National Training Requirements

BULGARIA

Specialty

Clinical Pharmacology and Therapy

Клинична Фармакология и Терапия

Deposited:	19.12.2017
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On behalf of (organisation):	Bulgarian Medical Association
Original language:	Bulgarian
NMA responsible for training:	Bulgarian Medical Association *(Български Лекарски Съюс)*
English translation:	UEMS Section of Pharmacology Executive Committee (TG)

APPROVED: /P/ Date: 09.12.2016

DR PETAR MOSKOV
MINISTER OF HEALTH

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

4.1.1.1. Drug action and drug effect. Experimental methods for assessing the efficacy of biologically active substances.

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 pharmacoeconomic analyses

Duration: 2 months

4.1.3.5. Drug therapy individualisation – therapeutic drug monitoring: pharmaco-kinetics 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 osteo-arthritis, 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 nephro-lithiasis

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 hypothalamo-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)

4.2.1.3.3. Seminar: Biostatistic approaches in planning and evaluation of clinical trials results. Tests for assessment of statistical significance. Identification of the required number of participants. Defining a zero hypothesis. Determination of confidence intervals.

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)

4.2.1.3.9. Seminar: Pharmacotherapy based on evidence (evidence-based therapy): Criteria for proof. Evidence and recommendation degrees. Application in clinical practice.

Duration: 1 day (8 academic hours)

4.2.1.3.10. Seminar: Clinical pharmacodynamics. Surrogates and end effects indicators. Criteria for effectiveness and efficacy of drug action. Modelling of dose/effect dependence. Reasons for ineffectiveness of therapy.

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)

4.2.1.3.12. Seminar: Pharmacovigilance. Adverse drug reactions: definition, types. Significance for clinical practice. Pharmacoepidemiology – essence, types of pharmacoepidemiological studies: advantages and disadvantages. Determination of the benefit/risk ratio.

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)

4.2.1.3.14. Seminar: Pharmacoeconomics. Approaches in planning and conducting pharmacoeconomic studies. Types of pharmacoeconomic studies: cost/decrease, cost/effectiveness, cost/benefit, cost/utility.

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

4.2.2.2. Internal diseases

4.2.2.2.1. 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

4.2.2.2.2. 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

4.2.2.2.3. 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 Cocroft-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

– Randomisation, stratification, and blinding of participants in clinical trials

– Approaches to standardise conditions during clinical trials

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.

4.2.2.3.14. Regulation of drug use. Approaches for registration of medicinal products for use in the EU. Principles of preparation of a hospital drug nomenclature.

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

4.2.2.3.16. Clinical-pharmacological approaches to conducting rational pharmaco-therapy in gastroenterological and liver diseases

4.2.2.3.17. 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 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

19. Regulatory and ethical requirements for planning and conducting clinical trials of medicines. Declaration by Helsinki. Good Clinical Practice (GCP).
20. Statistical aspects of planning clinical trials of medicines. Definition of hypotheses, alpha and beta-error, test strength. Determination of confidence intervals
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.
26. Design of clinical bioequivalence studies of formulations with modified 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.
33. Clinical pharmacokinetics: Zero and first order reactions. Features.
34. Compartmental models. Relevance to clinical practice.
35. Clinical pharmacokinetics: Determination of pharmacokinetic parameters: distribution volume, terminal half-life, clearance and steady-state plasma concentrations. Relevance to clinical practice.
36. Clinical pharmacodynamics. Surrogates and end points. Hysteresis curves.
37. Therapeutic drug monitoring: pharmacokinetic and pharmacodynamic. Principles and application in clinical practice.
38. Methods for determining the concentrations of drugs in biological environments. Types, features, requirements.
39. Principles of rational choice of medicines. WHO approach to choosing personal drugs (P-drug).
40. Principles of rational choice of antimicrobials. Algorithm for rational choice of antimicrobials.
41. Principles for the combined use of antimicrobials.
42. Performance criteria during treatment with antimicrobials. Pharmaco-kinetic/pharmacodynamic parameters (Pk/Pd) of effectiveness.
43. Principles for the prophylactic application of antimicrobials. Antimicrobial surgical prophylaxis.
44. Causes of ineffectiveness of antimicrobial therapy. Microbial Resistance: species, meaning for clinical practice.
45. Clinical pharmacogenetics and pharmacogenomics.
46. Adverse drug reactions (ADRs). Definition, classifications, meaning for clinical practice. Qualitative methods for registration of ADR – Yellow card method: advantages and disadvantages. Side effects of medicines.

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).
48. Pharmacoepidemiology. Definition. Methods for quantifying the degree of risk of ADR occurrence. Cohort studies: types, peculiarities, advantages and disadvantages.
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.
51. Principles of combination drug therapy. Drug interactions. Types, relevance to clinical practice.
52. Kidney failure as a factor changing the effect of drugs.
53. Hepatic failure as a factor changing the effect of drugs.
54. Features of pharmacotherapy in children and elderly age.
55. Features of pharmacotherapy in pregnancy and lactation.
56. Pharmacoeconomics. Definition. Principles of planning and implementation of pharmacoeconomic studies. Types of cost, modelling, discounting.
57. Pharmacoeconomics. Types of pharmacoeconomic analyses: cost/reduction, cost/performance. Growth index.
58. Pharmacoeconomics. Types of pharmacoeconomic analyses: cost/benefit and cost/utility. Approaches to assessing quality of life.
59. Hospital drug policy. Preparation and management of hospital drug lists. Determination of drug use by the method defined daily dose (DDD).
60. Procedures for registration of medicinal products in the EU: centralised, decentralised, mutual recognition, national.

6. RECOMMENDED LITERATURE FOR PREPARATION

6.1. Bulgarian sources:

1. Фармакология- Учебник за студенти по медицина. Под редакцията на проф.Н.Бояджиева. Изд. АРСО- София, 2015 г.
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.
4. Basic & Clinical Pharmacology with Toxicology. Под редакцията на проф. д-р Н.Бояджиева. Изд. АРСО – София, 2012 г.
5. Вътрешна медицина, Под редакцията на проф.д-р Захари Кръстев. Изд. Иван Сапунджиев-ЕООД, С, 2010 г.
6. Фармакокинетика. Под редакцията на проф. Д.Михайлова, Д.Станева-Стойчева. Изд. Венимекс-София, 2001 г.
7. Лекарствени взаимодействия Под редакцията на Проф. Д. Станева-Стойчева, Проф.Ц.Стойчев. Изд. Венемекс-София, 2001 г.
8. Еврофарма. Под редакцията на Нешев Г., Изд. ГорексПрес-София, 1997 г.
9. Фармакоикономика. Под редакцията на Нешев Г., Изд. ГорексПрес-София,1999 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.
12. Болнична лекарствена политика. Под редакцията на проф. д-р Д.Дамянов, проф. д-р В.Влахов и авт.колектив: Гърбев Г., Димитрова З., Хаджиева Н., Кантарджиев Т., Иванова Д., Изд. Медарт- 1998 г.
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