

Diaplant: Manufacturing technology and rationalization of costs of acute intestinal infection pharmacotherapy

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Abstract

Aim: To the development of the technological scheme of a new drug Diaplant, and rationalization of the costs of the acute intestinal infection (AII) pharmacotherapy. **Materials and Methods:** Development of the technological scheme of the new drug in tablets called Diaplant; analysis of the Ukraine pharmaceutical market of the analogs of Diaplant; pharmacoeconomic advantages of Diaplant compared with its analogs. **Results and Discussion:** In the pharmaceutical market of Ukraine, there are groups A07 antidiarrheals, intestinal anti-inflammatory/anti-infective agents according to Anatomical Therapeutic Chemical (ATC)-classification. ATC/defined daily dose (DDD)-analysis showed that the cost for DDD of Diaplant was 9.60 UAH. The total cost of the average recommended daily doses of separate drugs (nifuroxazide and plantaglucidum) ranged from 14 to 27.42 UA. The use of the drug Diaplant for the treatment 1000 patients requires 9600 UAH daily and 288000 UAH monthly. The use of other drugs with nifuroxazide and plantaglucidum requires from 14000 to 27420 UAH daily and from 420,000 to 822,600 UAH monthly. Savings of financial resources can be from 4400 to 17,820 UAH/day and – from 132,000 to 534,600 UAH/month for 1000 patients receiving Diaplant. It has been found that the Diaplant can provide the treatment from 1460 to 2860 patients instead of only 1000 patients receiving its analogs at the pharmaceutical market of Ukraine. **Conclusion:** The technological scheme of production of the drug in capsules Diaplant that contains nifuroxazide and plantaglucidum were developed for pharmacotherapy of AIIs. The use of Diaplant in clinical practice allows reducing the cost of pharmacotherapy from 46% to 286%.

Key words: Acute intestinal infections, pharmacoeconomic advantages, technological scheme

INTRODUCTION

One of the modern infectious problems in the world is the high level of morbidity of acute intestinal infections (AII). According to the WHO from 68.4 to 275 million cases of diarrheal diseases are registered in the world annually. More over diarrheal diseases kill around 525,000 children from year to year.^[1]

It is known that antimicrobial agents are very important in the treatment of AII. There are nifuroxazide, ceftriaxone, cefotaxime, trimethoprim, metronidazole, furazolidone, and others. Nifuroxazide is the drug of choice^[2,3] in this case. It is active substance against most pathogens of intestinal diseases such as *Staphylococcus aureus*, *Streptococcus faecalis*, *Campylobacter jejuni*, *Citrobacter* spp., and *Enterobacter* spp., including *Enterobacter cloacae*, *Escherichia coli*, *Hafnia*

spp., *Salmonella* spp., *Shigella* spp., *Vibrio cholerae*, and *Yersinia enterocolitica*.^[4] In the complex therapy of AII plantaglucidum can be used due to antispasmodic, anti-inflammatory activity has enveloping, hemostatics effects, ability to regulate the secretion of gastric juice and pectin substances has a protective effect in gastric ulcers.^[5] That is why we developed the new drug Diaplant, as a combination of the following substances: Nifuroxazide and pantaglugidum (leaf extract of *Plantago major*).^[6]

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Diaplant allows extending the spectrum of action and has a complex affect in the treatment of AII.^[7-9] To optimize the drug provision in the limited financing of the Ukraine Health Care System and low solvency of the population of Ukraine, it is necessary to use pharmacoeconomic justified drugs and treatment regimens.^[10-12]

The purpose of the research was the development of the technological scheme of a new drug Diaplant, and rationalization of the costs of the AII pharmacotherapy.

Objectives

The objectives of the study were the development of the technological scheme of the new drug Diaplant; analysis of the Ukraine pharmaceutical market of the analogs of Diaplant; research of the average recommended daily dose cost (defined daily dose [DDD]), the study of pharmacoeconomic advantages of Diaplant in comparison with the analogs.

MATERIALS AND METHODS

The material of the study was nifuroxazide and plantaglicidum (leaf extract of *P. major*); pharmaceutical market of the drugs for the treatment AII; DDD of drugs included in the study was determined according to data of the WHO by Anatomical Therapeutic Chemical (ATC)/DDD-methodology;^[13] average retail price data of medicines published in the weekly journal "Pharmacy" in Ukraine in May, 2017.^[14] Methods: Analysis of the pharmaceutical market of Ukraine, ATC/DDD-methodology; cost minimization analysis, calculation of NNT-coefficient.

The new original drug Diaplant^[6] was developed [Table 1].

In the modern pharmaceutical market, it has been founded the presence of Diaplant analogs such as nifuroxazide, nifuroxazide-zdorovie, enterofuryl, stopdiar (international nonproprietary names [INN] nifuroxazide), and plantaglicid-zdorovyie (INN leaf extract of *P. major*).

DDD of nifuroxazide was determined according to the WHO data, 2017. DDD of plantaglicidum was not determined according to the WHO, so average daily doses were calculated as average manufacturer recommended daily dose for adults. The cost of the average recommended daily dose of the Diaplant was calculated as the sum of the cost of the average recommended daily doses of nifuroxazide and plantaglicidum, considering the practice in the previous studies.^[15]

Calculation of cost of the average daily dose for adults in UAH by the formula:

$C = P/T \times D$, where,

C – Cost of average daily doses for adults, UAH;

P – Cost of medicine packing of investigated drugs, UAH;

Table 1: Composition of Diaplant

Agents	g
Nifuroxazide	0.200
Leaf extract of <i>Plantago major</i>	0.200
Excipients	
Povidone 29/32	0.005
Saccharose	0.200
Pectin	0.009
Corn starch	0.003
Magnesium stearate	0.003
	0.002
Total	0.620

T – Number of tablets in medicine packaging, units;

D – Average daily dose for adults.

Cost-minimization analysis was performed in the context of analogs cost (in their equal efficacy) by the formula:^[10-12]

$CMA = DC_1 - DC_2$, where,

CMA – The difference in the cost of compared drugs, UAH,

DC_1 – Direct costs when using the cheapest drugs, UAH,

DC_2 – Direct costs when using the most expensive drugs, UAH,

NNT - Coefficient (number need to treat) shows the ratio of the number of patients receiving the most expensive drugs to the number of patients receiving the cheapest drugs, and it was calculated by the formula:^[16]

$NNT = C_1/C_2$, where,

NNT - Coefficient of the number of patients receiving the most expensive drugs to the number of patients receiving the cheapest drugs,

C_1 – Direct costs when using the most expensive drugs, UAH,

C_2 – Direct costs when using the cheapest drugs, UAH.

RESULTS AND DISCUSSION

In the pharmaceutical market of Ukraine, there are groups A07 antidiarrheals, intestinal anti-inflammatory/anti-infective agents according to ATC-classification:^[10]

1. A07A – Intestinal anti-infective (antibiotics, sulfonamides, imidazole derivatives, and nifuroxazide);
2. A07B – Intestinal adsorbents (charcoal preparations);
3. A07C – Electrolytes with carbohydrates (salt solutions for oral rehydration);
4. A07D – Antipropulsives (loperamide);
5. A07E – Intestinal anti-inflammatory agents (corticosteroids of locally action);
6. A07F – Antidiarrheal microorganisms (*Lactobacilli*, and *Saccharomyces boulardii*);
7. A07X – Other antidiarrheals (racecadotril).

The technological scheme of production of the drug in capsules Diaplant shows the technological process at each stage [Figure 1].

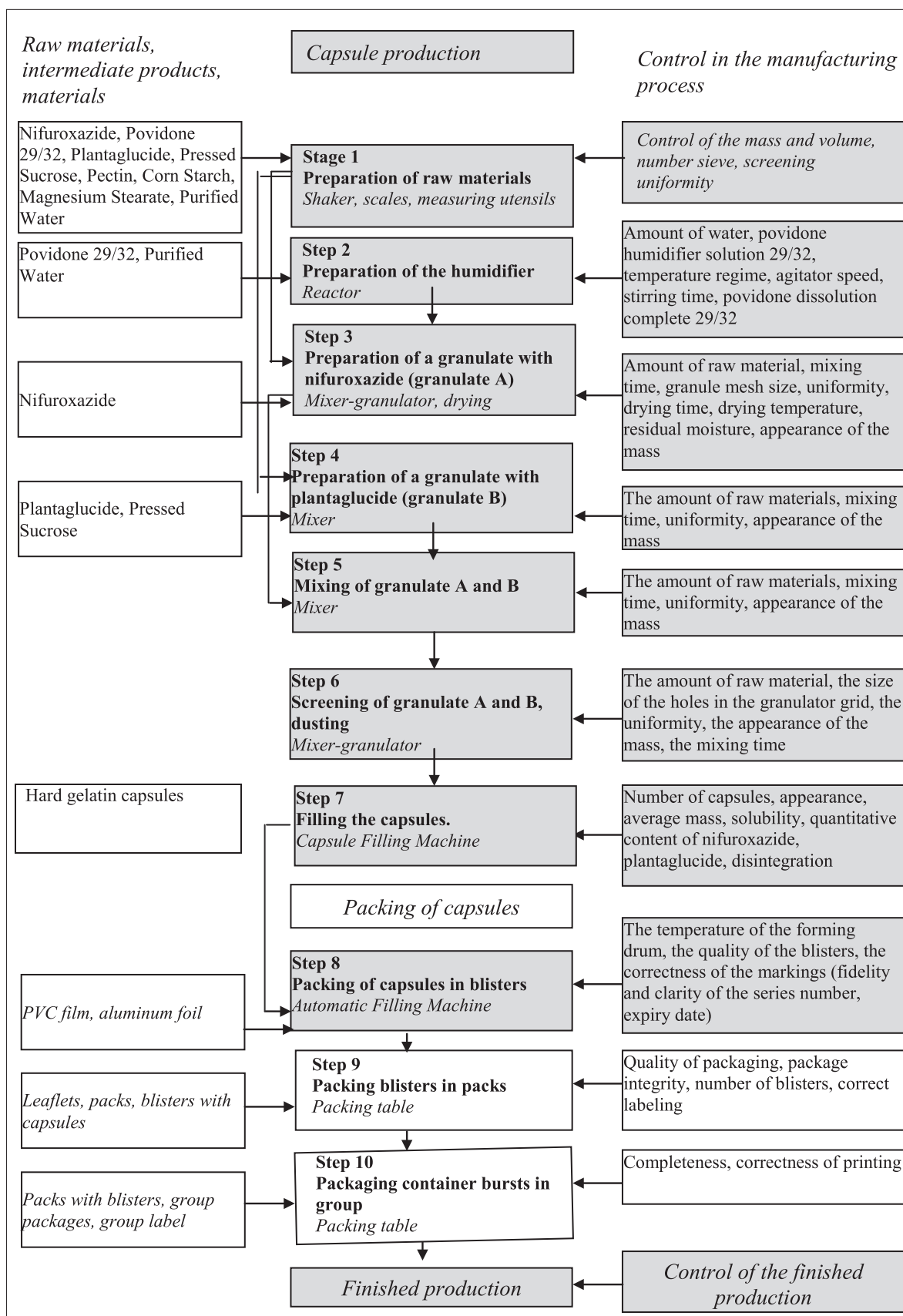


Figure 1: Technological scheme of production of the Diaplant

There are granules of 2 g No. 25 for the preparation of oral solution, the cost of package is 204.46 UAH, and the average daily dose recommended by the manufacturer is 8.18 UAH. DDD cost of drugs with INN nifuroxazide ranged from 5.82 to 19.24 UAH in the pharmaceutical market of Ukraine [Table 2].

ATC/DDD-analysis showed that the cost for DDD of Diaplant was 9.60 UAH. The total cost of the average recommended daily doses of separate drugs (nifuroxazide and plantaglucidum) ranged from 14 to 27.42 UAH [Table 3].

According to the methodology of cost minimization analysis, it has been found that the savings of financial resources ranged from 4.40 to 17.82 UAH per 1 patient/day in the context of the minimum and maximum cost of the researched drugs:

$$CMA_{\text{minimum cost}} = DC_1 - DC_2 = 14 - 9.60 = 4.40 \text{ UAH,}$$

$$CMA_{\text{maximum cost}} = DC_1 - DC_2 = 27.42 - 9.60 = 17.82 \text{ UAH}$$

The use of the drug Diaplant for the treatment 1000 patients requires 9600 UAH daily and 288,000 UAH monthly. The

use of other drugs with nifuroxazide and plantaglucidum requires from 14,000 to 27,420 UAH daily and from 420,000 to 822,600 UAH monthly [Graph 1].

Savings of financial resources can be from 4400 to 17,820 UAH/day and – from 132,000 to 534,600 UAH/month for 1000 patients receiving Diaplant.

The obtained results became the basis for further pharmacoeconomic research by cost minimization analysis and calculation of NNT-coefficient.

$$NNT_{\text{minimum cost}} = C_1/C_2 = 14/9.60 = 1.46$$

$$NNT_{\text{maximum cost}} = C_1/C_2 = 27.42/9.60 = 2.86.$$

Hence, it has been found that the Diaplant can provide the treatment from 1460 to 2860 patients instead of only 1000 patients receiving its analogs at the pharmaceutical market of Ukraine.

Thus, the use of Diaplant in clinical practice allows reducing the cost of pharmacotherapy of AII from 46% to 286% considering the prices of the cheapest and most expensive analogs of Diaplant.

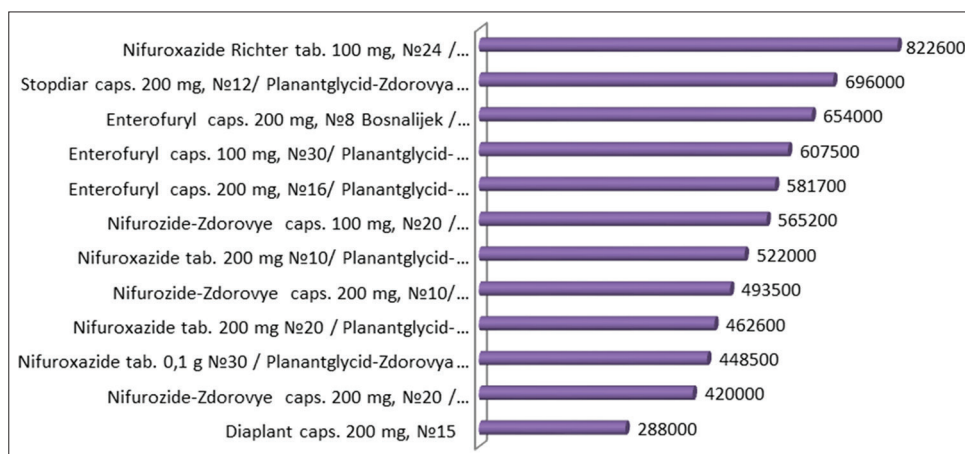
Table 2: Cost of average manufacturer recommended daily dose of research drugs

Trade name	INN	Cost of average recommended daily dose, UAH
Diaplant capsules 200 mg, No. 15	Nifuroxazide/leaf extract of <i>Plantago major</i>	9.60
Plantaglucid-Zdorovie 2 g No. 25	Leaf extract of <i>Plantago major</i>	8.18
Nifuroxazide-Zdorovie capsule 200 mg, No. 20	Nifuroxazide	5.82
Nifuroxazide tablet 0.1 g No. 30 Terno parma (Ukraine, Ternopil)	Nifuroxazide	6.77
Nifuroxazide tablet 200 mg No. 20 Kyivmedpreparat (Ukraine, Kiev)	Nifuroxazide	7.24
Nifuroxazide-Zdorovie capsule 200 mg, No. 10	Nifuroxazide	8.27
Nifuroxazide tablet 200 mg No. 10 Kyivmedpreparat (Ukraine, Kiev)	Nifuroxazide	9.22
Nifuroxazide-Zdorovie capsule 100 mg, No. 20	Nifuroxazide	10.66
Enterofuryl capsule 200 mg, No. 16 Bosnalijek (Republic of Bosnia and Herzegovina)	Nifuroxazide	11.21
Enterofuryl capsule 100 mg, No. 30 Bosnalijek (Republic of Bosnia and Herzegovina)	Nifuroxazide	12.07
Enterofuryl capsule 200 mg, No. 8 Bosnalijek (Republic of Bosnia and Herzegovina)	Nifuroxazide	13.62
Stopdiar capsule 200 mg, No. 12 Gedeon Richter (Hungary)	Nifuroxazide	15.02
Nifuroxazide Richter tablet 100 mg, No. 24 Gedeon Richter (Hungary)	Nifuroxazide	19.24

INN: International nonproprietary names

Table 3: Cost of average recommended daily dose of research drugs

Trade name	INN	Cost of average recommended daily dose, UAH
Diaplant capsule 200 mg, No. 15	Nifuroxazide/leaf extract of <i>Plantago major</i>	9.60
Nifuroxazide-zdorovie capsule 200 mg, No. 20/ Plantaglucid-Zdorovie 2 g No. 25	Nifuroxazide/leaf extract of <i>Plantago major</i>	14
Nifuroxazide tablet 0.1 g No. 30 Terno parma (Ukraine, Ternopil)/Plantaglucid-Zdorovie 2 g No. 25	Nifuroxazide/leaf extract of <i>Plantago major</i>	14.95
Nifuroxazide tablet 200 mg No. 20 Kyivmed preparat (Ukraine, Kiev)/Plantaglucid-Zdorovie 2 g No. 25	Nifuroxazide/leaf extract of <i>Plantago major</i>	15.42
Nifuroxazide-Zdorovie capsule 200 mg, No. 10/ Plantaglucid-Zdorovie 2 g No. 25	Nifuroxazide/leaf extract of <i>Plantago major</i>	16.45
Nifuroxazide tablet 200 mg No. 10 Kyivmedpreparat (Ukraine, Kiev)/Plantaglucid-Zdorovie 2 g No. 25	Nifuroxazide/leaf extract of <i>Plantago major</i>	17.4
Nifuroxazide-zdorovie capsule 100 mg, No. 20/ Plantaglucid-Zdorovie 2 g No. 25	Nifuroxazide/leaf extract of <i>Plantago major</i>	18.84
Enterofuryl capsule 200 mg, No. 16 Bosnalijek (Republic of Bosnia and Herzegovina)/Plantaglucid-Zdorovie 2 g No. 25	Nifuroxazide/leaf extract of <i>Plantago major</i>	19.39
Enterofuryl capsule 100 mg, No. 30 Bosnalijek (Republic of Bosnia and Herzegovina)/Plantaglucid-Zdorovie 2 g No. 25	Nifuroxazide/leaf extract of <i>Plantago major</i>	20.25
Enterofuryl capsule 200 mg, No. 8 Bosnalijek (Republic of Bosnia and Herzegovina)/Plantaglucid-Zdorovie 2 g No. 25	Nifuroxazide/leaf extract of <i>Plantago major</i>	21.8
Stopdiar capsule 200 mg, No. 12 Gedeon Richter (Hungary)/Plantaglucid-Zdorovie 2 g No. 25	Nifuroxazide/leaf extract of <i>Plantago major</i>	23.2
Nifuroxazide Richter tablet 100 mg, No. 24 Gedeon Richter (Hungary)/Plantaglucid-Zdorovie 2 g No. 25	Nifuroxazide/leaf extract of <i>Plantago major</i>	27.42

**Graph 1:** The cost of monthly pharmacotherapy (UAH)

CONCLUSIONS

1. The technological scheme of production of the drug in capsules Diaplant that contains nifuroxazide and plantaglucidum were developed for pharmacotherapy of AIIIs

2. Modern pharmaceutical market of Ukraine of group A07 according ATC-classification was analyzed, and it was established the presence of drugs – analogs of Diaplant

3. It has been found that the cost for DDD of Diaplant was 9.60 UAH. The total cost of the average recommended

daily doses of Diaplant analogs ranged from 14 to 27.42 UAH

4. The use of Diaplant in clinical practice allows reducing the cost of pharmacotherapy from 46% to 286%.

PROSPECTS FOR FURTHER RESEARCH

It will be possible to identify cost-effectiveness and cost-utility advantages of investigated drugs based on the obtained data of the research.

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