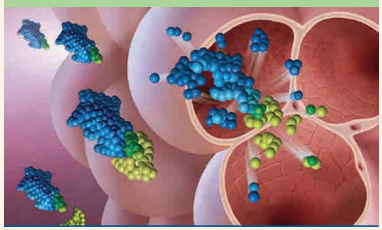
THE ROLE OF NEUTROPHILS

Neutrophils mobilize, delivering elastase at the alveolar surface in response to bacterial infections, environmental pollutants, or tobacco exposure



NORMAL

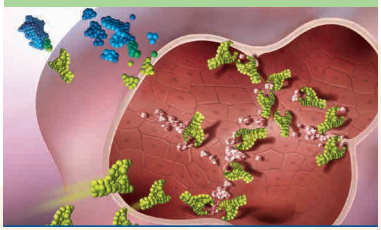
Normal AAT levels keep neutrophil elastase in check



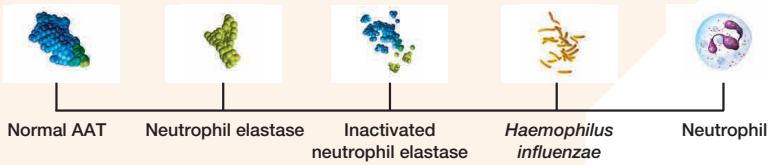
AAT inhibits excess neutrophil elastase by binding to it irreversibly, thereby preventing lung damage and preserving lung structure

DEFICIENT

Low levels of AAT leave lung tissue unprotected



Excess elastase cannot be neutralized; lung elastin is destroyed, and lung function compromised



Indications and Clinical Use:

PROLASTIN®-C is indicated for chronic replacement therapy of individuals having congenital deficiency of alpha1-PI (alpha1-antitrypsin deficiency), related to deficiency causing alleles, and with clinically demonstrable emphysema. Subjects with the PiMZ or PiMS phenotypes should not be considered for treatment. Only adult subjects have received Alpha1-Proteinase Inhibitor (Human) to date.

Contraindications:

- Hypersensitivity to Alpha1-Proteinase Inhibitor (Human) or to any ingredient in the formulation or component of the container
- Selective immunoglobulin A (IgA) deficiencies

Relevant Warnings and Precautions:

- Risk of transmitting infectious agents
- Product administration and handling of needles
- Circulatory Overload
- Sexual Function/Reproduction
- Cacinogenesis and Mutagenesis
- Special Populations: Pregnant women, nursing mothers, pediatrics

For More Information:

Please consult the Product Monograph at www.pm.prolastin-c.ca. The Product Monograph is also available through our medical department, which can be reached at 1-866-482-5226.

REFERENCES:

1. Wewers MD, Casolaro MA, Sellers SE, et al. Replacement therapy for alpha1-antitrypsin deficiency associated with emphysema. *N Engl J Med.* 1987;316:1055-1062. **2.** PROLASTIN® C Product Monograph, June 30,2017. Grifols Canada Ltd. **3.** Stocks JM, Brantly ML, Wang-Smith L, et al. Pharmacokinetic comparability of PROLASTIN® C to PROLASTIN® in alpha1-antitrypsin deficiency: a randomized study. *BMC Clin Pharmacol.* 2010;10:1-11. **4.** The Alpha1-Antitrypsin Deficiency Registry Study Group. Survival and FEV1 decline in individuals with severe deficiency of alpha1-antitrypsin. *Am J Respir Crit Care Med.* 1998;158:49-59. **5.** Köhnlein T, Welte T. *Alpha1-Antitrypsin Deficiency-Clinical Aspects and Management*. Introduction. Bremen, Germany; Uni-Med Verlga AG; 2007:19-39. **6.** Dirksen A, Piitulainen E, Parr DG, et al. Exploring the role of CT densitometry: a randomised study of augmentation therapy in α1-antitrypsin deficiency. *Eur Respir* J 2009;33(6):1345-53.

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