Analysis of The Consumption of Drugs for The Treatment of Peptic Ulcer and Gastroesophageal Reflux Issued on Prescription in A Four-Year Period

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ABSTRACT
Medicines indicated for the treatment of peptic ulcer and GERD are H2 blockers, proton pump inhibitors, antacids and mucoprotective agents. The analysis of the market of the medicines used for treatment of peptic ulcer and GERD, implies analysis of the range of these medicines registered in RNM, their presence on the list of medicines which costs are covered by the Health Insurance Fund, their financial and physical availability, as opposed to treatment recommendations of the above conditions according to MBD as well as a comparison of the range of these drugs available on the world markets. For the analysis of the consumptions of drugs issued at the expense of the Health Insurance Fund in pharmacies of the Republic of North Macedonia for a period of four years by number of realized prescriptions and total amounts of funds, we used the data published on the official website of the Health Insurance Fund of RNM. The increase in the total number of prescription drugs is probably due to the large number of patients diagnosed with peptic ulcer and GERD, as well as the recent regimen for issuing such medicines without a prescription. The total amounts for issued medicines at the expense of the Health Insurance Fund depend on the price and the number of issued prescriptions. The RNM is a county with a low standard and limited budget for medicine, in which the health policies are oriented towards saving the funds for procurement of drugs.

Key words: registered drugs, blockers, proton pump inhibitors, treatment

INTRODUCTION
Peptic ulcer - is a damage or lesion in the mucosa of the digestive tract, typically in the stomach or duodenum.
Gastroesophageal reflux disease - as a consequence of the return of gastric acid and the remaining gastric contents, there is a burning sensation in the chest, which can sometimes be accompanied by severe pain.
The analysis of the market of medicines used for the treatment of peptic ulcer and gastroesophageal reflux, includes analysis of the range of these medicines registered in our country, their presence on the List of medicines for which costs are covered by the Health Insurance Fund, financial and physical availability, as opposed to recommendations for treatment of the above conditions according to Evidence-Based Medicine as well as a comparison of the range of these medicines available on the world market.
Peptic ulcer occurs as a result of the inability of the gastroduodenal mucosa to protect epithelial cells from the action of hydrochloric acid and the enzyme pepsin.
The peptic ulcer may occur as a result of the following factors: hypersecretion of hydrochloric acid and pepsin, presence of Helicobacter pylori, certain medications, genetic factors and lifestyle factors. The most common complication of ulcer disease that occurs as an accompanying symptom is gastrointestinal bleeding.
Gastroesophageal reflux disease is a consequence of weakness of the lower esophageal sphincter, which forms a ring around the lower esophagus. Causes that can lead to weakness of the lower esophageal sphincter are: application of certain drugs (beta blockers, calcium channel blockers, nitrates, estrogen, progesterone), smoking, emotional stress, improper chewing.
The most serious complication that can occur in patients as a result of constant exposure to acid reflux is Barrett’s esophagus.
The main objectives of this paper are:
To make an analysis of the range of medicines used for the treatment of peptic ulcer and Gastroesophageal reflux on the market in the Republic of North Macedonia compared to the registered medicines in the world.
To compare the registered medicines in RNM and the medicines for which the costs are covered by the Health Insurance Fund of RNM, with the recommendations from Medicine based on evidence for medicine treatment of the above conditions.
To analyze the consumption of medicines for which the costs are covered by the Health Insurance Fund in the pharmacies of RNM in the period from 2015 to 2018 by number of realized prescriptions and total paid amount of funds per medicine.
To perceive the physical and financial availability of the recommended medicines to patients and doctors as an opportunity to choose the most appropriate medicine

**MATERIALS AND METHODS**
In order to achieve the set goals, we reviewed relevant literary data from primary, secondary and tertiary literature, the recommendations of Evidence-Based Medicine, official data from international and national medicine registers and the published reports on medicine consumption from the List of medicines which costs are covered by the Health Insurance Fund. For analysis of the consumption of drugs issued at the expense of the Fund in the pharmacies of RNM in the period from 2015 to 2018 by number of realized prescriptions and total paid amount of funds per drug, we used the data published on the official website of the Health Insurance Fund.

**RESULT AND DISCUSSION**
Obtained results are presented on Table 2, Table 3, Figure 1 and Figure 2.

### Table 1: Pharmacotherapy

<table>
<thead>
<tr>
<th>Peptic ulcer</th>
<th>Gastroesophageal reflux</th>
</tr>
</thead>
<tbody>
<tr>
<td>➢ Non-pharmacological methods</td>
<td>➢ Non-pharmacological methods</td>
</tr>
<tr>
<td>➢ Pharmacological methods</td>
<td>➢ Pharmacological methods:</td>
</tr>
<tr>
<td>H2 blockers</td>
<td>Antacids</td>
</tr>
<tr>
<td>Proton pump inhibitors</td>
<td>H2 blockers</td>
</tr>
<tr>
<td>Prokinetic drugs</td>
<td></td>
</tr>
<tr>
<td>Eradication of Helicobacter pylori:</td>
<td>Proton pump inhibitors</td>
</tr>
<tr>
<td>✓ Antibiotics- Triple therapy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>In patients with resistant and complicated gastroesophageal reflux disease:</td>
</tr>
<tr>
<td></td>
<td>- Surgical method (laparoscopic Nissen fundoplication)</td>
</tr>
</tbody>
</table>

### Table 2: Medicines used for the treatment of peptic ulcer and gastroesophageal reflux in RNM which costs are covered by Health Insurance Fund

<table>
<thead>
<tr>
<th>ATC code</th>
<th>International nonproprietary name - INN</th>
<th>Defined Daily Dose (DDD)</th>
<th>Administration route</th>
<th>Dosage form</th>
</tr>
</thead>
<tbody>
<tr>
<td>A02BA02</td>
<td>Ranitidine</td>
<td>0,3 g</td>
<td>O</td>
<td>Tablets</td>
</tr>
<tr>
<td>A02BA03</td>
<td>Famotidine</td>
<td>40 mg</td>
<td>O</td>
<td>Tablets</td>
</tr>
<tr>
<td>A02BC01</td>
<td>Omeprazole</td>
<td>20 mg</td>
<td>O</td>
<td>Capsules</td>
</tr>
<tr>
<td>A02BC02</td>
<td>Pantoprazole</td>
<td>40 mg</td>
<td>O</td>
<td>Tablets</td>
</tr>
<tr>
<td>A02BC03</td>
<td>Lansoprazole</td>
<td>30 mg</td>
<td>O</td>
<td>Capsules</td>
</tr>
</tbody>
</table>
Table 3: Recommended drugs for treatment of peptic ulcer and gastroesophageal reflux according to MBD, present on the worldwide, in RNM and on the positive list in RNM

<table>
<thead>
<tr>
<th>Recommended medicine according MBD</th>
<th>Registered medicine worldwide</th>
<th>Registered medicine in RNM</th>
<th>Medicines which costs are covered by the HIF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omeprazole</td>
<td>Omeprazole</td>
<td>Omeprazole</td>
<td>Omeprazole</td>
</tr>
<tr>
<td>Pantoprazole</td>
<td>Pantoprazole</td>
<td>Pantoprazole</td>
<td>Pantoprazole</td>
</tr>
<tr>
<td>Lansoprazole</td>
<td>Lansoprazole</td>
<td>Lansoprazole</td>
<td>Lansoprazole</td>
</tr>
<tr>
<td>Rabeprazole</td>
<td>Rabeprazole</td>
<td>Rabeprazole</td>
<td>Rabeprazole</td>
</tr>
<tr>
<td>Esomeprazole</td>
<td>Esomeprazole</td>
<td>Esomeprazole</td>
<td>Esomeprazole</td>
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<td></td>
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</tbody>
</table>

Comparison of the consumption of H2 blockers and proton pump inhibitors in RNM in relation to realized prescriptions for a period of four years

Fig.1: Realized prescriptions for a period of four years (2015-2018)

In the examined period:
The most commonly prescribed drug is: Ranitidine 150 mg
The largest increase in prescribed recipes is observed for: Pantoprazole 20 mg and Pantoprazole 40 mg
The least prescribed drugs are: Lansoprazole 15 mg and Famotidine 20 mg
Comparison of the consumption of H2 blockers and proton pump inhibitors in the Republic of North Macedonia in relation to the total amount by the HIF
The largest amount of funds are paid for: Lansoprazole 30 mg - 24,358,758 denars (2018)
The largest increase in funds paid for: Pantoprazole 40 mg - increase of 274.7%, Pantoprazole 20 mg - increase of 223.7%
Decreased value in funds paid for: Omeprazole 20 mg - reduced by 9.67%, Famotidine 20 mg - reduced by 9.58%

CONCLUSION

10 INN medicines for treatment of ulcer disease and gastroesophageal reflux have been registered in the Republic of North Macedonia, with a total of 40 names and 9 dosage forms.

Compared to the world market, according to current knowledge there are about fifty medicines from this group that are not registered in our country.
The list of the medicines which costs are covered by the Health Insurance Fund includes five INN medicines for the treatment of peptic ulcer and gastroesophageal reflux. All medicines which are recommended according to MBD are on the market in RNM.
The supply of insured persons with medicines used for the treatment of peptic ulcer and GERD is continuously moving upwards.

In the period from 2015 to 2018, most of the prescriptions were realized for Ranitidine, while the largest amounts were paid for Lansoprazole 30 mg

In the last ten years, in order to save funds in the Republic of N. Macedonia, the principle of generic drug policy has been implemented.
Newer generation medicines are lacking on the market in RNM.

REFERENCES


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