National Training Requirements

BULGARIA

Specialty
Clinical Pharmacology and Therapy

Клинична Фармакология и Терапия

Deposited: 19.12.2017
Prepared by (name): Ellie Genova
On behalf of (organisation): Bulgarian Medical Association
Original language: Bulgarian

NMA responsible for training: Bulgarian Medical Association (Български Лекарски Съюз)
English translation: UEMS Section of Pharmacology Executive Committee (TG)

Note: This is not a legally binding document. Any current official regulations must be obtained from the responsible National Medical Association or other organisation in charge of the training of medical specialists.
CURRICULUM
FOR THE SPECIALTY
CLINICAL PHARMACOLOGY AND THERAPY

2016
1. INTRODUCTION

1.1. Name of the specialty – Clinical Pharmacology and Therapy

1.2. Duration of training – 4 years, including:
   - 6 months of Pharmacology training
   - 12 months of Internal Medicine training
   - 30 months of Clinical Pharmacology and Therapy training

1.3. Required basic education for admission to specialty training Clinical pharmacology and therapy – tertiary education degree "Master" in "Medicine" and acquired professional qualification "Doctor"

1.4. Definition of the specialty

Clinical Pharmacology and Therapy is a scientific discipline and an independent medical specialty that studies and evaluates the action of drugs in humans – both in the general population and in specific subgroups and individuals. The evaluation of the action of drugs aims to establish the link and provide an optimal correlation between the therapeutic effect, adverse drug reactions and cost of treatment.

The methods used in clinical pharmacology and therapy include both methods and approaches specific to the subject, as well as methods used in the field of clinical medicine, pharmacology, drug epidemiology and economics.

2. GOAL OF TRAINING

The goal of the clinical pharmacology and therapy training is learning approaches on efficient, safe, economically feasible and individualised pharmacotherapy as well as approaches for planning, conducting, analysis and evaluation of the results of clinical trials of medicines.

3. KNOWLEDGE, SKILLS AND COMPETENCES WHICH THE SPECIALIST SHOULD OBTAIN

3.1. Understanding the theoretical knowledge and practical skills for choosing rational drug therapy based on objective benefit / risk criteria

3.2. Understanding the theoretical knowledge and practical skills to individualise drug therapy, based on specific individual pharmacokinetic and pharmacogenetic indicators

3.3. Understanding the theoretical knowledge and practical skills to assess and monitor drug safety
3.4. Understanding the theoretical knowledge and practical skills to assess the economic aspects of drug therapy and to prepare pharmacoeconomic analyses

3.5. Understanding the theoretical knowledge and practical skills for designing, conducting, analysing and evaluating the results of clinical trials of medicinal products in their development phase as well as of registered medicinal products in order to optimise their usability

4. TRAINING

4.1. Curriculum (name of the modules and their duration)

1st year:
1. Module of Pharmacology
2. Module of Internal Diseases:
   • Module of Nephrology:
   • Module of Gastroenterology
   • Module of Pulmonary diseases

2nd year:
3. Module of Internal Diseases:
   • Module of Cardiology
   • Module of Endocrinology
4. Module of Clinical Pharmacology and Therapy

3rd year:
5. Module of Clinical Pharmacology and Therapy

4th year:
6. Module of Clinical Pharmacology and Therapy

4.1.1. Module of Pharmacology: Duration of the module: 6 months

   Duration: 3 months

4.1.1.2. Experimental methods for assessing the safety of biologically active substances: determination of acute, sub-chronic and chronic toxicity
   Duration: 3 months
4.1.2. **Module of Internal Diseases**: Duration of the module: 12 months

4.1.2.1. Evaluation and optimization of pharmacotherapy in patients with kidney disease
   Duration: 2 months

4.1.2.2. Evaluation and optimization of pharmacotherapy in patients with liver and gastrointestinal diseases
   Duration: 2 months

4.1.2.3. Evaluation and optimization of pharmacotherapy in patients with pulmonary diseases
   Duration: 2 months

4.1.2.4. Evaluation and optimization of pharmacotherapy in patients with cardiovascular diseases
   Duration: 3 months

4.1.2.5. Evaluation and optimization of pharmacotherapy in patients with metabolic-endocrine diseases
   Duration: 3 months

4.1.3. **Module for Clinical Pharmacology and Therapy**: Duration of the module: 30 months

4.1.3.1. Planning, conducting, analysing and evaluating the results of clinical trials of medicines
   Duration: 12 months

4.1.3.2. Principle to conduct rational pharmacotherapy. WHO approach for personal medicine
   Duration: 2 months

4.1.3.3. Monitoring of drug efficacy and safety
   Duration: 2 months

4.1.3.4. Analysis of the economic aspect and of drug therapy and preparation of pharmaco-economic analyses
   Duration: 2 months

4.1.3.5. Drug therapy individualisation – therapeutic drug monitoring: pharmacokinetics and pharmacogenetics
   Duration: 2 months

4.1.3.6. Analysis of concentrations of medicinal products in biological media
Duration: 2 months
4.1.3.7. Regulation of drug use. Registration for the use of medicinal products in the EU. Principles of preparation of hospital drug nomenclature.
Duration: 2 months
4.1.3.8. Optimization and individualization of drug therapy in problem patients
Duration: 6 months

4.2. Curriculum

4.2.1. Theoretical part

4.2.1.1. Pharmacology

4.2.1.1.1. General pharmacodynamics

4.2.1.1.1.1. Course: Drug action and drug effect. Types of drug effects.
Duration: 2 days (16 academic hours)
4.2.1.1.1.2. Course: Receptor and non-receptor mechanisms of drug action
Duration: 2 days (16 academic hours)
4.2.1.1.1.3. Course: Benefits for proving pharmacological activity
Duration: 5 days (40 academic hours)

4.2.1.1.2. Drug Toxicology: Assessment of toxicity of biologically active substances

4.2.1.1.2.1. Course: Approaches for the study of acute toxicity
Duration: 2 days (16 academic hours)
4.2.1.1.2.2. Course: Approaches for the study of chronic toxicity
Duration: 2 days (16 academic hours)

4.2.1.2. Internal diseases

4.2.1.2.1. Fundamentals of therapy in nephrologic diseases

4.2.1.2.1.1. Course: Diagnosis, differential diagnosis and therapy of osteoarthritis, chronic glomerulonephritis and nephropathies in systemic diseases
Duration: 1 day (8 academic hours)
4.2.1.2.1.2. Course: Diagnosis, differential diagnosis and therapy of kidney and urinary tract infections
Duration: 1 day (8 academic hours)
4.2.1.2.1.3. Course: Diagnosis, differential diagnosis and therapy of acute and chronic kidney disease  
Duration: 1 day (8 academic hours)

4.2.1.2.1.4. Course: Diagnosis, differential diagnosis and therapy of nephrolithiasis  
Duration: 1 day (8 academic hours)

4.2.1.2.2. Fundamentals of therapy in liver and gastroenterological diseases

4.2.1.2.2.1. Course: Diagnosis, differential diagnosis and therapy of diseases of the gastrointestinal tract: ulcerative stomach and duodenum  
Duration: 1 day (8 academic hours)

4.2.1.2.2.2. Course: Diagnosis, differential diagnosis and therapy of liver diseases: hepatitis and cirrhosis  
Duration: 1 day (8 academic hours)

4.2.1.2.2.3. Course: Diagnosis, differential diagnosis and therapy of diseases of the biliary system: cholecystitis  
Duration: 1 day (8 academic hours)

4.2.1.2.2.4. Course: Diagnosis, differential diagnosis and therapy of pancreatic diseases: pancreatitis  
Duration: 1 day (8 academic hours)

4.2.1.2.3. Fundamentals of therapy in pulmonary diseases

4.2.1.2.3.1. Course: Diagnosis, differential diagnosis and therapy of acute and chronic bronchitis  
Duration: 1 day (8 academic hours)

4.2.1.2.3.2. Course: Diagnosis, differential diagnosis and therapy of pneumonia acquired in society  
Duration: 1 day (8 academic hours)

4.2.1.2.3.3. Course: Diagnosis, differential diagnosis and therapy of nosocomial pneumonia  
Duration: 1 day (8 academic hours)

4.2.1.2.3.4. Course: Diagnosis, differential diagnosis and therapy of COPD  
Duration: 1 day (8 academic hours)

4.2.1.2.3.5. Course: Diagnosis, differential diagnosis and therapy of tuberculosis  
Duration: 1 day (8 academic hours)
4.2.1.2.4. **Fundamentals of therapy of cardiovascular diseases**

4.2.1.2.4.1. Course: Diagnosis, differential diagnosis and therapy of essential hypertension  
Duration: 2 days (16 academic hours)

4.2.1.2.4.2. Course: Diagnosis, differential diagnosis and therapy of ischemic heart disease  
Duration: 1 day (8 academic hours)

4.2.1.2.4.3. Course: Diagnosis, differential diagnosis and therapy of congestive heart failure  
Duration: 1 day (8 academic hours)

4.2.1.2.4.4. Course: Diagnosis, differential diagnosis and therapy of heart rhythm disorders  
Duration: 1 day (8 academic hours)

4.2.1.2.5. **Basics of therapy in metabolic-endocrine diseases**

4.2.1.2.5.1. Course: Diagnosis, differential diagnosis and therapy of metabolic syndrome and dyslipidaemias  
Duration: 2 days (16 academic hours)

4.2.1.2.5.2. Course: Diagnosis, differential diagnosis and therapy of diabetes  
Duration: 2 days (16 academic hours)

4.2.1.2.5.3. Course: Diagnosis, differential diagnosis and therapy of thyroid diseases and parathyroid glands  
Duration: 1 day (8 academic hours)

4.2.1.2.5.4. Course: Diagnosis, differential diagnosis and therapy of hypothalmo-pituitary-adrenal axis  
Duration: 1 day (8 academic hours)

4.2.1.2.5.5. Course: Diagnosis, differential diagnosis and therapy of gonadal diseases  
Duration: 1 day (8 academic hours)

4.2.1.3. **Clinical pharmacology and therapy**

4.2.1.3.1. Seminar: Regulatory and ethical requirements for planning and conducting clinical trials of medicines. Good Clinical Practice (GCP).  
Duration: 5 days (40 academic hours)
4.2.1.3.2. Seminar: Approaches to planning and organising clinical trials of medicines. Types of design of clinical studies. Methods for limiting "external influences": placebo, randomisation, stratification, blinding. Selection of participants – inclusion and exclusion criteria.
Duration: 2 days (16 academic hours)

Duration: 5 days (40 academic hours)

4.2.1.3.4. Seminar: Clinical studies on bioavailability and bioequivalence – definition and calculation of primary, secondary and additional target parameters
Duration: 5 days (40 academic hours)

4.2.1.3.5. Seminar: Clinical studies for bioequivalence – types: mean, population and bioequivalence. Design of clinical studies for bioequivalence of fast release drugs.
Duration: 5 days (40 academic hours)

4.2.1.3.6. Seminar: Clinical bioequivalence studies: design of bioequivalence studies for modified release drugs and drugs with high variability
Duration: 5 days (40 academic hours)

4.2.1.3.7. Seminar: Phases of drug action. Pharmacokinetic criteria for evaluation of efficacy from drug therapy. Dose-dependent and dose-independent pharmacokinetics.
Duration: 2 days (16 academic hours)

4.2.1.3.8. Seminar: Determination of drug concentrations in biological media. Methods, peculiarities, normative requirements
Duration: 5 days (40 academic hours)

Duration: 1 day (8 academic hours)
Duration: 1 day (8 academic hours)

4.2.1.3.11. Seminar: Clinical Pharmacogenetics, pharmacogenetics. Significance for clinical practice.
Duration: 2 days (16 academic hours)

Duration: 2 days (16 academic hours)

4.2.1.3.13. Seminar: Factors modifying the action of drugs. Influence of:
– disease process
– diet
– use of tobacco and alcohol
– childhood
– elderly
– pregnancy and lactation
Duration: 2 days (16 academic hours)

Duration: 5 days (40 academic hours)

4.2.1.3.15. Essential medicines. Strategy for the establishment of a hospital drug nomenclature.
Duration: 5 days (40 academic hours)

4.2.1.3.16. Seminar: Clinical-pharmacological approaches for the treatment of essential hypertension
Duration: 2 days (16 academic hours)

4.2.1.3.17. Seminar: Clinical-pharmacological approaches for the treatment of ischemic heart disease
Duration: 1 day (8 academic hours)
4.2.1.3.18. Seminar: Clinical-pharmacological approaches for the treatment of congestive heart failure  
Duration: 1 day (8 academic hours)  
4.2.1.3.1 9. Seminar: Clinical-pharmacological approaches for the treatment of chronic obstructive pulmonary disease  
Duration: 1 day (8 academic hours)  
4.2.1.3.20. Seminar: Clinical-pharmacological approaches for the treatment of ulcerative stomach and duodenal disease  
Duration: 1 day (8 academic hours)  
4.2.1.3.21. Seminar: Clinical-pharmacological approaches for the treatment of diabetes mellitus  
Duration: 2 days (16 academic hours)  
4.2.1.3.22. Seminar: Clinical-pharmacological approaches for the treatment of metabolic syndrome and dyslipidemias  
Duration: 2 days (16 academic hours)  
4.2.1.3.23. Seminar: Clinical-pharmacological approaches for the treatment of infectious diseases of the urinary system  
Duration: 1 day (8 academic hours)  
4.2.1.3.24. Seminar: Clinical-pharmacological approaches for the treatment of infectious lung and bronchial diseases  
Duration: 2 days (16 academic hours)  
4.2.1.3.25. Seminar: Clinical-pharmacological approaches in conducting antimicrobial surgical prophylaxis  
Duration: 2 days (16 academic hours)  
4.2.1.3.26. Seminar: Clinical-pharmacological approaches for the treatment of pain syndromes  
Duration: 1 day (8 academic hours)  

4.2.2. Practical part  
4.2.2.1. Pharmacology  
4.2.2.1.1. Experimental approaches to demonstrating pharmacological activity:  
– psychopharmacological activity  
– antiparkinsonian and anti-inflammatory activity  
– anti-exudative and antiproliferative activity
– cholinomimetic and cholinolytic activity
– adrenomimetic and adrenolytic activity
– influence on vegetative ganglia and neuromuscular transmission
– antiarrhythmic and antianginal activity
– antihypertensive activity
– diuretic activity
– antiulcer activity
– spasmolytic and spasmogenic activity on isolated smooth muscle cells in vitro

4.2.2.1.2. Experimental approaches to assessing the toxicity of biologically active substances:
– acute toxicity
– chronic toxicity

4.2.2. Internal diseases

4.2.2.1. Therapy of nephrologic diseases:
– Acute and chronic glomerulonephritis and nephropathies in systemic diseases
– Infections of the kidneys and the urinary tract
– Acute and chronic renal failure
– Nephrolithiasis

4.2.2.2. Therapy of gastroenterological and hepatic diseases:
– Diseases of the gastrointestinal tract: Ulcer disease of the stomach and duodenum
– Liver diseases: hepatitis and cirrhosis
– Diseases of the biliary system: cholecystitis
– Diseases of the pancreas: pancreatitis

4.2.2.3. Therapy of pulmonary diseases:
– Acute and chronic bronchitis
– Pneumonia acquired in the community
– Nosocomial pneumonia
– COPD
– Tuberculosis
4.2.2.2.4. Cardiovascular Therapy:
   – Essential hypertension
   – Ischemic heart disease
   – Congestive heart failure
   – Heart rhythm disorders

4.2.2.2.5. Treatment of metabolic-endocrine diseases:
   – Metabolic syndrome and dyslipidaemias
   – Diabetes
   – Diseases of the thyroid gland and parathyroid glands
   – Diseases of the hypothalamic-pituitary-adrenal axis
   – Diseases of the gonadal glands

4.2.2.3. Clinical pharmacology and therapy

4.2.2.3.1. WHO approach for choosing a personal drug (P-drug). Assessment of the benefit/risk ratio. Individualisation of therapy.

4.2.2.3.2. Normative and ethical aspects of planning and conducting clinical trials.
   Good clinical practice. Informed consent and information for participants in clinical trials.

4.2.2.3.3. Conducting screening studies of participants in clinical trials:
   – Definition and evaluation of inclusion and exclusion criteria in a clinical study
   – Calculation of the Body Mass Index (BMI)
   – Carrying out tests for drug use; alcohol; smoking and pregnancy
   – Measuring vital signs
   – Making and reading ECG results
   – Calculation of creatinine clearance: the formulas of Cockroft-Gault and MDRD, as by means of a quantitative method
   – Staging of liver cirrhosis in Child-Pugh
   – Functional analysis of the pulmonary function, by carrying out spirometric tests

4.2.2.3.4. Clinical trial design approaches (of fast and modified release drugs as well as of high variability drugs):
   – Choice of: design; number and type of participants
   – Choosing a reference medicinal product
4.2.2.3.5. Pharmacokinetic aspects of clinical trials of drugs. Definition, calculation and evaluation of target pharmacokinetic parameters in studies of bioavailability and bioequivalence. Construction of pharmacokinetic curves.

4.2.2.3.6. Pharmacodynamic aspects of clinical trials. Selection of indicators to assess the effect (surrogate endpoints).

4.2.2.3.7. Statistical aspects of clinical trials. Calculate the required number of participants in clinical trials. Defining the null hypothesis, alpha and beta error and power of the statistical test. Calculation of 90% and 95% confidence intervals.

4.2.2.3.8. Methods for determining the concentrations of drugs in biological environments, species, regulatory requirements. Approaches for the validation of the analytical methods.

4.2.2.3.9. Drafting of a clinical trial to assess the bioavailability and bioequivalence of drugs, including research file protocol, clinical patient card and a form of informed consent.

4.2.2.3.10. Drafting of the final report of a clinical study to evaluate the bioavailability and bioequivalence of drugs.

4.2.2.3.11. Management of drug therapy in dependence of the measured concentrations of drugs in biological fluids – therapeutic drug monitoring.

4.2.2.3.12. Planning and evaluation of the results of pharmacoepidemiological studies to determine the risk of adverse drug reactions: calculating indicators of absolute risk, relative risk, odds ratio and number needed to treat (NNT).

4.2.2.3.13. Planning and conducting pharmacoeconomic analysis. Types of pharmacoeconomic analyses: cost/reduction, cost/effectiveness, cost/utility and cost/benefit. Types of expenses. Approaches to assessing quality of life.


4.2.2.3.15. Clinical-pharmacological approaches to conducting rational pharmacotherapy in nephrologic diseases

4.2.2.3.16. Clinical-pharmacological approaches to conducting rational pharmacotherapy in gastroenterological and liver diseases
4.2.2.3. Clinical-pharmacological approaches to conducting rational pharmacotherapy of bronchopulmonary diseases
4.2.2.3.18. Clinical-pharmacological approaches to conducting rational pharmacotherapy in cardiovascular diseases
4.2.2.3.19. Clinical-pharmacological approaches to conducting rational pharmacotherapy in metabolic-endocrine diseases

4.3. Required colloquia and deadlines for their application

4.3.1. Pharmacology

4.3.1.1. Pharmacological action and pharmacological effect. Experimental approaches to demonstrating pharmacological activity – 3 months after the start of the module
4.3.1.2. Experimental approaches to assess the toxicity of biologically active substances – 3 months after the first colloquium

4.3.2. Internal diseases

4.3.2.1. Rational pharmacotherapy of nephrological diseases – 2 months after the start of the module
4.3.2.2. Rational pharmacotherapy of gastroenterological and liver diseases – 2 months after the first colloquium
4.3.2.3. Rational pharmacotherapy of lung diseases – 2 months after the second colloquium
4.3.2.4. Rational pharmacotherapy of cardiovascular diseases – 3 months after the third colloquium
4.3.2.5. Rational pharmacotherapy of metabolic-endocrine diseases – 3 months after the fourth colloquium

4.3.3. Clinical Pharmacology and Therapeutics

4.3.3.1. Regulatory and ethical requirements in planning and conducting clinical trials of drugs. Declaration of Helsinki, Good Clinical Practice (GCP). Approaches to limit the impact of external factors in planning and conducting clinical trials – 3 months after starting the module
4.3.3.2. Statistical aspects when planning clinical trials of drugs. Defining null and alternative hypotheses. Alpha and beta error, power of the test, confidence
intervals. Determining the necessary number of participants in clinical trials – 3 months after the first colloquium

4.3.3.3. Clinical studies on bioavailability and bioequivalence: types, peculiarities.
Generic and biosimilar medicines – 3 months after the second colloquium

4.3.3.4. Clinical trials of therapeutic comparability: type, characteristics – 3 months after the third colloquium

4.3.3. 5. Clinical trials of drugs: phases, objects, features, types of design – 3 months after the fourth colloquium

4.3.3.6. Chemical analysis of the concentrations of drugs in biological fluids and media. Therapeutic drug monitoring: pharmacokinetic and pharmacodynamic.
Preparation of individual dosing regimens – 3 months after the fifth colloquium

4.3.3.7. The disease process as a factor changing the pharmacokinetic and pharmacodynamic characteristics of drugs. Criteria for assessing the effectiveness and safety of drug therapy. Physiological factors that change the effect of drugs – 3 months after the sixth colloquium

4.3.3.8. Pharmacoepidemiology. Adverse reactions and side effects of drugs. Monitoring of drug safety. Qualitative and quantitative approaches to assess the degree of risk of adverse reactions to drugs – 3 months after the seventh colloquium

4.3.3.9. Pharmacoeconomics, types of pharmacoeconomic studies. Approaches to planning and conducting pharmacoeconomic studies. Rating the quality of life – 3 months after the eighth colloquium

4.3.3.10. Drug regulation. Hospital drug policy. Preparation and management of hospital drug lists. Monitoring of drug use. Procedures for registration of medicinal products in the EU – 3 months after the ninth colloquium

5. SCHEME FOR STATE EXAMINATION FOR SPECIALTY

I. Questions from module Pharmacology

1. Drug action and drug effect
2. Receptor and non-receptor mechanisms of drug action
3. Experimental methods for investigation of psychopharmacological, antiparkinsonian and anti-inflammatory activity of biologically active substances
4. Experimental methods for the study of cholinergic and adrenergic activity of biologically active substances
5. Experimental methods for the study of antiarrhythmic, antianginal, antihypertensive and diuretic activity of biologically active substances
6. Evaluation of the toxicity of biologically active substances – Experimental methods for the assessment of acute, subacute and chronic toxicity

II. Questions from module Internal Medicine
7. Diagnosis and rational therapy of urinary tract infections
8. Diagnosis and rational treatment of glomerulonephritis
9. Diagnosis and rational therapy of COPD
10. Diagnosis and rational therapy of Pneumonia acquired in the community
11. Diagnosis and rational treatment of nosocomial pneumonia
12. Diagnosis and rational therapy of essential hypertension
13. Diagnosis and rational therapy of chronic congestive heart failure
14. Diagnosis and rational treatment of coronary artery disease
15. Diagnosis and rational therapy of hepatitis and cirrhosis
16. Diagnosis and rational treatment of ulcers of the stomach and duodenum
17. Diagnosis and rational therapy of dyslipidaemias
18. Diagnosis and rational therapy of diabetes mellitus – type 2

III. Questions from module Clinical Pharmacology
21. Approaches to limit the influence of external factors in planning and conducting clinical trials: placebo blinding, randomisation, stratification. Types of design of clinical trials.
22. Design of clinical trials from Phase I.
23. Bioequivalence and therapeutic equivalence of drugs. Types of bioequivalence studies of drugs: mean, population and individual bioequivalence.
24. Target parameters in studies of bioequivalence: types, meaning.
25. Design of clinical bioequivalence studies of formulations with fast release.
27. Design of clinical bioequivalence studies of formulations with a high degree of variability
28. Design of clinical trials from Phase II.
29. Design of clinical trials from Phase III.
30. Design of clinical trials from Phase IV. Non-interventional clinical trials.
31. Medicine, based on evidence (Evidence-Based Medicine). Evidence and recommendation degrees. Application in clinical practice
32. Phases of drug action: ADME, characteristics and features.
34. Compartmental models. Relevance to clinical practice.
38. Methods for determining the concentrations of drugs in biological environments. Types, features, requirements.
41. Principles for the combined use of antimicrobials.
42. Performance criteria during treatment with antimicrobials. Pharmacokinetic/pharmacodynamic parameters (Pk/Pd) of effectiveness.
43. Principles for the prophylactic application of antimicrobials. Antimicrobial surgical prophylaxis.
45. Clinical pharmacogenetics and pharmacogenomics.
47. Undesirable effects. Methods for assessing the degree of risk of ADRs. Determination of absolute risk, relative risk, Odds ratio and the number needed to treat (NNT).


49. Pharmacoepidemiology. Definition. Methods to quantify the degree of risk of ADRs. Method of control cases (Case control studies): peculiarities, advantages and disadvantages.

50. Diet, alcohol and smoking as factors changing the actions of drugs.


52. Kidney failure as a factor changing the effect of drugs.

53. Hepatic failure as a factor changing the effect of drugs.


55. Features of pharmacotherapy in pregnancy and lactation.


60. Procedures for registration of medicinal products in the EU: centralised, decentralised, mutual recognition, national.

6. RECOMMENDED LITERATURE FOR PREPARATION

6.1. Bulgarian sources:


2. Клинична фармакология. Учебник и ръководство за практически упражнения. Под редакцията на проф. д-р В. Влахов. Изд. Медицина и физкултура- София, 1996 г.
3. Клинична фармакология. Д.Терзииванов, И. Атанасова. Университетско издателство „Св.Климент Охридски”, 2013 г.


5. Вътрешна медицина, Под редакцията на проф.д-р Захари Кръстев. Изд. Иван Сапунджиев-ЕООД, С, 2010 г.


8. Еврофарма. Под редакцията на Нешев Г., Изд. ГорексПрес-София, 1997 г.


10. Атанасова, Ив., Д. Терзииванов. Проблеми при взаимозаменяемостта на лекарствените препарати. Средна (популационна) и индивидуална биоеквивалентност. Изд. НИХФИ, С, 1999 г.

11. Актуални проблеми на терапията. Под редакцията на Н.Беловеждов и П.Пешев С.1998 г.


13. Актуална терапия 98, том І. Под ръководството на проф.д-р Чудомир Начев, Изд.“Знание” ЕООД, 1998 г.

14. Д. Свинаров. Наръчник- терапевтичен лекарствен мониторинг и индивидуализиране на лекарствената терапия. Изд. Знание ООД, 1996 г.

15. Лечение на синдромите и болестите във вътрешната медицина и клиничната фармакология. Беловеждов Н., Терзииванов Д. Архе ООД и ARSO-София, 1996 г.

16. Закон за лекарствените продукти в хуманната медицина. ДВ Бр.31/13.04.2007 г.

17. Наредба № 31 от 12 август 2007 г. за Определяне на правилата за Добра Клинична Практика. ДВ Бр.67/17.08.2007 г. с Приложения 1-3.

18. Директива 536/2014 г на Европейския парламент и Съвета.
6.2. Foreign sources:

19. Handbook of clinical pharmacokinetics
20. The pharmacological basis of therapeutics. Goodman & Gilman
21. Clinical Pharmacology
22. Applied clinical pharmacokinetics
23. Clinical Pharmacy & Therapeutics
24. Physician Drug Reference
25. Clinical Evidence
26. Klinische Pharmakologie
27. Kompendium der Klinischen Pharmakologie
28. EMA (CPMP/EWP/QWP/1401/98 Rev. 1/ Corr **) Guideline on the investigation of bioequivalence
29. EMA (CPMP/ICH/135/95 Topic E 6) (R1) Note for guidance on Good Clinical Practice
30. EMA (CPMP/ICH/291/95 Topic E 8) Note for guidance on general considerations for clinical trials
31. EMA (ICH E9, CPMP/ICH/363/96) Statistical Principles for Clinical Trials
32. EMA (ICH E3, CPMP/ICH/137/95) Structure and Content of Clinical Study Reports