

## Pharmacoutilization and costs of nucleoside and nucleotide analog inhibitors for hepatitis B treatment in the Vesuvian area of South Italy

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### ABSTRACT

Hepatitis B virus (HBV) infection is an important sanitary problem due to its worldwide distribution and high social impact; severe complications of chronic hepatitis induced by HBV are cirrhosis and hepatocellular carcinoma (HCC). We conducted a survey with the aim i) to show the updated prevalence of the disease and ii) to evaluate the economic impact of treatment with oral agents (nucleoside and nucleotide analog inhibitors) in a region of the South Italy comprising 1.012.304 inhabitants. Between January and December 2012, 778 patients with hepatitis B (prevalence: 0.08%) were treated. The total pharmaceutical cost was € 2.082.926 (3% of the total sanitary expense). Oral drugs against HBV have a moderate impact on the pharmaceutical spending. The major economic impact associated with HBV infection is primarily represented by the later development of cirrhosis and HCC.

**Key words:** Hepatitis B, pharmacoutilization, pharmaceutical spending, prevalence.

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### INTRODUCTION

Hepatitis B Virus (HBV) is an important sanitary problem due to its worldwide distribution and development of adverse *sequelae* after liver infection, including acute liver failure (< 1%), cirrhosis (5 - 10%) and hepatocellular carcinoma - HCC - (5-year cumulative HCC risk in cirrhosis is 15% in high endemic areas and 10% in the West).<sup>[1]</sup> There are an estimated 370 million chronic carriers of HBV world-wide. However, the incidence of HBV infection, complications and patterns of transmission vary greatly in different geographical areas. It has been estimated that the prevalence of chronic infection is low (< 1%) in North West Europe, while intermediate (1 - 8%) in southern Europe. In some African countries the prevalence of HBV infection is very high (> 8%).<sup>[1]</sup> The average prevalence in Italy lies between 2 and 3%; rates are higher in

the South (4 - 4.5%) than in the North (1 - 2%).<sup>[2]</sup>

Significant improvements for the therapy of HBV have been obtained in the last decade with the introduction of new and effective oral drugs.<sup>[3-5]</sup> Currently, there are five oral agents approved for the treatment of HBV by the U.S. Food and Drug Administration (FDA): the nucleoside (lamivudine, entecavir, and telbivudine) and nucleotide (adefovir and tenofovir) analogues.<sup>[3-5]</sup> The goal of the therapy is to suppress HBV replication in order to arrest the progression of liver injury and to prevent the development of cirrhosis and HCC.

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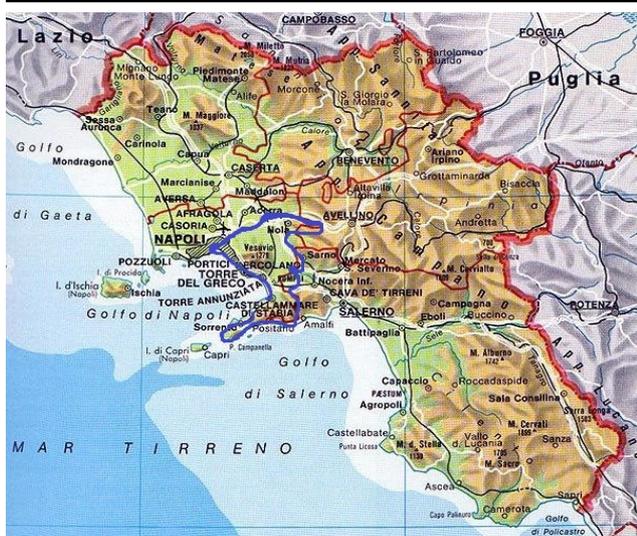
Given the significant social and economic impact of HBV infection in South Italy, we conducted a survey with the aim i) to show the updated prevalence of the disease and ii) to evaluate the economic impact of specific therapy in a population of 1,012,304 inhabitants of the Local Sanitary Agency (LSA) Naples 3 South Italy (LSA - NA 3 South).

## MATERIALS AND METHODS

According to ISTAT (Istituto nazionale di STATistica, National Institute of Statistics), the LSA - NA 3 South (Italy) comprises a population of 1,012,304 inhabitants, 491,406 males (M) and 520,898 females (F) within the Vesuvian area of about 680 km<sup>2</sup> (**Figure 1**), 56 municipalities and 12 sanitary districts.

Data were retrieved from a database of a specific monitoring program of the LSA - NA 3 South reporting all patient demographics and treatment plans for drugs against hepatitis B (drug, dosage and expenditure for single tablet) prescribed between January and December 2012. The analysis shown in this study is descriptive.

**Figure 1: The population of the study is comprised into the area marked with the blue line**



## RESULTS

Seven hundred seventy-eight patients with hepatitis B (prevalence: 0.08%) were

treated between January and December 2012; 579 were M (0.12%) and 199 F (0.04%). One hundred forty-five patients (111 M and 34 F) were treated with lamivudine 100 mg, for a total of 55,482 tablets (total expenditure: € 21.195); 289 patients (215 M and 74 F) were treated with entecavir 0.5 mg, for a total of 73,440 tablets (total expenditure: € 1,070,097); 196 patients (140 M and 56 F) were treated with tenofovir 245 mg, for a total of 48,210 tablets (total expenditure: € 444,737); 49 patients (35 M and 14 F) were treated with telbivudine 600 mg, for a total of 13,216 tablets (total expenditure: € 192,953); finally, 99 patients (78 M and 21 F) were treated with adefovir 10 mg for a total of 25,560 tablets (total expenditure: € 353,944) (**Table 1**).

**Table 1: A comparison of nucleoside and nucleotide analog inhibitors according to gender and costs**

Drug, dose in mg	No. of patients	Total expenditure in €
Lamivudine 100	145 (111 M, 34 F)	21.195
Entecavir 0.5	289 (215 M, 74 F)	1.070.097
Tenofovir 245	196 (140 M, 56 F)	444.737
Telbivudine 600	49 (35 M, 14 F)	192.953
Adefovir 10	99 (78 M, 21 F)	353.944

The total pharmaceutical cost was € 2,082,926. The most prescribed drug was entecavir 0.5 mg which had an impact on the total expenditure of 51%. Tenofovir 245 mg represented the 21%, adefovir 10 mg the 17% and telbivudine 600 mg the 9% of the total expense. The participation of lamivudine 100 mg to the total LSA expense was negligible (1%). In the observed population 42 patients switched to entecavir 0.5 mg treatment, 18 patients to tenofovir 245 mg and 10 patients to adefovir 10 mg because of a high rate of resistance (70% after 4 years).

**DISCUSSION**

Drugs against HBV have been developed independently and approved in clinic as monotherapy for patients with chronic hepatitis B.<sup>[3]</sup> Unfortunately, resistance resulting from the emergence of mutant strains of HBV is an important limitation in long-term administration of these drugs. Furthermore, other factors should be considered when choosing a first-line agent in the treatment of patients with HBV infection: efficacy of the treatment, patient tolerance to the therapy and safety of a specific regimen, cost of therapy.<sup>[6]</sup>

This study shows that the updated prevalence of HBV in our territory is low (< 1%). Furthermore, entecavir and tenofovir are currently the preferred oral antiviral agents for initial therapy due to their efficacy and low rate of HBV resistance; in the future, we expect an increase of their co-administration.

In 2012, the LSA - NA 3 South spent about € 70,000,000 for the pharmaceutical care of all patients referring to its sanitary districts. The costs for hepatitis B treatment (nucleoside/nucleotide analogues inhibitors) were € 2,082,926 (i.e. 3% of the total).

Thus, we can conclude that drugs against HVB have a moderate impact on the pharmaceutical spending. The major economic impact associated with HBV infection is primarily represented by the later development of cirrhosis and HCC. In fact, treatment of cirrhosis and HCC are about 2 and 6 times respectively more expensive than chronic hepatitis. Pharmaceutical research should be improved to identify new drugs as well as prognostic factors and specific molecular mechanisms<sup>[7]</sup> to arrest cirrhotic and neoplastic evolution of HBV infection.

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Not reported.

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