

## UTILIZATION AND COSTS OF REIMBURSED INHALED $\beta$ 2-AGONISTS IN ALBANIA DURING THE YEARS 2008-2010

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### Abstract

$\beta$ 2-agonists are bronchodilators that are used in the treatment of obstructive airway diseases as pathologies with high global prevalence and in constantly growing. **Objective:** In this retrospective study was assessed the trend of utilization of reimbursed inhaled  $\beta$ 2-agonists in Albania during the period 2008-2010. **Materials and Methods:** Data on quantities and costs of analyzed drugs were taken from Health Insurance Institute (HII) database. International ATC/DDD methodology and International Classification of Diseases (ICD-9) were used to quantify the use of inhaled  $\beta$ 2-agonists in DDD/1000 inhabitants/day according to drugs and diseases diagnoses. **Results:** Total consumption of inhaled  $\beta$ 2-agonists increased from 2.49 DDD/1000 inhabitants/day in 2008 to 3.43 DDD/1000 inhabitants/day in 2010. Increased consumption of these drugs was associated with almost reduplication of the cost. Inhaled  $\beta$ 2-agonists were reimbursed mainly for the treatment of bronchial asthma and COPD. Salbutamol was the most used drug in 2010 with 2.19 DDD/1000 inhabitants/day. Increased consumption of combinations of LABAs plus ICS was associated in parallel with decrease in the use of inhaled long-acting  $\beta$ 2-agonists (LABAs) during the years 2009-2010. **Conclusions:** The total use of inhaled  $\beta$ 2-agonists in Alba-

nia was at low level compared to other countries such as Italy and Norway. Combined inhaled  $\beta$ 2-agonists had the highest consumption in Italy and in Norway, but not in Albania.

**Key words:** Utilization of drugs, ATC / DDD methodology, ICD-9, inhaled  $\beta$ 2-agonists.

### Introduction

Bronchodilator drugs are most useful in the treatment of obstructive airway disease, of which bronchial asthma and chronic obstructive pulmonary disease (COPD) are the most common pathologies and important causes of global morbidity and mortality.

According to latest World Health Organization (WHO) estimates (2007), currently 300 million people worldwide have asthma and 210 million people have COPD. Furthermore, asthma is considered to be the most common chronic disease among children (1). It is estimated that the number of people with asthma could grow to as many as 400-450 million people worldwide by 2025 (2). WHO also predicts that, by 2020, COPD will be the third leading cause of mortality and the fifth leading cause of morbidity in the world (3).  $\beta$ 2-agonists belong to the class of bronchodilator drugs and are widely used in the treatment of obstructive airway diseases. Inhaled  $\beta$ 2-agonists have greater use than  $\beta$ 2-agonists for systemic use. The major advantage

of inhaled drugs is that these drugs are delivered directly to the airways, producing higher local concentrations with significantly less risk of systemic side effects (4).

We need drug consumption statistics because it is very difficult to work for improvements in drug use without proper knowledge about what is actually used (5). In this context, drug use statistics of reimbursed inhaled  $\beta_2$ -agonists in our country will allow us to appreciate current trends in the use of these drugs and to make international comparisons in order to improve the quality of using these drugs.

#### **Objective of the study**

The objective of this study is to evaluate the utilization of reimbursed inhaled  $\beta_2$ -agonists in Albania during the years 2008-2010 and to compare the statistics of the use of these drugs with those of other European countries.

#### **Methods and Materials**

In this study is used ATC/DDD methodology developed by WHO to measure drug use. Because the Anatomical Therapeutic Chemical (ATC) system separates drugs into groups at five levels, statistics on drug utilization grouped at the five different levels can be provided (6).

Inhaled  $\beta_2$ -agonists were divided into two groups at the fourth level of ATC classification, respectively: R03AC - Selective  $\beta_2$ -adrenoreceptor agonists and R03AK-Adrenergics and other drugs for obstructive airway diseases, until the fifth level of chemical substance.

The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults (6,7). The DDDs of plain inhaled products that are objects of this study were taken from the ATC/DDD Index-2010.

Plain products are defined as preparations containing one active

component (including stereoisomeric mixtures). Medicinal products which in addition to one active component contain auxiliary substances intended to increase the stability of the preparations, increase the duration and/or increase the absorption are also considered as plain products (7).

Products containing two or more active ingredients are regarded as combination products. The DDDs assigned for combination products are based on the main principle of counting the combination as one daily dose, regardless of the number of active ingredients included in the combination (7). For combined products, the DDDs were taken from List of DDDs for combined products which is available on the website [www.whocc.no](http://www.whocc.no).

The data on quantities and costs of reimbursed inhaled  $\beta_2$ -agonists drugs in Albania during the years 2008-2010 were obtained from the HII database. The use of inhaled  $\beta_2$ -agonists was presented also according to the disease diagnoses based on International Classification of Diseases (ICD-9). The data for the population in Albania were taken from the Albanian Institute of Statistics (INSTAT).

Drug consumption figures were presented as numbers of DDDs/1000 inhabitants/day and the cost figures, suitable for an overall analysis of drugs expenditures, were expressed in national currency (Lek). Sales or prescription data presented in DDD/1000 inhabitants/day may provide a rough estimate of the proportion of the population within a defined area treated daily with certain drugs (7).

#### **Results**

In our country the consumption of reimbursed inhaled  $\beta_2$ -agonists increased from 2.49 DDD/1000 inhabitants/day in 2008 to 3.43 DDD/1000 inhabitants/day in 2010.

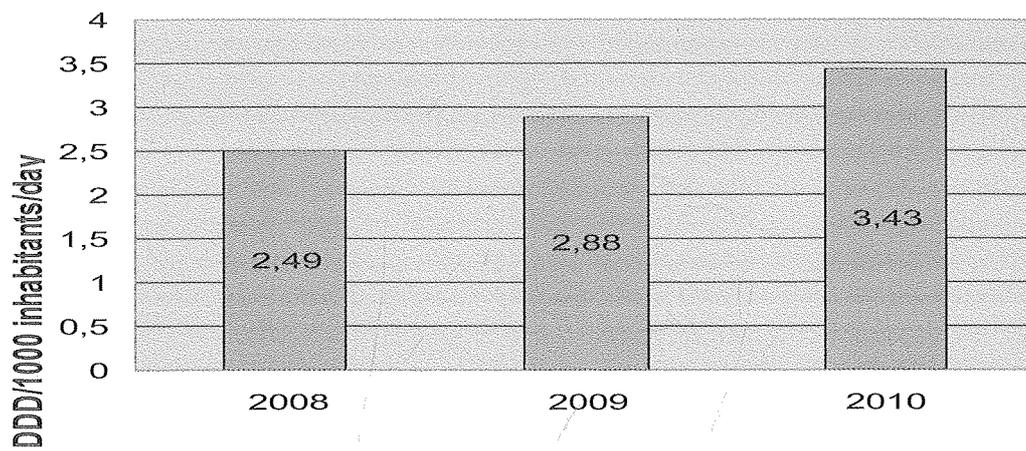


Figure nr.1. Total consumption of reimbursed inhaled  $\beta$ 2-agonists in Albania

The costs for these drugs increased from year to year respectively from 145 million Lek in 2008 to 180 million

Lek in 2009 and 283 million Lek in 2010.

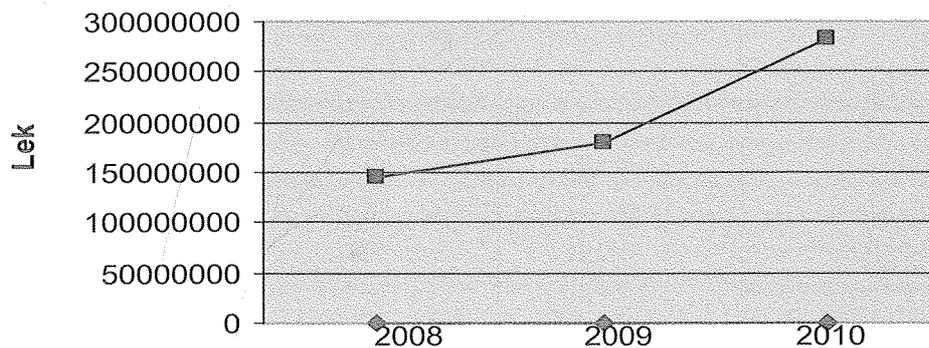


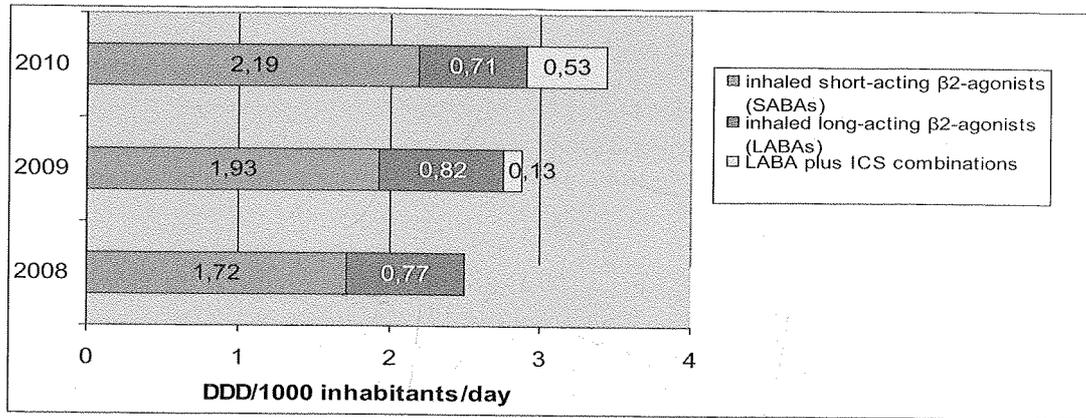
Figure nr.2 Total costs for reimbursed inhaled  $\beta$ 2-agonists in Albania

According to pharmacotherapeutical groups, the consumption of inhaled short-acting  $\beta$ 2-agonists (SABAs) increased every year. The consumption of SABAs, represented only by the active substance Salbutamol, increased from 1.72 DDD/1000 inhabitants/day in 2008 to 2.19 DDD/1000 inhabitants/day in 2010.

The consumption of inhaled corticosteroid/long-acting  $\beta$ 2-agonist combinations (ICS+LABA) increased from 0.13 DDD/1000 inhabitants/day

in 2009 to 0.53 DDD/1000 inhabitants/day in 2010. Preparations of inhaled long-acting  $\beta$ 2-agonists (LABAs) in combinations with inhaled glucocorticosteroids have been reimbursed for the first time in Albania in 2009, so this group of drugs does not represent consumption during 2008.

In contrast, inhaled long-acting  $\beta$ 2-agonists (LABAs) as plain preparations presented greater consumption in 2009 than in 2010.



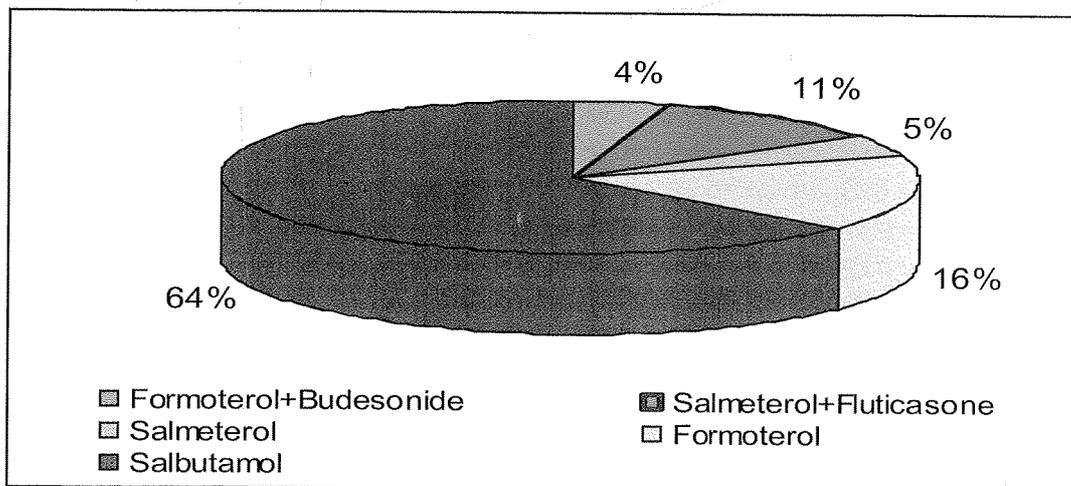
**Figure nr.3 Consumption of reimbursed inhaled β2-agonists by pharmacotherapeutical groups in Albania**

According to the active substances, in 2010 compared to the previous year, the largest increase in consumption belonged to inhaled long-acting β2-agonists (LABAs) and ICS combinations.

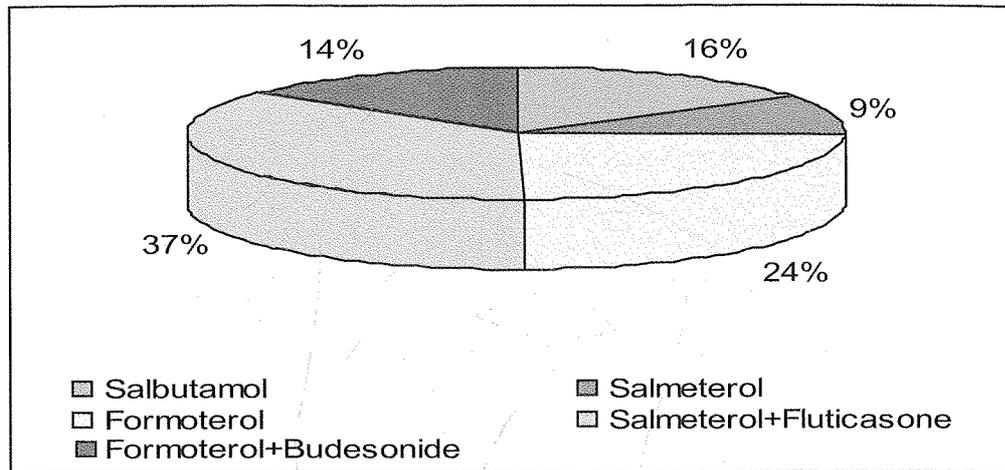
**Table nr.1 Consumption of reimbursed inhaled β2-agonists by active substances in Albania from 2009 to 2010**

Active substances	DDD/1000 inhabitants/day		Increase or Decrease in percentage of consumption
	2009	2010	
Salbutamol	1.93	2.19	13,4
Formoterol	0.58	0.55	-5
Salmeterol	0.24	0.16	-33
Salmeterol+Fluticasone	0.09	0.38	76
Formoterol+ Budesonide	0.04	0.15	76

Salbutamol was the most often used active substance and the combination of Salmeterol plus Fluticasone had the highest cost in 2010.



**Figure nr.4 Consumption in percentage of reimbursed inhaled β2-agonists in Albania in 2010**



**Figure nr.5. Costs in percentage of reimbursed inhaled  $\beta$ 2-agonists in Albania in 2010**

Inhaled  $\beta$ 2-agonists are mostly described for the treatment of asthma and COPD. 83% of the total consumption of these drugs was reimbursed for the treatment of asthmatic patients during the years

2008-2010. The use of inhaled  $\beta$ 2-agonists although was at low level for the treatment of patients with COPD, had increased as part of the total consumption, over the years.

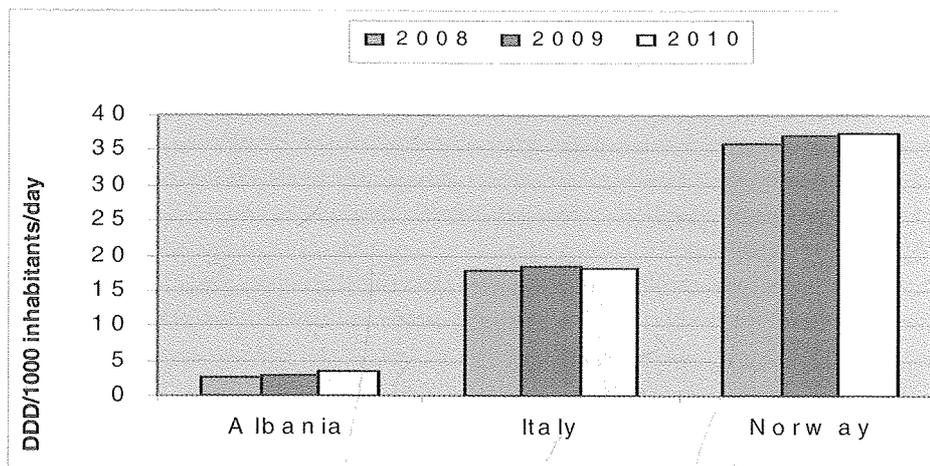
**Table nr.2. Consumption in percentage of reimbursed inhaled  $\beta$ 2-agonists according to the diagnoses of diseases in Albania**

Diagnoses Years	Diagnoses		
	Asthma	COPD	Other diagnoses treated
2008	83%	8%	9%
2009	83%	9%	8%
2010	83%	11%	6%

### Discussion

The use of inhaled  $\beta$ 2-agonists in Albania has low levels compared with Italy and Norway. Total consumption of these drugs has increased in the three compared states from 2008 to

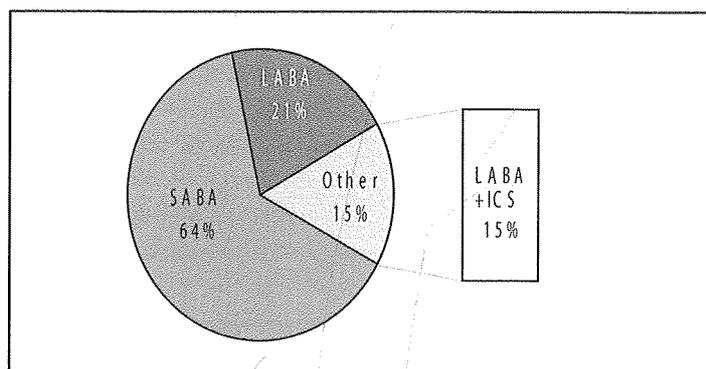
2010: in Albania from 2.49 to 3.43 DDD/1000 inhabitants /day, in Italy from 17.8 to 18.1 DDD/1000 inhabitants/day (8) and in Norway from 36 to 37.3 DDD/1000 inhabitants/day (9).



**Figure nr.6. Total consumption of inhaled  $\beta$ 2-agonists in Albania, Italy and Norway during 2008-2010**

In Albania inhaled short-acting  $\beta$ 2-agonists (SABAs) are the most used drugs in 2010. Their consumption represents 64% of total consumption of inhaled  $\beta$ 2-agonists. SABAs are followed by inhaled long-acting  $\beta$ 2-

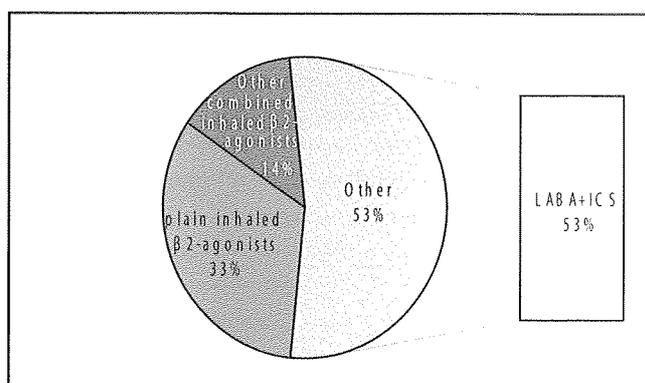
agonists (LABAs) with 21% of total consumption. The less used drugs are inhaled corticosteroid/long - acting  $\beta$ 2-agonist combinations. The consumption ratio of plain inhaled  $\beta$ 2-agonists to combined ones is 85:15.



**Figure nr.7. Consumption in percentage of inhaled  $\beta$ 2-agonists in Albania in 2010**

In Italy LABA/ICS combinations are the most used drugs in 2010 with 53% of total consumption of inhaled  $\beta$ 2-agonists. The consumption ratio of plain inhaled  $\beta$ 2-agonists to combined ones is 33:67.

**Figure nr.8. Consumption in percentage of inhaled  $\beta$ 2-agonists in Italy in 2010**



In Norway LABA plus ICS combinations dominate the consumption of this class of drugs with 54% of total consumption. After those, inhaled short-acting  $\beta$ 2-agonists (SABAs) and finally inhaled

long-acting  $\beta$ 2-agonists (LABAs) ranked with the use respectively 38% and 8% of total consumption. The consumption ratio of plain inhaled  $\beta$ 2-agonists to combined ones is 46:54 in Norway in 2010.

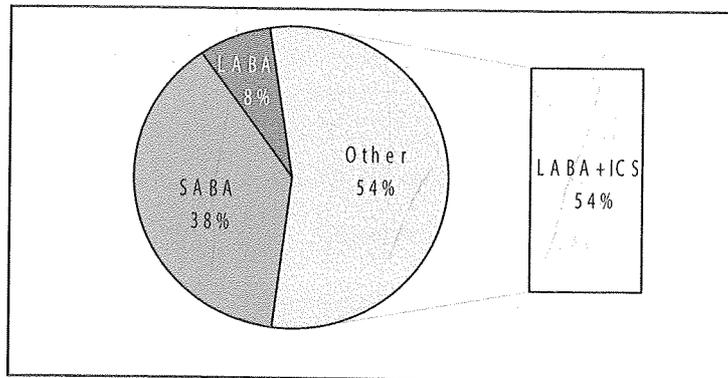


Figure nr.9. Consumption in percentage of inhaled  $\beta$ 2-agonists in Norway in 2010

By comparing the above statistics noted that in Italy and Norway dominate the use of combined inhaled  $\beta$ 2-agonists (especially LABA plus ICS combinations). The low level of consumption of these combined drugs in Albania, is also explained by the fact that these preparations have been reimbursed for the first time on 1 June 2009.

The addition of a long-acting  $\beta$ 2-agonist (LABA) to ICS rather than increasing the dose of ICS has become standard therapy in poorly controlled asthma. This is because the combination of these two

therapies appears to provide improved asthma control (10).

Current guidelines recommend ICS as add-on therapy in patients with stage III (severe,  $FEV_1 = 30\% - 50\%$  predicted) and stage IV (very severe,  $FEV_1 < 30\%$ ) COPD with chronic symptoms or repeated exacerbations (11).

However, based on recent findings of the TORCH study that FSC is associated with a reduced rate of exacerbations, improved lung function and health-related quality of life, and possible survival benefits,

European regulators recently approved its use in patients with milder COPD ( $FEV_1 < 60\%$  of predicted pre-bronchodilator value and history of exacerbations (12).

Combination therapy has become more feasible with the availability of single inhaler devices containing both LABA and ICS (13). Combined inhalers are more convenient for patients, they may increase compliance and ensure that the long-acting  $\beta$ 2-agonist is always accompanied by the glucocorticosteroid (4).

This is especially important for asthmatics. In asthma, a LABA should always be used together with an inhaled corticosteroid because of an association between LABA monotherapy and asthma-related hospital admissions and deaths (14).

Patients with COPD display significantly lower adherence to treatment than asthmatic patients (James et al 1985; Cochrane 1992; Haupt et al 2008). Because LABAs provide symptom relief, however, patients are more likely to comply with scheduled dosing regimens when ICS and LABAs are combined in the same inhaler device (15).

The combination of Salmeterol and Fluticasone is the most used drug in 2010 in Italy and Norway and represents the highest cost in the three compared countries. The cost of this combined drug makes up 37% of total expenditures of inhaled  $\beta_2$ -agonists in Albania. Salmeterol/

Fluticasone combination continues to be the most prescribed combination in 2010 in Italy and the only one that appears in the list of first 30 active substances with the highest costs (8). This combination ranks among the top 10 POMs (Prescription Only Medicines) ranged according to the sales in NOK in 2010 in Norway (9).

**Table nr.3. Consumptions and costs of Salmeterol plus Fluticasone combination in 2010**

Countries	DDD/1000 inhabitants/day	Costs
Albania	0,38	102 million LEK
Italy	6,1	302 million EURO
Norway	11,75	348 million NOK

When comparing the values of consumption of inhaled  $\beta_2$ -agonists, the different sources of the data should always be taken into account. Data represent the quantities of reimbursed drugs in Albania and Italy during the period 2008-2010. In Albania the data are taken from the HII database and in Italy data refer to drugs prescribed in charge of the National Health Service (NHS). In Norway, data represent total sales of medical products from wholesalers to retailers and such sales are not necessarily equal to what is actually consumed (9).

#### Conclusions

- Total consumption of reimbursed inhaled  $\beta_2$ -agonists in our country increased from 2.49 to 3.43 DDD/1000 inhabitants/day or 37,7% during the years 2008-2010 and the costs of these drugs almost doubled.

- The consumption of inhaled long-acting  $\beta_2$ -agonists (LABAs) decreased from 0.82 to 0.71 DDD/1000 inhabitants/day, while the consumption of LABA plus ICS combinations increased from 0.13 to

0.53 DDD/1000 inhabitants/day during 2009-2010.

- In 2010 Salbutamol was the most described active substance in Albania and made up 64% of total consumption of reimbursed inhaled  $\beta_2$ -agonists. Salmeterol plus Fluticasone combination had the highest cost with 37% of total expenditures for all these drugs.

- Reimbursed inhaled  $\beta_2$ -agonists were described mainly for patients with asthma and COPD.

- The utilization of inhaled  $\beta_2$ -agonists in our country is at low level compared with other European countries such as Italy and Norway.

- Combined inhaled  $\beta_2$ -agonists had the greatest use in Italy and in Norway, while in Albania the use of these preparations that had been reimbursed during the second half of 2009 was low.

- In 2010 Salmeterol plus Fluticasone combination which had the highest costs in the three compared countries, was the inhaled  $\beta_2$ -agonist with the greatest consumptions in Italy and in Norway.

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