The only alpha₁-proteinase inhibitor with more than 17 years of continuous commitment

- Elevates AAT levels\textsuperscript{12}
- Shown to improve survival rate and slow FEV\textsubscript{1} decline\textsuperscript{13,14*}
- Well tolerated
- Easy to dose

Free Talecris AlphaKit available for AAT testing

The most commonly reported side effect with Prolastin is flu-like symptoms, resolving spontaneously over 24 hours.\textsuperscript{15}

*Nonrandomized/uncontrolled trials.

Before prescribing, please see full Prescribing Information inside back pocket.

For clinical and technical questions on Prolastin, call Talecris Clinical Communications at 1-800-520-2807.

For information on Talecris Direct, call 1-800-305-7881.

To order free Talecris AlphaKits, call 1-800-562-7222.
...the tip of the iceberg

Alpha1-antitrypsin (AAT) deficiency: The fatal pulmonary disease undetected in 95% of cases

- North American/European prevalence: 1 in 2000 to 7000, comparable to cystic fibrosis
- Occurs in up to 3% of patients with chronic obstructive lung disease
- Caused by genetic mutation found primarily in patients of northern European descent
- Deficiency of AAT exposes lung tissue to erosion by AAT-neutralized enzyme

3000 to 5000 diagnosed

80,000 to 100,000 unidentified

5%

95%

AAT deficiency: Often misdiagnosed as asthma or chronic obstructive pulmonary disease (COPD)

<table>
<thead>
<tr>
<th></th>
<th>Signs and symptoms</th>
<th>Response: inhaled β agonists/steroids</th>
<th>Age of onset</th>
<th>Chest x-ray</th>
</tr>
</thead>
<tbody>
<tr>
<td>AAT deficiency</td>
<td>Dyspnea, wheeze, cough, weight loss, cor pulmonale, pneumonia</td>
<td>Poor</td>
<td>20-40</td>
<td>Bibasal bullous changes and avascularity, flattened diaphragm, pulmonary hypertension</td>
</tr>
<tr>
<td>Asthma</td>
<td>Dyspnea, wheeze, cough, flares, night symptoms</td>
<td>Good</td>
<td>2-20 and 40-50</td>
<td>Typically normal, no pulmonary hypertension</td>
</tr>
<tr>
<td>COPD</td>
<td>Same as for AAT deficiency</td>
<td>Variable</td>
<td>60-70</td>
<td>Upper-lobe bullous changes and avascularity, flattened diaphragm, pulmonary hypertension</td>
</tr>
</tbody>
</table>

Adapted from Pina and Horan.

Diagnosis, if it occurs, takes an average of 7.2 years after symptom onset

Lung function spirals down year after year, leading to early disability and mortality

Missed or late diagnosis deprives patient of proper care

Only a specific blood test can diagnose AAT deficiency
ATS/ERS recommendations for AAT deficiency testing:

- COPD (all subjects)
- Early-onset pulmonary emphysema (regardless of smoking history)
- Family members of known AAT-deficient patients
- Dyspnea and cough occurring in multiple family members (same or different generations)
- Liver disease of unknown cause
- Adults with bronchiectasis without evident etiology
- Patients with asthma whose spirometry fails to return to normal with therapy
- Unexplained panniculitis and antiproteinase-3 vasculitis

Talecris Biotherapeutics:
Committed to the identification and treatment of AAT deficiency

Test with our FREE Talecris AlphaKit

The Talecris AlphaKit contains: data form, special filter paper for sampling, device for obtaining blood sample from a fingerstick, full instructions, and return envelope for sending sample by regular mail

- Validated, simple testing method
- Measures AAT levels and, if needed, genetic phenotype
- Results in 10 working days
- All costs paid by Talecris Biotherapeutics

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1-800-562-7222
Treat with Prolastin, alpha₁-proteinase inhibitor (human)

- The only alpha₁-proteinase inhibitor with more than 17 years of continuous commitment

- Produced sustained elevation of AAT levels in the lower respiratory tract

- Slowed decline in forced expiratory volume in 1 second (FEV₁)*

- Improved survival versus no-replacement therapy*

- Easy to administer, usually reimbursable

Prolastin—alpha₁-proteinase inhibitor (human)—is contraindicated in individuals with selective immunoglobulin A (IgA) deficiencies who have known antibody against IgA (anti-IgA antibody), since these patients may experience severe reactions, including anaphylaxis, to IgA that may be present.

*Clinical trials simultaneously meeting all 4 criteria—prospective, long-term, controlled, and randomized—have not been performed to evaluate the effect of chronic replacement therapy with Prolastin on the regression or progression of emphysema in AAT deficiency. Prolastin does not correct any underlying lung damage induced by AAT deficiency, but may retard the progression of lung damage.

Prolastin

Raises AAT levels without compromising safety

Markedly increased patients’ levels of AAT

Over a 1-month period, treated patients averaged AAT levels within normal range (163 ± 4 mg/dL)

AAT levels in the epithelial-lining fluid of the lungs was significantly increased from baseline after 6 days of treatment (P<0.0001)

This product is prepared from pooled human plasma, which may contain the causative agents of hepatitis and other viral diseases. While collection and manufacturing procedures are designed to minimize risk of virus transmission, this risk cannot be completely eliminated.
Slower-than-expected long-term decline in FEV₁

Uncontrolled, prospective study of 20 patients with severe AAT deficiency followed during 36 months with alpha₁-proteinase inhibitor. Expected decline in FEV₁ in patients with nonaugmented AAT deficiency may range from 40 mL/y to 316 mL/y (120 mL/36 mo to 948 mL/36 mo).¹⁴

Prolastin, alpha₁-proteinase inhibitor (human), significantly delayed the decline in FEV₁ among patients with baseline FEV₁ 35% to 49% predicted (P=0.03)¹³

The most commonly reported side effect with Prolastin is flu-like symptoms, resolving spontaneously over 24 hours.¹⁵

Prolastin, alpha₁-proteinase inhibitor (human), significantly delayed the decline in FEV₁ among patients with baseline FEV₁ 35% to 49% predicted (P=0.03)¹³

Nonrandomized multicenter study evaluating AAT augmentation with Prolastin in a database of 1129 patients enrolled in the Alpha₁-Antitrypsin Deficiency Registry of the National Heart, Lung, and Blood Institute (NHLBI). Adapted from Alpha₁-Antitrypsin Deficiency Registry Study Group.⁹,¹³

* Patients partially receiving therapy either started therapy >3 months after study enrollment, permanently discontinued therapy, or temporarily stopped then restarted therapy.

Overall mortality risk significantly lower for Prolastin recipients than for nonrecipients — Risk ratio = 0.64:1, recipients versus nonrecipients, P=0.02.

Mortality risk especially reduced among patients with baseline FEV₁ 35% to 49% predicted — Risk ratio = 0.21:1, recipients versus nonrecipients, P<0.001.
Well tolerated in clinical studies at 60 mg/kg weekly

In clinical trials, only 6 reactions, none severe, were observed in 517 infusions of Prolastin, alpha1-proteinase inhibitor (human)

Mild transient leukocytosis and dilutional anemia also reported several hours after infusion

Since market entry, occasional reports of other flu-like symptoms, allergic-like reactions, chills, dyspnea, rash, tachycardia, and, rarely, hypotension have been received

### Flu-like symptoms the most common adverse reaction

<table>
<thead>
<tr>
<th>Adverse effect</th>
<th>% of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delayed fever (self-limiting within 24 h)</td>
<td>0.77%</td>
</tr>
<tr>
<td>Light-headedness</td>
<td>0.19%</td>
</tr>
<tr>
<td>Dizziness</td>
<td>0.19%</td>
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**Prolastin**

**Easy to dose**
- 60 mg/kg intravenously once weekly
- 30-minute infusion at home, in the hospital, or in the physician’s office

**Backed by Talecris Biotherapeutics**
- Ongoing support to the Alpha-1 community through grants, programs, educational materials, and sponsorship of Team Alpha-1

**Free Talecris AlphaKit**
- Talecris Biotherapeutics pays all costs for AAT testing
- To order Talecris AlphaKits, call 1-800-562-7222

**References:**