About Spiriva® (tiotropium) Respimat®* in asthma

4 key facts:

1. **New asthma indication in the EU**

2. **Improves asthma symptoms** (patients were 68% more likely to improve asthma control)

3. **Significantly reduces risk of severe asthma exacerbations** by 21% for patients with symptoms on current standard treatment

4. **Delivered via the Respimat® inhaler:** allowing gentle inhalation that makes it easy for patients to take their therapy

- In August 2014, a new indication for Spiriva® (tiotropium) Respimat®* in asthma was accepted by regulatory authorities in the EU
- Spiriva® Respimat®* is indicated as an add-on maintenance bronchodilator treatment in adult patients with asthma who are currently treated with the maintenance combination of inhaled corticosteroids (≥800 µg budesonide/day or equivalent) and long-acting beta2-agonist and who experienced one or more severe exacerbations in the previous year
- Spiriva® (tiotropium) is an inhaled long-acting, anticholinergic bronchodilator. There are currently no other long-acting anticholinergic bronchodilators indicated for the treatment of asthma

* The indication accepted by the EU regulatory authorities is for Spiriva® Respimat® as an add-on maintenance bronchodilator treatment in adult patients with asthma who are currently treated with the maintenance combination of inhaled corticosteroids (≥800 µg budesonide/day or equivalent) and long-acting β2-agonists and who experienced one or more severe exacerbations in the previous year

† At least inhaled corticosteroid (ICS)/long-acting beta2-agonist (LABA) therapy

‡ Severe asthma exacerbations were predefined in the clinical trial protocol as all asthma exacerbations that required treatment with systemic (including oral) corticosteroids for at least 3 days, or, in case of ongoing and pre-existing systemic corticosteroid therapy, that required at least a doubling of the previous daily dose of systemic corticosteroids for at least 3 days
• Pivotal, Phase III study results from the PrimoTinA-asthma® large-scale, Phase III clinical trials which investigated adults with asthma who continued to have symptoms despite taking at least ICS/LABA therapy, demonstrated that the addition of Spiriva® Respimat®:
  • Significantly improved asthma symptoms
    – patients were 68% more likely to improve asthma control5
  • Reduced the risk of patients having a severe asthma exacerbation by a fifth (21%)1
    – reducing the number of patients who experienced a severe asthma exacerbation1
  • Reduced the risk of a patients’ asthma worsening by nearly one third (31%)1
  • Delayed the time to patients’ first severe asthma exacerbation and first episode of asthma worsening1

![Graph showing significant reduction in time to first severe asthma exacerbation - pooled](image)

**Significant reduction in time to first severe asthma exacerbation - pooled**

- Tiotropium Respimat® n=122 (26.9%), Placebo Respimat® n=149 (32.8%)
- Tiotropium Respimat®: 282 days; Placebo Respimat®: 226 days (25th percentile)
- Number needed to treat: 15
- HR=0.79; Risk reduction of 21% (P=0.03)

- Patients at risk

Kerstjens et al. NEJM 2012;367:1198-1207.
HR, hazard ratio; ICS, inhaled corticosteroid; OR, odds ratio

• The safety of Spiriva® Respimat® has been shown to be balanced as compared to placebo1
• Spiriva® is delivered by the Respimat® Soft Mist™ Inhaler (SMI). Respimat® is the only inhaler delivering a slow-moving Soft Mist™ allowing gentle inhalation – making it easy for patients with asthma to take their therapy2-4
UniTinA-asthma® clinical trial programme

3 key facts:

1. Designed to evaluate efficacy and safety of Spiriva® Respimat® in asthma added on to at least ICS therapy

2. Consists of 18 studies

3. Involved more than 6,000 patients

18x1000

3 key facts:

- UniTinA-asthma®: a comprehensive Phase II and III clinical trial programme designed to evaluate the efficacy and safety of Spiriva® Respimat® in patients with asthma
- Includes 18 clinical studies investigating Spiriva® Respimat® added to usual care in adults, adolescents and children (age 1+) with asthma across asthma severities
About asthma and the unmet need for innovative treatments in asthma

3 key facts:

1. Almost one in two patients with asthma still experience asthma symptoms.

2. Symptomatic asthma patients have ~6 greater chance of having an asthma attack in the next few weeks than those with minimal to no daytime symptoms.

3. Words people with asthma use to describe how they feel:
   - Embarrassed
   - In the shadow of asthma
   - Anxiety
   - Uncertain
   - Blamed
   - Fear

- The goal of asthma therapy is to achieve and maintain clinical control, which includes improving lung function, and reducing symptoms and exacerbation risk.

- The current standard treatment for asthma includes inhaled corticosteroids (ICS), which treat the underlying inflammation. Long-acting beta2-agonists (LABA) bronchodilators may be prescribed in addition to ICS to prevent or relieve symptoms.

- Despite current treatment options, almost one in two patients with asthma still experience asthma symptoms and may experience frightening and life-threatening asthma exacerbations.

- People suffering from asthma experience recurrent episodes of wheezing, breathlessness, chest tightness and coughing. These episodes may be punctuated by periods of more severe and sustained deterioration of symptoms, termed an asthma exacerbation.

- Asthma can, and does, still kill and many of these deaths may be preventable.

- According to the GINA guidelines an estimated 300 million people worldwide have asthma – ~30 million people in Europe have asthma.
References

5. Boehringer Ingelheim. Data on file