Semester I.
Seminar 3.

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Exam topics 5-6

5.

- Antagonism. Non-receptorial antagonism
- Non-selective α-adrenoceptor blockers
- General description of antiarrhythmic drugs. Vaughan Williams classification

6.

- Control of receptor expression. Receptor diseases and receptors and disease
- ß-adrenoceptor blockers
- Treatment of myocardial ischemia especially the treatment of angina pectoris

Combinative drug-effects

- Addition: the combined effect is the sum of the effects produced separately
  - E.g.: ß-blockers + verapamil
    decreased atrio-ventricular leading/transition
  - E.g.: ß-agonists + muscarinic rec-blockers
    bronchodilator effect
  - E.g.: codein + non narcotic pain killers
- Potentiation: the combined effect is more, than the sum of the effects produced separately
  - E.g.: ethanol + CNS-depressing agents
- (Drug-)Antagonism: the combined effect is less, than the sum of the effects produced separately
  - Every antagonist acts like this

So called drug-interactions
See also: Seminar 10 - Drug interactions

Drug-antagonism I.

- Receptorial antagonisms (see the former seminar)
  - Reversible, competitive antagonism
  - Irreversible „non-competitive” antagonism
  - Allosteric antagonism (non-competitive)

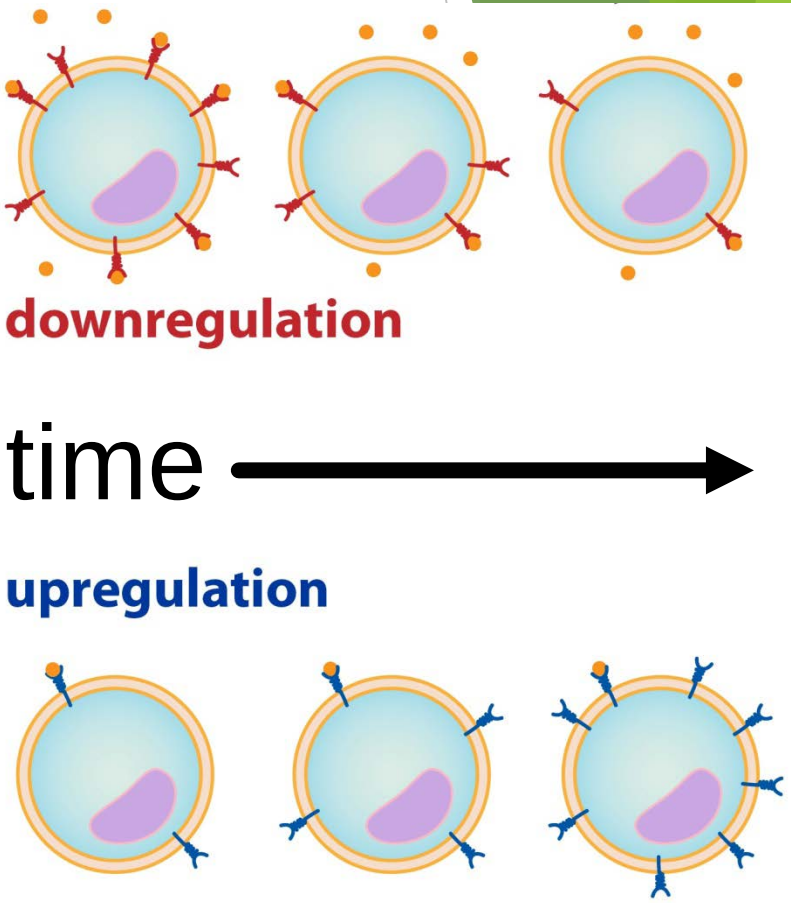
Drug-antagonisms II.

- Non-receptorial antagonisms
  - Inhibition of signal transduction (with site of action other than on the receptor)
    - E.g.: Li+ inhibits the synthesis of PIP2
  - Functional antagonsim
    - Opposite effect on different receptor
    - E.g.: ACh vs adrenaline
  - Pharmacokinetic antagonism
    - One of the drugs influence pharmacokinetic processes, which affects the other drug(s)
    - E.g.: furosemid ➔ forced diuresis ➔ drugs eliminated through the kidneys eliminated faster ➔ their effect decreases
  - Chemical antagonism
    - Two (or more) drugs react with each other
    - Occurs *in vitro* as well
    - E.g.: protamine + heparine

Control of receptor expression, Receptor diseases and receptors and disease

Change in receptor-density

- This is autoregulation, a local feedback mechanism. One possible reason of reduction of effect of drugs.
  - Down-regulation
    - May develop due to long-term use of the receptor (e.g.: long-term agonist exposure)
    - Mechanism: internalisation (endocytosis of the receptor)
    - Tissue sensitivity decreases
  - Up-regulation
    - May develop due to long-term disuse of the receptor (e.g.: long-term antagonist exposure, or lack of agonist)
    - Mechanism: externalisation of new receptors to the cell surface
    - Tissue sensitivity increases (hypersensitivity) e.g.: ß-blockers have to be discontinued gradually



Receptor-diseases

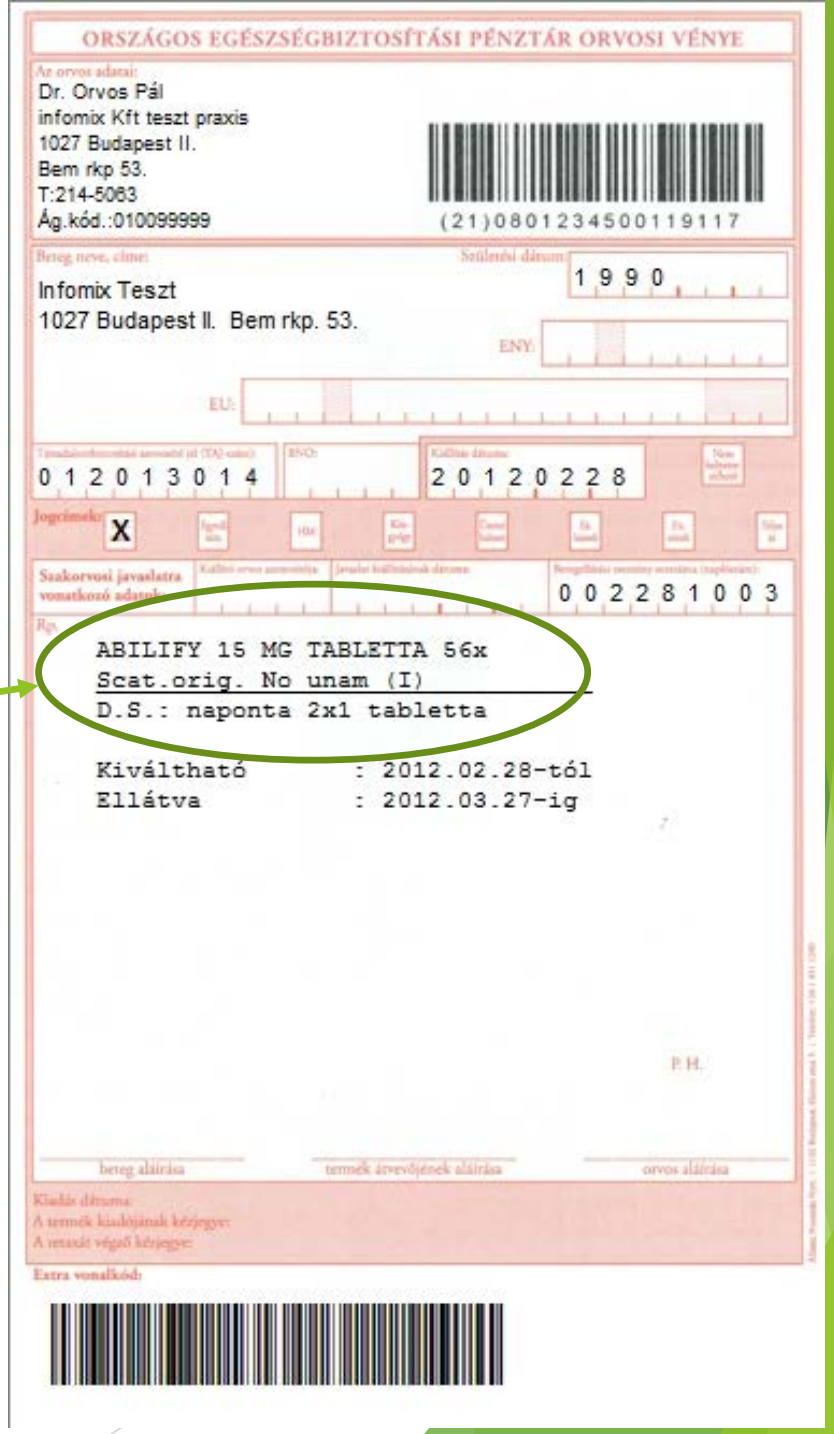
- Receptors and disease:
  Down-/Up-regulation may develop without agonist/antagonist exposure as well e.g.:
  - Hyperthyreosis ➔ ß-rec. upregulation in myocardium
  - Glucocorticoids ➔ stimulate ß-rec. synthesis, but inhibit synthesis of some cytokine receptors
- Receptor-diseases: the cause of the disease is the overactivity or hypofunctioning of a receptor e.g.:
  - Myastenia gravis – autoantibodies are formed against the nAChR-s of the neuromuscular junction (antagonist effect)
  - one type of insuline-resistent diabetes mellitus – inhibitory autoantibody against insuline-receptor
  - Basedow-disease – stimulatory antibodies are formed against TSH-receptors
  - Testicular Feminisation – secondary sexual characteristics does not develop due to lack of androgen-receptors
  - Pseudo-hypoparathyreosis – singal transduction (cAMP increase) is inhibited
  - diabetes insipidus renalis – singal transduction (cAMP increase) is inhibited

Receptura

The knowledge of writing a prescription.

Let’s learn how to write a precription in Hungary!

- Ordinatio (praescriptio) (*Latin*)
  &
- Signatura (*patient’s language*)


ORSZÁGOS EGÉSZSÉGBIZTOSÍTÁSI PÉNZTÁR ORVOSI VÉNYE

Az orvos adatai:
Dr. Orvos Pál
infomix Kft teszt praxis
1027 Budapest II.
Bem rkp 53.
T:214-5083
Ág.kód.:010099999

(21)080123450011911 7

Beteg neve, címe:
Infomix Teszt
1027 Budapest II. Bem rkp. 53.

Születési dátum: 1990

ENY:

EU:

0120130 14

Kiállítás dátuma: 20120228

Jogcímek: X

Szakorvosi javaslatra vonatkozó adatok:

00228100 3

Rp.

ABILIFY 15 MG TABLETTA 56x
Scat.orig. No unam (I)
D.S.: naponta 2x1 tabletta

Kiváltható : 2012.02.28-tól
Ellátva : 2012.03.27-ig

P.H.

beteg aláírása | termék átvevőjének aláírása | orvos aláírása

Kiadás dátuma:
A termék kiadójának kézjegye:
A receptet végző kézjegye:

Extra vonalkód:

Prescribable medicines

- Individually compounded medicines prescribed as components (**magistral**)
- Official components (= compounding materials) found in the Pharmacopoeia Hungarica (either basic substances or compounded base materials (”**galenicums”**)) prescribed alone
- Standardized magistral medicines found in the „Formulae Normales” (**FoNo**)
- Proprietary Medicinal Products (**”specialities”**)

Forms of prescriptions

- Formula magistralis
- Formula officinalis
- Formula normalis
- Formula originalis

General rules for „ordinatio” / ”praescriptio” (for all kinds of prescription forms)

- 1. Writing and reading prescriptions are inseparable from each other.
- 2. On the prescriptions the names of the medicaments are put in the genitive case, the quantities in the accusative.
- 3. The names of the medicaments may be simple (e.g.Ichthammolum), or compounded of 2-4 words (e.g. Cera alba, Vaselinum album ophthalmicum).
- 4. The adjective qualifying the noun must agree with the noun in gender, number and case.
- 5. The quantity must be written in letters and numbers, and should be underlined. The order is usually letters first, followed by numbers, except if the quantity is preceded by ”No.”, in which case numbers first, followed by letters.
- 6. Numbers of quantity must be written in parenthesis.
  In case of ”No.” letters of quantity are put in parenthesis.
- 7. The quantities of mass have to be written in Arabic numerals and always in grams, while the countable numbers (e.g. drops and pieces) in Roman numerals. Prescribing volume is prohibited (e.g. ~~ml~~).
- 8. The sign ”g” (gram) is written before the quantity.
- 9. Quantities of mass should be given to decimal accuracy, even if it is an integer (e.g.: (g 6,0)) (=decimal point (decimal comma in Hungarian) must be used even if after the decimal point we write zero–tenth gram)

Formula magistralis I.

- The prescription is compiled by the doctor ➔
- Every component should be listed one by one together with their respective quantities (usually grams)
- The used components should be official (either in the Pharmacopoeia Hungarica, or licensed by the National Institute of Pharmacy and Nutrition (OGYÉI))

Rp./

Codeini hydrochloridi dihydrici

centigrammata decem (g 0.10)

Metamizoli natrici

grammata duo (g 2.00)

Saccharini natrici

tablettas duas (II)

Aquae purificatae

ad grammata centum (ad g 100.0)

Misce fiat solutio

Detur ad vitrum fuscum

Signetur: 5x 5ml daily

- The doctor should define the formulation of the medicine e.g.: solution, powder, drops etc.
- The doctor should define the packaging material for the medicine e.g.: dark bottle, packet, box etc.
- The doctor must indicate the exact dosing. This, the signatura, must be in the patients' own language.

Formula magistralis II.

- In case the quantity of two or more component is the same, we may write the amount once and use "ana" (abbreviation: "aa", meaning: equally)

  Phenacetini

  Acidi acetylsalicylici

  ana centigrammata triginta (aa g 0,30)

- If we want the product to be a whole number, e.g. 100 gramms we use "ad„ (meaning: make up to)

  Aqae destillatae

  ad grammata centum (ad g 100,0)

- If we don’t want to specify the exact amount of a carrier material (only this is allowed no other component!), it will be calculated by the pharmacist

  Adipis solidi

  quantum satis (qu.s.) = the sufficient amount

Formula magistralis III.

- In a magistral prescription the order of components are as follows:
  - *remedium cardinale* (primary agent)
  - *remedium adjuvans* (adjuvant agent(s)),
  - *remedium corrigens* (flavoring, color-corrector, odor improver, etc. excipients),
  - finally the *remedium vehiculum* (carrier excipient = basis material)

Formula magistralis IV.

Rp.

remedium cardinale Aminophenazoni *(Sing. Gen.)*

gramma unum (g 1,0) *(Acc.)*

remedium adjuvans Extracti belladonnae sicci *(Sing. Gen.)*

centigrammata viginti (g 0,20) *(Acc.)*

Calcii bromati *(Sing. Gen.)*

grammata septem (g 7,0) *(Acc.)*

remedium corrigens Sirupi simplicis *(Sing. Gen.)*

grammata viginti (g 20,0) *(Acc.)*

remedium vehiculum Aquae destillatae *(Sing. Gen.)*

ad grammata centum (ad g 100,0) *(Acc.)*

Misce fiat solutio

Da ad vitrum fuscum

S.: 4 óránként 1 kávéskanállal bevenni

Formula magistralis V.

- Giving strictly exact orders in *Ordinatio* is inevitable.
  Because this defines the formulation of the medicine (i.e. „Misce fiat solutio, emulsio, suspensio, …") as well as this defines site of application (e.g. eardrops, nasal drops, eyedrops).
- Some extra labels (depending on the components):
  - „Da sub signo veneni" (= Dispense with poison sign),
  - „Da ad vitrum fuscum" (= Dispense in dark bottle),
  - „Detur in vitro guttatorio" (= Dispense in bottle with dropper attachment)
- In case of prescribing emulsions or suspensions „To be kept in a cool place! Shake before use!" extra labels are mandatory.
  (this is part of the Signatura, so should be written in the language of the patient)

Formula magistralis VI.

On magistral prescription „single-dose” and „multidose” medicines can be prescribed:

- *Multidose pharmaceutical formulations* (solution, ointment, undivided powders, etc.): The dispensing of medication is done by the patient.
- *Single-dose pharmaceutical formulations* (dosed powders, pills, suppositories) can be prescribed in two ways:
  - Dispensed form
    - The doctor defines the mass of components for one dose, and then using the phrase "Dentur tales doses No **...**" (make **...** more identical doses) instructs how many doses are needed.
      This is more logical for the doctor.
  - Divided form
    - The doctor defines the mass of the components of the whole medication, then using the phrase "Divide in doses aequales No **...**„ (divide it in **...** identical doses) instructs how many doses should it be divided to.
      This is more logical for the pharmacist.

Formula magistralis VIII.

Dispensed form

Rp./

Codeinii chlorati

centigrammata quattuor (g 0,04)

Acidi acetylsalicylici

Phenacetini

aa gramma semis (aa g 0,5)

Vehiculi

quantum satis

Misce fiat suppositorium

Dentur tales doses No III (tres)

Da ad scatulam

S.: Rectal suppository! To be kept in a cool place! In case of pain apply 1 suppository rectally, max 3 times daily!

Divided form

Rp./

Codeinii chlorati

centigrammata duodecim (g 0,12)

Acidi acetylsalicylici

Phenacetini

aa gramma unum et semis (aa g 1,5)

Vehiculi

quantum satis

Misce fiant suppositoria

Divide in doses equales No III (tres)

Da ad scatulam

S.:Rectal suppository! To be kept in a cool place! In case of pain apply 1 suppository rectally, max 3 times daily!

OR Misce fiant suppositoria No III (tres)
OR Ut fiant suppositoria No III (tres) = to be 3 suppositories

Formula magistralis VII.

Advices for prescribing single-dose pharmaceutical formulations

- **Do not forget!**
  In case of dispensed form ➔ single dose (dosis singularis),
  in case of divided form ➔ the total dose (dosis totalis) should be written!
- In case of prescribing suppositories or pills in divided form, never use the usual singular phrases
  - Because „Misce fiat suppositorium/pilula" together with „Divide in doses aequales No …" means that the pharmacist is instructed to make one giant suppository/pill and to divide it (cut it) in parts ☺ ☺
- In case carrier excipient is not defined „Vehiculum" or „Massa suppositorii" / „Massa pilulae" should be written to instruct the pharmacist – trusting his/her professional knowledge – to choose the carrier.
- Suppositories must be marked with „Rectal/vaginal suppository!" and „To be kept in a cool place!" labels (in the language of the patient).

Formula officinalis

- This is the form of prescription of basic substances and the so called Galenicums, each are official in the Pharmacopoeia Hungarica.
- Galenicums are complex, multi-component products,
  - some of which are used as compounded base materials for further magistral drug compounding,
  - OR used alone having effects on their own.
- On the prescription name of the product in the Pharmacopoeia and the required amount (in gramms) should be indicated (but not the components).
- „misce fiat" is not needed (because the pharmacopoeia defines the pharmaceutical formulation of the product)
- these are usually kept ready in storage of pharmacies, so they just need to be dispensed;

Rp./

Unguenti Hydrophylici nonionici

grammata ducenta (g 200,0)

Detur ad fictile

Signetur: For external use only. Ointment for bathing.

Fictile = ointment jar

Formula normalis

- This is the form of prescription of standardized magistral products
- These can be found in Formulae Normales = „collection of standard prescriptions”
  - FoNo is a collection of recognized, often prescribed magistral prescriptions and
  - contains directions for their use and their making.
  - The 7th edition of the FoNo has been official since 2003. Two editions of FoNo VII. are available, one for pharmacists and the other one for doctors.
    A (IV. edition) veterinarian FoNo also exists.
  - Pharmacist Fono available online:
    https://www.ogyei.gov.hu/dynamic/FoNo_1020.pdf
- On the prescription name of the product in the FoNo and number of FoNo doses should be indicated (e.g.: „FoNo dosim unam” = one dose according to FoNo; „FoNo doses duas” = two doses etc.)
- „misce fiat” is also not needed here (as the pharmaceutical form is defined here as well)

Rp./

Spiritus iodosalicylati

FoNo dosim unam (I)

Detur ad vitrum fuscum

Signetur: For external use only. Antimycotic dermatologic spread

Modified FoNo-prescriptions I.

- Adding a new active ingredient: After the Formula Normalis prescription „adde” should be written (meaning = add)

Rp./

Mixturae pectoralis

FoNo dosim unam (I)

D.S.: 1 spoonful t.i.d.p.c.

Adde

Codeini hydrochloridi dihydrici

cgta viginti (0,20g)

t.i.d.p.c. = Take 1 spoonful 3 times daily after meals
(see last seminar: Pharmaceutical Latin Abbreviations)

Modified FoNo-prescriptions II.

- To omit (leave out) a component from a FoNo preparation write „sine” after the name of the FoNo product (meaning = without) (after „sine” we use Ablativus case)

Rp./

Solutionis castellani sine fuchsino

FoNo doses duas (II)

D.S.: For external use only. Antimycotic dermatologic spread

SOLUTIO CASTELLANI
(Sol. Castellani)

I. Fuchsinum	0,25	g	
I. Acidum boricum	0,50	g	
I. Resorcinum	2,0	g	
II. Alcoholum 96%	5,0	g	
II. Aqua destillata	25,0	g	
III. Phenolum liquefactum	1,0	g	
IV. Acetonum	2,5	g	
V. Aqua destillata	ad 50,0	g	(13,7 g)

Modified FoNo-prescriptions III.

- Changing the vehicle/carrier of the FoNo preparation: write „cum” after the name of the FoNo product (meaning = with) (after „cum” we also use Ablativus case)

Rp./

Unguenti anaesthetici cum unguento macrogoli

FoNo dosim unam (I)

D.S.: For external use only. Anaesthetic ointment to ease pain and itching

Unguentum anaestheticum

(Ung. anaesth.)

— 10 g —

Rp. Norcaini
(Aethylii aminobenzoici)
gramma unum (g 1,00)
Adipis lanae hydrosi
Vaselini flavi
aa grammata quattuor
et semis (g 4,5)

Modified FoNo-prescriptions IV.

- If we change the dose of a component in a FoNo prescription = it should be written like Formula Magistralis
  (so every component should be listed one by one together with their respective quantities)

Formula originalis I.

- This is the prescription form of precompounded, factory products (called ”specialities”) which are official in the so called Drug Compendium.
  - The Drug Compendium lists every precompounded, factory medicine that has Marketing Authorisation in Hungary together with its Application, Product Characteristics and the package leaflet for informing the patient.
- On Formula Originalis type prescriptions the following three should be written: the pharmaceutical form of the drug (genitivus), the Factory Name (= the trademarked name; this should not be conjugated grammatically), and the quantity (accusativus)
- Quantity:
  - Either in original packing: „scatulam/tubum originalem No …” = in original box/tube No. …”
  - Or in case of opened package unit: „No …” = No. …
  - Here, because of the use of No., first written with Roman numbers (!), then in parenthesis with letters

Rp./

Tablettarum Algopyrin

scatulam originalem No. I (unam)

D.S.: In case of fever take 1. Maximum 1 per every 4 hours.

Formula originalis II.

Used only if the box contains only 1 tablet
e.g.: emergency contraceptives, some anthelmintics

Rp./

Tablett { -ae *(Sing. Gen.)* / -arum *(Plur. Gen.)*

”Tradename”

Nowadays usually written after Tradname

continent { -is *(Sing. Gen.)* / -ium *(Plur. Gen.)*

mg { -ma unum (g 0,001) *(Sing. Acc.)* / -mata duo (g 0,002), tria (g 0,003)… *(Plur. Acc.)*

Scatul { -am / -as

original { -em *(Sing. Acc.)* / -es *(Plur. Acc.)*

No { I. (unam) *(Sing. Acc.)* / II. (duas), III. (tres)… *(Plur. Acc.)*

Detur, Signetur:

Formula originalis III.

- In case more than one concentration and/or packaging unit of the factory product exists, the doctor should indicate precisely
- If not indicated, the pharmacist will give the smallest one.

Rp./

Capsularum Olicard

Scatulam Originalem No I (unam) ➔ Olicard 40mg 30x

D.S.: S.i.d.

Rp./

Capsularum Olicard 60mg 50x

Scatulam Originalem No I (unam)

D.S.: S.i.d.

Supplied for 50 days ➔ This is required if quantity exceeds 1 month

(s.i.d. = semel in die = 1x1 daily)

Combinations of prescription formulas

Rp.

Unguenti „Flucinar”

seu

Unguenti „Elocom"

tubos originales No II (duos)

Cerae albae

Cholesterini

aa grammata tria (aa g 3,0)

Aluminii acetici tartarici soluti 1%

Paraffini solidi

aa grammata viginti (aa g 20,0)

Paraffini liquidi

ad grammata centum (ad g 100,0)

M. D. S.: For external use only. Cooling ointment containing steroids.

Rp.

Unguenti „Hydrocortison 2,5% 5g”

tubos No II (duos)

Unguenti refrigerantis FoNo VII

ad grammata centum (ad g 100,0)

M. D. S.: For external use only. Haemorrhoidal ointment.

Others:

- FLUCINAR ointment + Ung. refrigerans
- FASTUM gel + Ung. contra dolor.
- FTOROCORT + Ung. hydrophilicum nonion.
- ELOCOM + Ung. hydrophil. nonion.

Prescription of narcotic drugs I.

- What is narcotic, what is not? ➔ 66/2012 Korm. rend. (Korm. rend. = government regulation) lists official narcotics
- K1, K2 register = narcotic drugs
  K1 e.g.: morphine, cocaine K2 e.g.: codeine, ethyl-morphine
- K3 register = narcotic-containing exclusions (products) these hold such low amounts of narcotics in a complex product form, that is too low to retrieve significant amount from the narcotic
  e.g.: low-concentrate codein-product (antitussivum)
- P1, P2, P3, P4 – psychotropic substances
  e.g.: amphetamine, ketamine, amobarbital, diazepam
- And the so called C-register, which is part of this government regulation, and which is a list of psycho-active substances or substance-groups
- This C-register was needed due to the spreading of the so called „designer narcotics"
  Designer narcotic = is produced by chemical modifcation of a strictly controlled, official narcotic (see above) , so that the effect is similar to the original narcotic, but they are legit, and can be marketed and used legally (as dye dissolver, pesticide or censer etc.)

Prescription of narcotic drugs II.

- Current law (as of 2017 september) : 43/2005 EüM. Rend.
  (EüM. rend. = regulation published by Minister of Health)
- Nowadays duplicate prescription is not needed (but the practice is slowly changes)
- Concentration have to be indicated! (arabic numbers)
  (in case of hand-written prescription: concentration should be written with letters as well)
- Always dosage units (e.g.: tablets, ampules, patches) have to be prescribed (the quantity of which has to be written with letters (in latin) and with roman numbers)
  the prescribed amount must match the amount found in one packaging unit (e.g. box contains 5 patches ➔
  5 patches must be prescribed or 10 or 15 etc.)
- In the case of Prn (Pro re nata =„use as necessary") ➔ daily maximal dose have to be indicated
- In the case the ordered dose differs from the summary of product characteristics (SPC) ➔ it has to be indicated by the doctor with an exclamation mark, stamp and signature of the doctor
- On one prescription doctors may order a dose for only 15 days („statim" have to be written on the prescription) (meaning = immediately) Exception: family doctor / general practitioner (see below)
- If narcotic is needed over 15 days:
  - Only general practitioner may prescribe (except if only some other specialist is allowed to prescribe the given product)
  - Upon first prescription of the narcotic, a notification form (attached to the above mentioned regulation) should be filled out. The patient chooses a pharmacy, and the notification form notifies this specific pharmacy about the narcotic use of the patient. The form is valid for three months. The patient may only buy the prescribed narcotic from this pharmacy.
  - The general practitioner have to maintain a register of patients using narcotics. (this is also an attachment of the above mentioned regulation)
  - In this case the general practitioner may prescribe a 30-day dose at once
  - In the case of any change, a new notification form have to be filled out (e.g.: need of narcotic over 3 months; change in the concentration of the product; or change to another active ingredient etc.)