UMECLIDINIUM BROMIDE

▼Incruse® for COPD
Very little efficacy

dtbn
DRUG ASSESSMENT REPORT
www.dtb.navarra.es
@DTB_Navarre.es

ABSTRACT

Umeclidinium is a long acting muscarinic antagonist (LAMA) authorized for symptom relief in patients with Chronic Obstructive Pulmonary Disease (COPD).

They are no comparative data available with tiotropium, or with other LAMA or LABA.

It has not shown to reduce the number of exacerbations. Neither does it improve quality of life or reduce the need for rescue treatment in studies lasting more than 12 weeks.

There is concern on safety regarding its cardiovascular profile and the possible higher risk of pneumonia.

Indications[3]

This drug is indicated as maintenance bronchodilator treatment to relieve symptoms in adult patients with COPD.

Mecanismo de acción[3]

This is a long acting antimuscarinic agent that acts by inhibiting the action of acetylcholine in smooth muscle cells, producing bronchodilation.

Posology and administration[3]

The recommended dose is one inhalation per day using the dry powder inhaler (Ellipta®) (for an inspiratory flow of 60ml/min for 4 seconds) providing a release dose of 55mcg of umeclidinium which corresponds to a pre-dispensed dose of 62.5mcg. It should be applied at the same time every day.

Clinical efficacy[5,6]

The clinical development program included 4 trials which compared the authorized doses to placebo.

In the two main trials, the primary endpoint was change with respect to initial values in Forced Expiratory Volume in 1 second (FEV1). The minimum value considered clinically relevant is a difference of 100ml. The results were in the order of 120ml. Clinical relevance of the results was not conclusive given that the lower limit of the confidence interval was less than the clinically relevant difference. Only in one of the trials were an improvement in quality of life and a reduction in the use of rescue treatment found. In the longest study (24 weeks) no significant differences were found with regard to these endpoints. None of the studies showed evidence of a reduction in exacerbations.[7,9] In two other crossover studies no clinically relevant differences were found in either FEV1 or exercise resistance.[10,11]

No studies have been carried out comparing other LAMA.

Safety
Adverse reactions

The adverse reactions described most frequently in clinical trials include nasopharyngitis, and cefalea.[5] Upper respiratory infections, sinusitis, cough, urinary tract infections and tachycardia were also frequent.[3]

In the integral analysis of all clinical trials, the incidence of cardiovascular events was greater compared to placebo (13 cases per 100 patients per year), tachycardia and heart arrhythmias were reported more frequently followed by hypertension and cardiac ischemia. Patients with clinically relevant uncontrolled cardiovascular disease were excluded from the trials.[3]

One clinical trial on long term safety at 125 mcg found an increase in the incidence of pneumonia compared to placebo (42 cases per 1000 patients per year).[12]

Scarce efficacy shown when compared to placebo and no comparative data with other LAMA

Contraindications[3]

Hypersensitivity to the drug or its excipients.

Warnings and precautions[3]

- Do not prescribe concomitantly with other muscarinic antagonists.
- Do not prescribe in asthma patients.
- Precaution should be taken in patients with narrow angle glaucoma or urinary retention.
- Precaution should be taken in patients with severe cardiovascular disorders, especially cardiac arrhythmias.
- It contains lactose.

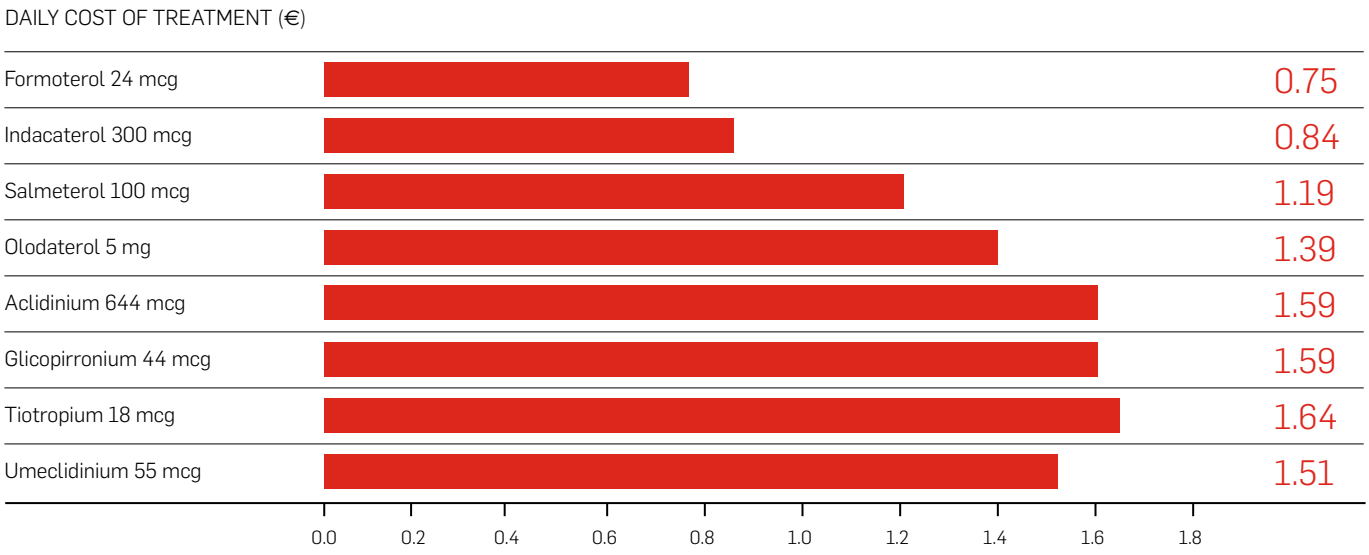
Use in special situations[3]

Pregnancy and lactation: There are no data available in pregnant women and its excretion in breast milk is unknown. **Renal failure:** No dose adjustments are necessary. **Liver failure:** no dose adjustments are required in case of

CLASSIFICATION

4	IMPORTANT THERAPEUTIC INNOVATION
3	MODEST THERAPEUTIC INNOVATION
2	SOME ADDED VALUE IN SPECIFIC SITUATIONS
1	NO THERAPEUTIC INNOVATION
0	**INSUFFICIENT EVIDENCE**

The qualification assigned to the drug was agreed by the Drug Assessment Committees of Andalusia, Basque Country, Catalonia Institute of Health, Aragon and Navarre. The current report is based on the available information and is susceptible to be updated according to the latest evidence. Let us remind the reader about the importance of notifying the Pharmacovigilance Centre when there are suspicions of adverse reactions to drugs.



mild and moderate liver dysfunction. There are no studies in patients with severe liver failure and therefore it should be used with precaution. **Children:** There are no specific recommendations in patients under 18 years.

Interacciones[1]

No se recomienda su administración concomitante con otros anticolinérgicos.

Interactions[1]

Concomitant use with other anticholinergic agents is not recommended.

EMA´s Risk Management Plan[5]

The potential important risks identified include cardiovascular and cerebrovascular disorders, paradoxical bronchospasm, narrow angle glaucoma, urinary retention and lower respiratory tract infections like pneumonia. The EMA considers the need for research through a post-approval observational study on cardiovascular and cerebrovascular events and pneumonia in comparison with tiotropium. There is also no information available on patients with liver failure and on long term safety.

Comparators

Long acting bronchodilators, LAMA or LABA.

Place in therapeutics

Pharmacological management of COPD is used to reduce symptoms and/or complications. After diagnosis treatment can be introduced progressively based on the severity of the obstruction and symptoms, where bronchodilation represents the first step in the management of this disease. Inhaled bronchodilators such as long acting beta-2 adrenergic agonists(LABA) and long acting anti-muscarinic agents (LAMA) constitute the basis of symptomatic treatment of patients with COPD and permanent symptoms.[1]

Umeclidinium is a LAMA that has only shown statistically significant differences in variables that evaluate lung function compared to placebo. With regard to symptom related variables (dyspnea, quality of life), the minimum differences considered clinically relevant were not reached in the majority of the studies.

No improvement in either quality of life or a reduction in the use of rescue medication after 24 weeks have been observed. Now has it shown a reduction in exacerbations and it has not been compared to other bronchodilators.

The main concern on safety is the cardiovascular effects. More data is required to compare its safety profile to that of tiotropium. Therefore, given the poor evidence available on efficacy and safety, it is not clear whether this drug has a role in the management of COPD.

Presentations

Incruse® (GlaxoSmithKline) 55 mcg 30 doses (45.27 €)

References

This information is based on the therapeutic positioning report of the AEMPS.

Servicio Navarro de Salud
Osasunbidea

INTERNATIONAL SOCIETY OF DRUG BULLETINS

Information: Servicio de Prestaciones Farmacéuticas Plaza de la Paz s/n, 4ª planta 31002 Pamplona Teléfono 848429047 Fax 848429010
New Drugs Assessment Committee: Iñaki Abad, Mª José Ariz, Ana Azparren, Mª Concepción Celaya, Juan Erviti, Javier Garjón, Isabel García, Isabel Aranguren, Rodolfo Montoya, Mikel Moreno, Lourdes Muruzábal