

# Lignin based product research

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## Evaluation of the efficacy of Filtrum and Lactofiltrum in patients with irritable bowel syndrome

Indication / Claim	Product / Ingredient studied	Dosage and administration route	Duration of treatment
Irritable Bowel Syndrome	Filtrum (lignin) Lactofiltrum (lignin 85% + lactulose 15 %)	The aim of the study was the development of dosages, the course of therapy and the time of administration. In order to select the optimal dose, the drugs were prescribed in gradually increasing doses: from 3 to 9 tablets per day for 1 - 1.5 hours before meals and other drugs. Optimum therapeutic dose was 2 tablets 3 times a day.	10 days
Type of evidence (scientific evidence)	Study design	Study population	Limitations of the study
Clinical research	Open label, comparative	25 - 80 years old with stool disorder of various origin 60 subjects (16 male/44 female)	GCP non-compliant; Not randomised; Open; No results for control group assessed; No method description on dose finding part of the study; no statistical analysis description;

### Summary of findings

Four groups of subjects:

- 30 subjects with IBS with diarrhoea or with constipation or with inconsistent stool pattern; on standard therapy; control group (15 with IBS with diarrhoea, 10 with IBS with constipation and 5 with inconsistent pattern)
- 15 subjects with IBS with diarrhoea on FILTRUM
- 10 subjects with IBS with constipation on LACTOFILTRUM
- 5 subjects with IBS with inconsistent stool pattern on LACTOFILTRUM

Seven symptoms' dynamics was recorded: abdominal pain, meteorism, dyspepsia, abdominal tenderness, constipation, diarrhoea, inconsistent stool.

It is shown that on the 14-th day of treatment in all patients with irritable bowel syndrome, who administrated Lactofiltrum tablets constipations, abdominal distensions and borborygmus were stopped completely. Constipations remained in 2 patients, as well as in two patients on baseline therapy, but intestinal pains, distensions, borborygmus were reduced. In group administered Lactofiltrum tablets, effect was achieved to the 10th day. In patients on baseline therapy these symptoms disappeared by the 14th day. In Filtrum group, all the symptoms in all patients disappeared on day 10, while in the control group symptoms did not disappear in 3 subjects on day 10, and in 2 subjects on day 14.

## Clinical research of Filtrum and Lactofiltrum

Indication / Claim	Product / Ingredient studied	Dosage and administration route	Duration of treatment
1. Atopic Dermatitis	1. Lactofiltrum	1. 6 months to one year: 1/3 of a tablet 3 times a day	1. 14 days
2. Intestinal Dysbacteriosis	2. Lactofiltrum	2. 1 to 3 year: 1/2 of a tablet 3 times a day	2. 14 days
3. Acute Enteric Infections	3. Filtrum	3. >3 years: 1 tablet 3 times a day	3. 7 days

Type of evidence (scientific evidence)	Study design	Study population	Limitations of the study
Clinical research	NA	Children aged 6 months to 3 years 120 subjects: 1. 40 AD 2. 40 Dysbiosis 3. 40 AEI	GCP non-compliant; Not randomized; not controlled;

### Summary of findings

1. In the more than 50% patients in 7 days from beginning intake of Lactofiltrum tablets edema, exudation, and excoriation were stopped, the skin itch was reduced, and the sleep was normalized. On the 14th day of treatment light erythema remained in the 2 (5%) patients.

2. In 32 patients (80%) the abdominal pains and the tenderness were stopped in two days. In 4 patients (10%) stool frequency more than 3 times a day remained for 7 days. The complete normalization of intestines passage to the 14-th day of treatment was observed in all patients. Analysis of dynamics of changes of feces for bacteriosis showed that in the 12 children happened complete normalization of micro flora composition. Initially this group had gruel or liquid stool with changes (reduction) of the level of lacto and bifidobacteria. In 15 patients, reduction of specific weight of coccal flora on the background of growth of lacto- and bifidoflora was noted. Opportunistic pathogenic flora was disappeared in the 7 patients.

3. In all patients, admission was accompanied by dyspeptic Syndrome, manifested in unstable liquid stool, meteorism, and regurgitation. Changes in the stool were accompanied by the appearance in the fecal masses of leukocytes 10-15 in the field of view, mucus undigested fiber, neutral fat. During treatment on days 3-4, more than 50% of children had normalized frequency and consistency of stool. On the 7th day. All patients had complete normalization of intestinal dysfunction. All patients underwent monotherapy on the background of oral rehydration, carried out according to the standard scheme (saline solutions, glucose, physiological saline).

## Clinical research of Filtrum and Lactofiltrum

Indication / Claim	Product / Ingredient studied	Dosage and administration route	Duration of treatment
1. Atopic Dermatitis accompanied by constipation or diarrhoea.	Group 1: Standard therapy + Lactofiltrum 1A: 3 times a day / 1B: 4 times a day Group 2: Standard therapy + Filtrum 2A: 3 times a day / 2B: 4 times a day Group 3: 3A: Filtrum 3 times a day 3B: Lactofiltrum 3 times a day Group 4: Standard therapy	Group 1A and 2A: children 3 to 7 years - 1 tablet 3 times a day children 7 to 12 years – 1-2 tablets 3 times a day children 12 years – 2-3 tablets 3 times a day Group 1B and 2B: children 3 to 7 years - 1 tablet 4 times a day children 7 to 12 years – 1-2 tablets 4 times a day children 12 years – 2-3 tablets 4 times a day	14 days
Type of evidence (scientific evidence)	Study design	Study population	Limitations of the study
Clinical research	NA	48 children, 3-15 yrs. Old Group 1A: 7 / Group 1B: 8 Group 2A:7 / Group 2B: 8 Group 3A: 4 / Group 3B: 4 Group 4: 10	GCP non-compliant; Not randomized; Inappropriate design; Poor statistical analysis; Results for control group are not presented properly;

### Summary of findings

Dynamics of clinical manifestations of atopic dermatitis in the group 1 and 2 were better than in control group. The reliable differences between two schemes of intake of the drug (3 times and 4 times a day) were not found. Administration of Lactofiltrum tablets is recommended at functional constipations, meteorism in children with atopic dermatitis. Constipation resolved in 78.6% of subjects in Lactofiltrum group, comparing 36.4 in control group. In Filtrum group, diarrhoea disappeared in 90% of subjects during 1-2 days, while in control group it happened in 26% of subjects. In the analysis of two schemes of administration - three times a day and four times a day, significant differences between these schemes was not identified. No AE were recorded in Lactofiltrum groups. In Filtrum groups, one subject experienced allergic reaction in a form of papular rash and exacerbation of AD. After discontinuation of Filtrum, the reaction disappeared in a few days.

## Clinical research of Filtrum and Lactofiltrum

Indication / Claim	Product / Ingredient studied	Dosage and administration route	Duration of treatment
2. Bronchial asthma	Group 1: Standard therapy + Lactofiltrum 1A: 3 times a day / 1B: 4 times a day Group 2: Standard therapy + Filtrum 2A: 3 times a day / 2B: 4 times a day Group 3: Standard therapy	Group 1A and 2A: children 3 to 7 years - 1 tablet 3 times a day children 7 to 12 years – 1-2 tablets 3 times a day children 12 years – 2-3 tablets 3 times a day Group 1B and 2B: children 3 to 7 years - 1 tablet 4 times a day children 7 to 12 years – 1-2 tablets 4 times a day children 12 years – 2-3 tablets 4 times a day	14 days
Type of evidence (scientific evidence)	Study design	Study population	Limitations of the study
Clinical research	NA	40 children, 3-16 years old Group 1A: 7 / Group 1B: 8 Group 2A:7 / Group 2B: 8 Group 3: 10	GCP non- compliant; Not randomized; Inappropriate design; Poor statistical analysis; Results for control group are not presented properly;

### Summary of findings

When analyzing two therapy regimens (using enterosorbent-and without them) significant differences in the timing relief of bronchial obstruction syndrome was not recorded. In the analysis of two schemes of administration - three times a day and four times a day, significant differences between these schemes was not identified.

## CLINICAL STUDY OF EFFECTIVENESS OF THE PHARMAC COMPOSITION WHICH INCLUDES PROTON PUMP INHIBITOR (OMEPRAZOLE) AND PREBIOTIC (LACTULOSE) IN THE COMPLEX THERAPY OF DUODENAL ULCER

Indication / Claim	Product / Ingredient studied	Dosage and administration route	Duration of treatment
Pylori eradication in Duodenal Ulcer patients	Omeprazole Lactulose Filtrum	Group 1: Omeprazole 20 mg 2 times a day (40mg) / Lactulose 500mg 2 times a day (1000mg) Group 2: Omeprazole 20 mg 2 times a day (40mg) / Lactulose 1000mg 2 times a day (2000mg) Group 3: Omeprazole 20 mg 2 times a day (40mg) / Filtrum 800mg 3 times a day (1600mg) Group 4 (historical control): Standard of care	40 days
Type of evidence (scientific evidence)	Study design	Study population	Limitations of the study
Clinical research	Open label, randomised, comparative	40 adults 16-51 years Group 1: 10 / Group 2: 10 Group 3: 10 / Group 4 (historical control): 10	GCP non-compliant; no description of randomisation; poor statistical analysis; no statistical analysis description;

### Summary of findings

Research objective was to evaluate efficacy of complex eradication therapy for *Helicobacter pylori* using combined administration of proton pump inhibitor and prebiotic, in duodenal ulcer patients without the use of antibiotic therapy. Three groups of subjects and as a "historical control", 10 medical records of the patients with duodenum ulcer illness, who in the process of treatment received standard ulcer therapy were used. In patients with DU, associated with *Helicobacter pylori*, use of prebiotic lactulose in complex therapy, without using antibiotics, there is a reported significant clinical effect, as compared to the group of patients who received standard therapy. Differences are marked with different time for disappearance of dyspeptic conditions, stopping the pain syndrome and improving intestinal function. According to the results of endoscopic examinations in patients with the administration of lactulose there is a marked positive influence in endoscopic visible condition of the mucous tissues of stomach and duodenum, which is shown as scarring of ulcers earlier than in the control group, as well as disappearing of the inflammation signs and decreasing lesions in the stomach and duodenum. Complete eradication of *Helicobacter pylori* from the mucous tissue of the duodenum after administration of 2.0 g of lactulose daily was achieved in 100% of cases (in the control group only in 29% of cases), with distinct clinical improvement of patients' conditions. Including Filtrum does not affect significantly the reparation process and eradication of *Helicobacter pylori* from the duodenum mucous tissues.

## Study of clinical efficacy of enterosorbent “FILTRUM- SAFARI” in the complex treatment of moderate forms of acute intestinal infections of viral etiology of “osmotic” diarrhea in children.

Indication / Claim	Product / Ingredient studied	Dosage and administration route	Duration of treatment
Viral AEI in children	Filtrum Safari	NA	3-5 days

Type of evidence (scientific evidence)	Study design	Study population	Limitations of the study
Clinical research	Open label, comparative	Children age 3-13, 45 subjects Group 1: 30 Group 2: 15	GCP non- compliant; Not randomized; Inappropriate design; Poor statistical analysis; Results for control group are not presented properly;

### Summary of findings

“FILTRUM-SAFARI” enterosorbent during basic therapy of acute enteric infection of viral etiology among children significantly increase clinical and sanitate efficiency of the conducted therapy. An “excellent” clinical effect with stool frequency and character normalization on the 3-rd day during enterosorbent treatment took place among 80% of patients, while using the background therapy – only in 33.3% of cases. In case of clinical recovery after 4-5 days of treatment the therapy efficiency was assessed as “good” and in the comparison group it was among 66.7% of patients, while in the patient group with enterosorbent treatment – only in 20% of cases. No significant adverse reactions presented.

## CLINICAL EFFICIENCY OF FILTRUM-STI IN THERAPY OF ACUTE ENTERIC INFECTIONS IN CHILDREN AND ITS INFLUENCE ON BIO-CHEMICAL VALUES OF ENDOTOXICOSIS AND MICROBIOCENOSIS OF INTESTINAL TRACT

Indication / Claim	Product / Ingredient studied	Dosage and administration route	Duration of treatment
Bacterial AEI in children	Filtrum + standard therapy Standard therapy	Oral tablets: a. 1 to 3 – 1/2-1 tablet 3 times a day; b. 4 to 7 – 1-1.5 tablets 3 times a day; c. older than 7 – 2 tablets 3-4 times a day. to be taken 1-1.5 hours after meal	5 days
Type of evidence (scientific evidence)	Study design	Study population	Limitations of the study
Clinical research	Open label, comparative	Children age 1-14 with bacterial AEI 50 subjects (30+20)	GCP non-compliant; Not randomized; Aetiology in different groups is not described;

### Summary of findings

Clinical efficiency of therapy was estimated according to dynamic of main syndromes of acute period of AEI which included duration of fever, intoxication and local signs of bacterial diarrhea. All patients underwent combination treatment, which included antibacterial and pathogenetic therapy. Antibacterial therapy was administered with due regard to regional sensitivity of causative agents of enteric infections and included cephalosporins of III generation (cefotaxime), aminoglycosides of II-III generation (netilmicin sulfate, amikacin). The course of etiotropic treatment lasted 7 days. Pathogenetic measures included diet correction, rehydration therapy, enzyme replacement therapy, probiotics. Positive influence of the drug on duration of local syndrome, that was characterized by faster reduction of flatulence and diarrhea syndrome, was observed. If enterosorption was not used, those symptoms were present for longer time. Visualization of pathological foreign matters in stool associated with therapy by means of Filtrum-STI decreased substantially.



## Filtrum STI in the presence of enteric infection in children

Indication / Claim	Product / Ingredient studied	Dosage and administration route	Duration of treatment
Bacterial AEI in children	Filtrum	Daily dosage was from 0.04 to 0.12 g per 1 kg of the body weight Oral tablets: <3 yr: 1/3 - 1 tablet >3 yr:1 - 2 tablets	3 - 6 days 3 days:8 4 days : 11 5 days: 28 6 days: 2
Type of evidence (scientific evidence)	Study design	Study population	Limitations of the study
Clinical research	Open label, comparative	Children age 6 months -14 years with bacterial AEI 50 subjects	GCP non- compliant; Not randomized; No dose finding method description, to justify dosing recommendation;

### Summary of findings

Good tolerance of Filtrum STI and the effects of its influence over the course of acute enteric infection in children from 6 months permit to evaluate it as a separate pathogenetic factor that can be used for treatment of mild and moderately severe acute enteric infections that is mostly affecting upper segments of the gastrointestinal tract.

The curative effect of Filtrum STI that reduces the term of showing symptoms of acute enteric infection including symptoms of intoxication can give a considerable economic effect. Duration of treatment is 5-7 days. It is advisable to develop a paediatric form of this drug calculating the dosage based on the patient's body weight (0.07 g/kg is a daily dosage).

## EFFICIENCY OF FILTRUM STI IN TREATMENT OF ACUTE ENTERIC INFECTIONS IN CHILDREN

Indication / Claim	Product / Ingredient studied	Dosage and administration route	Duration of treatment
AEI in children	Filtrum STI	Less 6 months – 1/4 of a tablet 3-4 times a day; 6 months to 1 year – 1/3 of a tablet 3-4 times a day; 1 to 3 years – 1/2 - 1 tablet 3 times a day; 4 to 7 years – 1-1.5 tablets 3 times a day; Older than 7 years – 2 tablets 3-4 times a day	3-5 days
Type of evidence (scientific evidence)	Study design	Study population	Limitations of the study
Clinical research	Open label, comparative	Children age between 2 months and 13 years old with AEI 119 subjects	GCP non-compliant; Not randomized;

### Summary of findings

Filtrum STI showed a positive impact on general toxicity syndrome of AEI in the form of fever relief, reduction in severity of intoxication symptoms, termination of nausea and vomiting, and appetite improvement. When using Filtrum STI, normalization of stool improved and by 4-6 days of illness it became normal; children's pain abdominal syndrome and meteorism reduced. Filtrum STI provided the best therapeutic effect in viral diarrhea: febrile reaction was reduced faster and painfulness in abdomen palpation was the lowest. The use of Filtrum STI enterosorbent in the treatment of AEI in children significantly increases the effectiveness of treatment and leads to a more rapid clinical recuperation. The method of enterosorption with prescription of Filtrum STI in the treatment of AEI in children can be recommended for use in clinical practice.

## Clinical Trial of Filtrum

Indication / Claim	Product / Ingredient studied	Dosage and administration route	Duration of treatment
AEI in adults	Filtrum	2 tablets 4 times a day within 5 days or shorter period in case of regression of main clinical signs.	5 days

Type of evidence (scientific evidence)	Study design	Study population	Limitations of the study
Clinical research	Open label, comparative	Adults, 17-80 years old with AEI 60 subjects (45+15)	GCP non-compliant; Not randomized; poor report quality;

### Summary of findings

Filtrum is characterized by high clinical efficiency in treatment of patients with acute enteric infections accompanied by diarrhea syndrome: acute dysentery, gastrointestinal form of salmonellosis, gastroenteritis form of food toxic infection that is marked by reduction of duration of core clinical signs in these infections associated with administration of the above-mentioned drug. In combination with traditional etiopathogenetic therapy in acute dysentery, therapy in gastrointestinal form of salmonellosis and food toxic infections, administration of Filtrum in a dose of 2 tablets 4 times a day within 5 days provides an adequate positive effect. Filtrum does not cause adverse effects in patients with acute enteric infections accompanied by diarrhea and requires extension of a range of indications to administration in case of the above-mentioned diseases. Filtrum can be recommended as a drug of choice in mild course of food toxicoinfections and salmonellosis, and in complex therapy of the lungs; moderate and severe forms of dysentery, food toxic infections and salmonellosis.

## Clinical efficacy of Filtrum in 51 patients with chronic lead intoxication

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Indication / Claim	Product / Ingredient studied	Dosage and administration route	Duration of treatment
Chronic Lead Intoxication	Filtrum	2 tablets 3 times a day	30 days

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Type of evidence (scientific evidence)	Study design	Study population	Limitations of the study
Clinical research	NA	51 subjects (42 male and 9 female) between 30 and 60 years of age	GCP non-compliant; Not randomized; not controlled; no statistical analysis description; poor safety analysis;

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### Summary of findings

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Efficacy parameters were: subjective status of the patient and coproporphyrin in urine. The efficacy was evaluated as very good by 21 patients (41%), as good by 19 patients (37%) and 11 people. (21%) were not able to specify. The main factors for improving subjective status: Headache relief - 70%, increase of working capacity - 60%, normalization of sleep - 40%, reduction of abdominal pain after ingestion of food - 17%, disappearance of flatulence - 10%, cessation of constipation - 13%, daily defecation - 100%, formed stool - 90%, reduction of heartburn - 10%, decrease in angina attacks - 2%, decrease in paraesthesia in extremities - 30%, reduction of pain in the joints - 34%, normalization of menstrual cycle - 1%. Positive effect of "Filtrum" on porphyrin metabolism was recorded in 45 patients, which is 88%. Six patients had porphyrins in the urine above normal values (more than 160), which was associated with increase in chronic intoxication caused by unhealthy lifestyle (consuming alcohol).

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## Clinical efficacy of Filtrum oral sorbent in patients with end-stage renal insufficiency on haemodialysis

Indication / Claim	Product / Ingredient studied	Dosage and administration route	Duration of treatment
End -Stage Kidney Disease	Filtrum	3 tablets 3 times a day Group 1: weight 40 to 60 kg (8 people), Filtrum with an interval of one month (April-pause-June-pause-August); Group 2: weight 60 to 80 kg (10 people), Group 3: weight of more than 80 kg (6 people), Group 4: weight of more than 80 kg (6 people), were treated for 3 months in a row and then after the one-month break for 30 days more (April-May-June-pause- August).	5 months
Type of evidence (scientific evidence)	Study design	Study population	Limitations of the study
Clinical research	NA	30 subjects 16-63 years of age	GCP non- compliant; Not randomized; not controlled; no statistical analysis description; poor design; no statistical analysis description;

### Summary of findings

All patients were divided into 4 groups. The best effect was observed in Group 2: 70% of patients had improvement in subjective well-being, increased physical activity (50%), reduction or disappearance of skin itch (40%) and normalization of sleep (20%). In Group 4 : iprovement of subjective well-being (improved appetite and sleep, reduced nausea in the mornings and itching) was observed in 50% of cases. Those changes in the state were observed in 37.5% of patients in the Group 1. In the Group 3 positive results were almost not observed. In all groups, the pre-dialysis urea significantly increased (at average of 14%) and the percentage of its removal during a dialysis session increased (at average of 5.2%), which fact may be explained by improvement of appetite (it constitutes a positive point in the treatment of patients with chronic renal failure), as well as the active implementation of used dialyzers clearance characteristics. Changes in serum creatinine level during treatment with sorbent showed an increase of 6% of its indicators before dialysis, in our opinion, do not represent a reliable confirmation of increased physical activity of patients, and increase of the excretion rate (an average of 4.6%) for the procedure can be explained by absolute increase of pre-dialysis level.

## Clinical and sanifying efficacy of food supplement FILTRUM SAFARI in children with laboratory-confirmed viral diarrhoea

Indication / Claim	Product / Ingredient studied	Dosage and administration route	Duration of treatment
Viral AEI in children	Filtrum Safari + Standard therapy Smectite + Standard therapy	<3 yr: 1/2 tablet 3 times a day >3 yr: 1 tablet 3 times a day NA	5 days

Type of evidence (scientific evidence)	Study design	Study population	Limitations of the study
Clinical research	NA	49 subjects 1-8 years of age	GCP non-compliant; Not randomized; no placebo;

### Summary of findings

A significant reduction in the duration of vomiting and, as a consequence – exsiccosis was detected in the group treated with FILTRUM SAFARI. Shorter terms of elimination of diarrhoea and normalization of stool were recorded. In the dynamics of the treatment, the proportion of children, sanitized from the initially detected viruses, was equal to 0.25 in the group treated with Filtrum SAFARI and 0.10 - in the control ( $p = 0.11$ ), the proportion of cases of nosocomial viruses contamination (new virus or increased amount of viruses) – was 0.31 and 0.55 ( $p = 0.08$ ) respectively. Difference between compared groups after treatment was detected by the number of threshold cycles of PCR indirectly reflecting the number of viruses in faecal samples (Mann-Whitney criterion: before the treatment  $Z = 0.96$ ,  $p = 0.34$ , after treatment  $Z = 1$ ,  $p = 0.047$ ), indicating the lower amount of viruses in the faeces of children receiving Filtrum SAFARI.

## Evaluation of clinical efficiency of Filtrum oral enterosorbent in treating children with acute enteric infections

Indication / Claim	Product / Ingredient studied	Dosage and administration route	Duration of treatment
AEI in children	Stage 1: Filtrum + Furazolidone  Furazolidone  Stage 2: Filtrum	Stage 1: Filtrum under 7 years - 1 tablet 3 times a day, 8 - 12 years - 1 tablet x 4 times a day, over 12 years - 2 tablets 3 times a day  Furazolidone NA  Stage 2: Filtrum under 7 years - 1 tablet 4 times a day, 8-12 years - 2 tablets 3 times a day, over 12 years - 2 tablets 4 times a day.	3-7 days
Type of evidence (scientific evidence)	Study design	Study population	Limitations of the study
Clinical research	NA	Stage 1: 40 children, 1-14 years with moderate AEI (20+20)  Stage 2: 20 children, 1-14 years with mild and moderate AEI	GCP non-compliant; Not randomized; no placebo; No dosing for furazolidone; No description of design - "second stage" and higher doses prescription;
Summary of findings			

The average duration of the presence of toxicity symptoms and diarrhoea in children administered Filtrum and Furazolidine significantly decreased in comparison with patients only treated with Furazolidone. There were no significant differences in the average duration of fever and the presence of abdominal pain. In the treatment of acute enteric infections in children, are accompanied with involvement only upper GI in the pathological process, with Furazolidone in combination with Filtrum, in 50% of patients stool frequency and nature were returned to normal, while in the treatment of acute enteric infections with Furazolidone without any supplement drugs – only in 16.6% of patients. Also was established that using Filtrum in the treatment of acute enteric infections in children as a single agent of etiotropic therapy led to a short-term (less than one day) constipation in 11 of 20 (55%) patients on the second and rarely the third day of treatment. However, the evacuation function of the intestine independently restores even on the background of taking the drug. The increasing of the daily dosage leads to the significant increasing of number of the patients with constipation, especially in mild forms of the AEI. Thus, the increasing of Filtrum daily dose should be considered as justified only for the moderate forms of the AEI, especially in cases where the clinical picture is dominated by symptoms of infectious toxicosis.