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

It is estimated that 15,000 Canadians have severe Alpha1-Antitrypsin Deficiency*,[1-4]

A Step-By-Step Guide to the Testing and Treatment of Alpha1-antitrypsin (AAT) Deficiency

* PiSZ and PiZZ, less than 11µM, not all patients will have emphysema.[4]

GRIFOLS

Step 1: Identifying Potential Patients

The Canadian Thoracic Society (CTS) recommends targeted AAT testing for certain individuals

Testing for AAT Deficiency should be considered in[5]:

- Patients diagnosed with COPD before age 65 or with a smoking history of less than 20 pack years
- Individuals with a family history of AAT Deficiency, in conjunction with genetic counselling
- Adult asthma patients with diagnostic uncertainty (i.e. persistent obstruction on lung function testing)

The CTS recommends that individuals identified by the criteria listed above be tested for serum levels of AAT[5]

- Serum (quantitative) testing determines the level of AAT in the blood
- Serum testing for AAT is available at most hospital and community labs (note on the requisition form)
- A serum level <1.13 g/L (20 µm) should be referred for confirmatory (qualitative) testing to avoid false negatives, as established in the CTS guidelines*,[5]
- AAT is an acute phase protein whose production can be influenced by various stimuli, including inflammatory mediators. Therefore, protein serum levels may vary depending on the medical condition of the individual[7]

* An AAT serum level below 20 µm (1.13 mg/dl) will detect PiMZ, PiSZ, PiMS, and PiSS with 92% sensitivity and 90% specificity. For labs with reflex confirmatory testing based on AAT serum level, the actual cut off values may differ.

Step 2: Confirming a Diagnosis of AAT Deficiency

A diagnosis of AAT Deficiency is established by confirmatory testing.

Once low serum AAT levels have been assessed, confirmatory testing (PCR, gene sequencing, isoelectric focusing) can be carried out to confirm the diagnosis.

Physicians in all Canadian provinces can access AAT testing. Respective Provincial AAT testing instructions are highlighted below. Additional information can be accessed through the "Alpha-1 Testing" webpage on the www.Grifols.com website.

British Columbia	Indicate "Alpha-1 genetic testing" on your standard hospital requistion form or private laboratory services requisition form. This can be done in writing or using the alpha-1 testing stickers.
Alberta	Testing is available through laboratory services (provincial or private). Indicate "Alpha-1 Phenotyping" on the requisition form.
Saskatchewan	Testing is available through laboratory services (provincial or private). Indicate "Alpha-1 Antitrypsin Level" using your local hospital requisition form or on the standard laboratory requisition form. If a low serum level is detected (below 1.15 g/L), request "Alpha-1 antitrypsin confirmatory genetic testing" for additional sample collection and testing.
Manitoba	Testing is available through laboratory services (public). Indicate "Alpha-1 Antitrypsin" on the standard laboratory services requisition form. If a low serum level is detected, proteotype will be performed. If discordant, phenotyping will be added and reported. If phenotyping is explicitly desired, indicate on requisition.
Ontario	Indicate "Alpha-1 Antitrypsin Serum Level" in "Other Tests" using the standard MOHLTC Laboratory Requisition. If the serum level is low, request genetic testing using the LifeLabs Contract Services Requisition - Grifols Confirmatory Testing form.
Quebec	Testing is available through 2 designated centres: CHUM and MUHC. Request services required on the laboratory testing requisition form for your local hospital or community lab.
Atlantic	Indicate "Alpha-1 Antitrypsin Serum Level" on the standard laboratory requisition form.

Alternatively, for in-office testing, the Grifols Alpha-1 test kit can be used. To get a FREE test kit, call 1-877-3 ALPHA1 (1-877-325-7421) or contact your Grifols Canada representative. Turnaround time for test results is between 14 and 21 days. Results are confidential and shared only with the patient's physician.

If further blood samples are required, this will be communicated to the patient's physician.

Step 3: Determining if Augmentation Therapy is Right

Low Levels of Alpha$_1$-antitrypsin (AAT) can Significantly Compromise Lung Function

Grifols has over 25 years of clinical experience in augmentation therapy with over 4 million infusions worldwide.[12]

Augmentation therapy has demonstrated clinical benefits and can significantly improve patient outcomes.*[,5,8-10]

In clinical trials, PROLASTIN-C has been shown to raise AAT levels above the protective threshold.†[,8,11]

CTS guidelines support use of augmentation therapy for AAT Deficiency in select patients.*

Long-term assessments of treated patients indicate significant clinical benefits from augmentation therapy for patients with COPD attributable to emphysema.*[,5,8]

Learn more about PROLASTIN-C by contacting your Grifols Canada representative, or visiting www.grifols.com

* Long-term open-label assessments of patient registries indicate that augmentation therapy significantly reduced mortality and slowed decline in FEV1 compared to untreated patients with alpha1-antitrypsin deficiency[5,8-9]

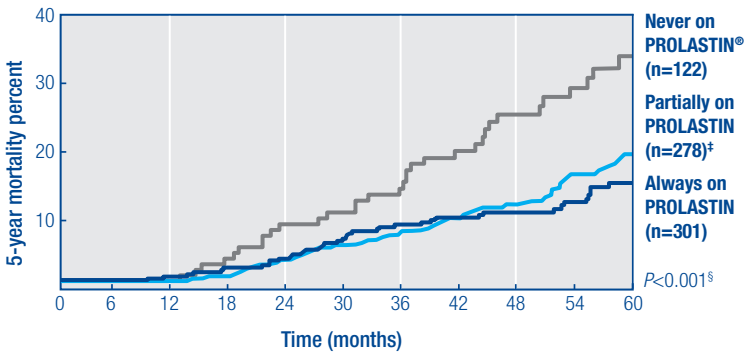
† Levels > 11µm are estimated to be protective[11]

‡ PROLASTIN-C is indicated for chronic replacement therapy of individuals having congenital deficiency of alpha1-PI (alpha1-antitrypsin deficiency) related to genotypes PiZZ, PiZ(null), Pi (null)(null), PiSZ, or other deficiency-causing alleles, and with clinically demonstrable emphysema.[8]

for Your Patient

PROLASTIN-C has been associated with improved survival versus no augmentation therapy*,8,9

Cumulative 5-year mortality for patients with baseline FEV_1 of <50% predicted



Data from assessment of long-term patient registry. Non-randomized, multicentre registry of 1,129 patients evaluating augmentation with Alpha1-PI. Analysis of patients who had follow-up contact for at least 6 months after enrolling in the registry.[9]

‡ Patients partially on Alpha1-PI received augmentation therapy for 66% of the total period; the majority of the discontinuations (59%) were attributed to receipt of a lung transplant.[9]

§ Log-rank P value is for comparison of subjects never receiving Alpha1-PI with subjects partly or always receiving Alpha1-PI.[9]

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)*,†,10

* 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.[8,11]

† 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).

Step 4: PROLASTIN DIRECT

Quality Care Within Reach

A program that works for patients by working *with* them.

PROLASTIN DIRECT is a confidential program sponsored by Grifols Canada Ltd. for patients who have been recommended PROLASTIN®-C.

Enroll your patient to ensure they get the support they need:

- Review PROLASTIN-C reimbursement options
- PROLASTIN-C infusion coordination
- Access to health management resources

3 easy ways to enroll your patients in the PROLASTIN DIRECT Program. Complete, sign and send the PROLASTIN DIRECT form:

1. PROLASTIN DIRECT Web Portal (www.prolastindirect.ca)
2. Phone: 1-877-3ALPHA1 and Fax: 1-888-345-ALPH
3. Email: ProlastinDirect@innomar-strategies.com

Contact your Grifols Canada representative for PROLASTIN DIRECT enrollment forms.

PROLASTIN
Alpha$_1$-Proteinase Inhibitor (Human)
DIRECT™
1-877-3 ALPHA1 (257421)

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
- Cacinogenesis and Mutagenesis
- Sexual Function/Reproduction
- 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.

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11. 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.

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Grifols. Expertise for the Future.

For more than 100 years, Grifols has been working to improve the health and well-being of people around the world.

We are committed to producing essential plasma-derived medicines for patients and to providing hospitals, pharmacies, and healthcare professionals with the tools, information, and services they need to deliver expert medical care.

For more information about GRIFOLS, visit **www.grifols.com**

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