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EMA completes review of inhaled corticosteroids for chronic obstructive pulmonary disease

Review finds no differences between products in risk of pneumonia

On 28 April 2016 EMA completed a review of the known risk of pneumonia (lung infection) in patients who take inhaled corticosteroid medicines to treat chronic obstructive pulmonary disease (COPD). COPD is a long-term disease of the lungs in which the airways and air sacs in the lungs become damaged or blocked, leading to breathing difficulties. Corticosteroid inhalers are widely used in the European Union (EU) to treat COPD and pneumonia is a common side effect of such treatment.

The review confirmed the risk of pneumonia with these products, which has been known for many years, and that it is common (can affect between 1 and 10 COPD patients in 100 using these medicines). The review did not find any conclusive evidence of differences in this risk for different products.

Overall the benefits of inhaled corticosteroid medicines in treating COPD continue to outweigh their risks and there should be no change to the way in which these medicines are used. Patients with COPD and their doctors should however be alert for signs and symptoms of pneumonia, bearing in mind that the clinical features of pneumonia overlap with those of a worsening (exacerbation) of the underlying disease.

The review was carried out by the Agency's Pharmacovigilance Risk Assessment Committee (PRAC), which recommended that the product information for these medicines should be updated to adequately reflect current knowledge about the risks. The PRAC recommendations were sent to the Committee for Medicinal Products for Human Use (CHMP), which adopted the Agency's opinion. The CHMP's opinion was then sent to the European Commission, which issued a final legally-binding decision valid throughout the EU.

Information for patients

- It has been known for some time that inhaled corticosteroid medicines increase the risk of pneumonia (infections of the lungs) in patients taking these medicines for the long-term lung disease COPD (chronic obstructive pulmonary disease).
- Corticosteroid inhalers reduce inflammation and swelling in the lungs and so help breathing in patients with COPD. In the EU, the available products include the active substances beclomethasone, budesonide, flunisolide, fluticasone furoate or fluticasone propionate.

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- EMA has reviewed the risk of pneumonia in COPD patients using corticosteroid inhalers and has concluded that this risk applies to all medicines of this class. The evidence did not confirm any differences in risk between products.
- Patients need to alert their doctors if they start to get symptoms that suggest they are developing pneumonia, so that it can be identified and treated early. These symptoms can be like those of an exacerbation (an episode of worsening COPD) and include fever or chills, increased amounts of mucus (phlegm) or a change in its colour, or worsening of cough or breathing difficulties.
- Patients who have any concerns should discuss them with their doctor or other healthcare professional. They should not stop using their inhaler or change the way they use it without consulting their prescriber.

Information for healthcare professionals

- Following a review of the available data, EMA has confirmed the risk of pneumonia with inhaled corticosteroids (ICS) in patients with COPD. There is no conclusive clinical evidence for intra-class differences in the magnitude of the risk among ICS products.
- There is some evidence of an increased risk of pneumonia with increasing steroid dose but this has not been demonstrated conclusively across all studies.
- The product information for all medicines of the class will be updated to reflect current knowledge about pneumonia risk.
- Healthcare professionals should remain vigilant for the possible development of pneumonia in patients with COPD as the clinical features of such infections overlap with the symptoms of COPD exacerbations.
- Patients should be advised to report any increased breathing difficulties or other symptoms suggestive of infection.
- The Agency's review included published data from randomised controlled clinical trials and a number of meta-analyses, as well as observational studies. No clinical trials directly examined the risk of pneumonia with ICS head to head, and only indirect comparison in meta-analyses/systematic reviews or from observational studies is available. Due to the variability in the clinical data and multiple uncertainties with study methodologies, this does not provide conclusive evidence for intra-class differences in the magnitude of risk.

More about the medicine

Corticosteroids, also known as steroids, are anti-inflammatory medicines used for a wide range of conditions. They are similar to natural hormones normally produced by the adrenal glands (two small glands located above the kidneys). When taken by inhalation they attach to receptors in the airways and cause a reduction in lung inflammation, which makes breathing easier. They are usually taken using inhalers which either contain a corticosteroid alone or a corticosteroid in combination with another medicine (such as a long-acting beta$_2$ agonist that widens the airways). Beclomethasone, budesonide, flunisolide, fluticasone propionate and fluticasone furoate are corticosteroids authorised

and marketed as inhalation formulations for use in COPD. Corticosteroid-containing medicines have been authorised in the EU through both central and national approval procedures.

More about the procedure

The review was initiated at the request of the European Commission on 7 May 2015, under Article 31 of Directive 2001/83/EC.

The review has been carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines, which made a set of recommendations. The PRAC recommendations were sent to the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use, which adopted the Agency's opinion. The CHMP opinion was forwarded to the European Commission, which issued a final legally binding decision applicable in all EU Member States.

Commission Decision dates: 29/06/2016 (nationally authorised products), 24/06/2016 (Relvar Ellipta, Revinty Ellipta), 04/07/2016 (BiResp Spiromax, DuoResp Spiromax), 06/07/2016 (Budesonide/Formoterol Teva, Vylaer Spiromax).

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