

# TRANSLATION OF CLINICAL PHARMACY AND PHARMACEUTICAL CARE RESEARCH INTO PRACTICE: SLOVENIAN CASE

***Prof. Dr. Aleš Mrhar, mag.farm.***

*Faculty of Pharmacy, University of Ljubljana*

*Aškerčeva 7, 1000 Ljubljana, Slovenia*

[ales.mrhar@ffa.uni-lj.si](mailto:ales.mrhar@ffa.uni-lj.si)

Asist. Prof. **Alenka Premuš Marušič**, mag.farm.,spec.clin.farm., General Hospital Murska Sobota

[alenka.premus@sb-ms.si](mailto:alenka.premus@sb-ms.si)

Asist. Prof. Dr. **Lea Knez**, mag.farm.,spec.clin.farm., University Clinic Golnik

[lea.knez@klinika-golnik.si](mailto:lea.knez@klinika-golnik.si)

**Polonca Drogenik**, mag.farm.,spec.clin.farm., University Medical Centre Maribor

[polonca.drogenik@ukc-mb.si](mailto:polonca.drogenik@ukc-mb.si)



# Goals of clinical pharmacy in Slovenia

The aim of clinical pharmacists in Slovenia is to ensure the correct and safe use of medicines and other medical products through the provision of various clinical pharmacy services.

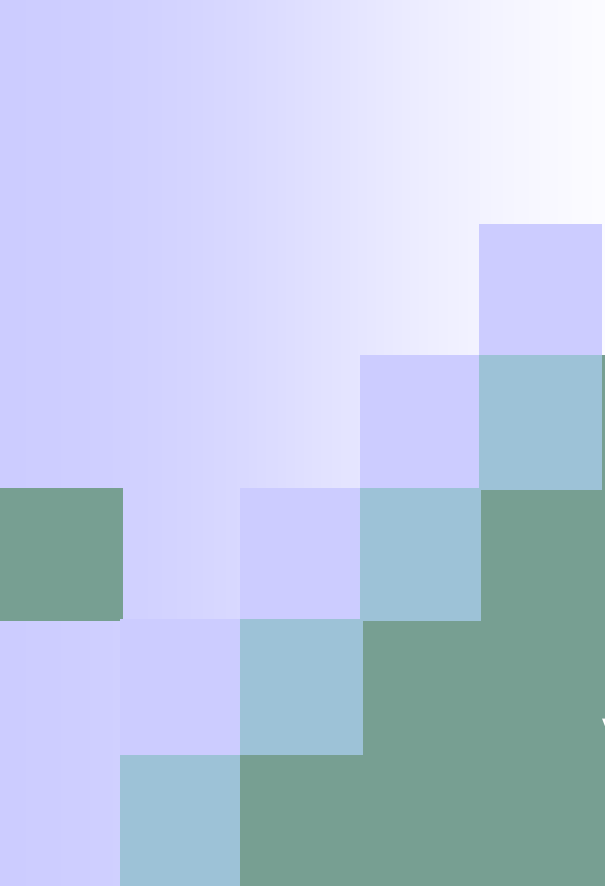
Their objective is to:

- maximise treatment efficacy by choosing the most appropriate medication for each condition and for each individual patient
- minimise the risk for adverse drug events by providing *drug monitoring* and assessing patient's medication adherence
- reduce drug expenditure by choosing the most cost-effective among all suitable strategies



# Clinical pharmacist

- Clinical pharmacist's role is to optimise drug treatment across the institutions of the Slovenian health care system (pharmacies, hospitals, clinics, nursing homes)
- Clinical pharmacist is entitled a pharmacist with Master of pharmacy degree and a three-year specialisation in clinical pharmacy



# Cases of good clinical pharmacy practice in various Slovenian settings



General hospital:  
*General hospital Murska  
Sobota*

# The beginning...

- **Polypharmacy is a main concern in Slovenia:** the number of medicines-prescribed per patient rises in average for 5,2% annually
- To address this concern, the clinical pharmacist in general hospital Murska Sobota was integrated into the healthcare team on various levels (as defined in the clinical pharmacist's work process):
  - Participation at healthcare meetings and ward rounds
  - Performing medication reconciliation at hospital admission
  - Performing advanced medication review in appointed patients called Pharmacotherapeutic review
  - Making patient follow-up
  - Performing medication reconciliation at hospital discharge



## FARMAKOTERAPIJSKI PREGLED

Bolnik MI: Zdravnik:

Ime, priimek:  
Datum rojstva:

Farmacevt:

Oddelek, soba: INT II  
Datum sprejema: 18.3.2011

### 1. OPIS, ANAMNEZA

Iz popisa ob sprejemu: Bolnik se je slabo počutil, težko dihal, trosile so se mu roke, soproga je opazila tudi slinjenje. Zavesti ni izgubil.

Prejšnje bolezni: Bolnik se zdravi zaradi arterijske hipertenzije, obravnavan večkrat zaradi cerebrovaskularnih insultov. Bolniku je bilo ugotovljeno tudi vnetje sečil, prejel je ciprofloksacin po antibiogramu. Prejema tudi Marevan po shemi.

### 2. DIAGNOZA

Collapsus, Stanje post ICV.

### 3. LABORATORIJ

21.3.2011 24.3.2011  
INR 4,9 (2-3) INR 1,5 (2-3)

### 4. PREGLED DOSEDANJE TERAPIJE ZDRAVIL

Apaurin p.p.	(diazepam)
Amoksiklav tbl. 2x1000mg	(amoksicilin+klav.kisl.)
Simvastatin Lek 40mg 1tbl. zvečer	(simvastatin)
Kornam 1 tbl. zvečer	(terazosin)
Lioresal 25mg 2x1 tbl	(baklofen)
Marevan – po shemi	(varfarin)
Tagren 2x1 tbl.	(tiklopidin)
Donepezilijev klorid Lek 1 tbl. zv.	(donepezil)
Kvelux 2x25mg	(kvetiapin)

Pred tem je jemal: Ciprofloksacin 500/12 ur in Ebixa 2x1 tbl.

### 5. INTERAKCIJE

#### Interakcije tipa D:

#### Benzodiazepini (diazepam) – tiklopidin (Tagren)

Tiklopidin je močan inhibitor encima CYP2C19, medtem ko je diazepam substrat na encimu CYP2C19. Metabolizem diazepama je zato znižan, njegova konc. v plazmi se lahko zelo poveča in neželeni učinki diazepama so lahko bolj izraženi.

#### Interakcije tipa C:

#### Baklofen (Lioresal) / kvetiapiin (Kvelux) / diazepam (Apaurin)

Uporabljanje več zdravil iz skupine zdravil, ki zavirajo CŽS lahko poveča stranske oz toksične učinke posameznih zdravil (zmedenost, vrtoglavica, ataksija, slabo počutje...), zato je potrebno skrbno opazovanje bolnika.

#### Ciprofloksacin / kvetiapiin (Kvelux)

Ciprofloksacin lahko povzroči podaljšanje QTC-intervalov, ko se uporablja z učinkovinami, ki že tako podaljšujejo QTC interval (kvetiapin)

- ⊗ B – ni potrebno ukrepanje;
- ⊗ C – potrebno je kontroliran terapijo, reden monitoring;
- ⊗ D – priporoča se zamenjava oziroma modifikacija terapije;
- ⊗ X – izogibanje kombinaciji, izjemno nevarna interakcija



### Ciprofloksacin / varfarin (Marevan)

Kinolonski antibiotiki lahko zvišajo antikoagulantni učinek varfarina, večja je verjetnost krvavitev. Ciprofloksacin namreč izpodriva varfarin s plazemskih beljakovin – možen mehanizem interakcije.

### Donepezil / kvetiapiin (Kvelux)

Centralni inhibitorji acetilholinesteraze (Yasnal tbl.) lahko zvišajo nevrotoksične učinke atipsihotikov (Loquem). Pojavijo se lahko ekstrapiramidalni simptomi.

### Simvastatin / varfarin (Marevan)

Statini lahko zvišajo antikoagulantni učinek varfarina. (inhibicija CYP2C9 izoenzimov). Potrebno je prilagajanje odmerka varfarina, ko se uvaja ali ukinja terapija s statini.

### Tiklopidin (Tagren) / varfarin (Marevan)

Pri tej kombinaciji zdravil je večja verjetnost krvavitev.

### 6. FARMAKOTERAPIJSKI NASVET

Zaradi interakcij tipa D priporočam ukinitvev zdravljenja z benzodiazepini (Apaurin).

Običajni učinkoviti odmerki Kvelux tbl. so med 300-400 mg na dan. Ker bolnik prejema veliko nižje odmerke, svetujem pregled psihiatra in nasvet, ali je terapija sploh potrebna. Bolnik prejema namreč več zdravil iz skupine, ki zavirajo CŽS in ima zato lahko te neželene učinke tudi izražene.

Bolnik je doma prejemal Ebixa tbl. 2x1, ki so indicirane za Alzheimerjevo bolezen. Če je dejansko imel postavljeno diagnozo Alzheimerjeve bolezni, svetujem nadaljevanje zdravljenja z zdravilom Ebixa 10mg tbl., vendar 2tbl. 1x na dan (vedno ob istem času). Memantin (Ebixa) namreč nima interakcij z ostalimi zdravili, medtem ko donepezil ima. Zato svetujem ukinitvev tbl. Donepezilijev klorid.

Tudi antibiotik amoksicilin s klavulnsko kislino je glede interakcij ustrezen, medtem ko je pred tem bolnik prejemal ciprofloksacin, ki pa lahko vpliva tako na INR kot na podaljšanje QTC intervala ob ostalih zdravilih (glej – interakcije).

Tudi trajanje zdravljenja s kombinacijo tiklopidina in varfarina je potrebno definirati. Če je indikacija, svetujem namesto tiklopidina raje uvedbo klopidogrela.

### 7. PREDLOG SPREMENJENE TERAPIJE

Apaurin p.p.	(diazepam) - ex
Amoksiklav tbl. 2x1000mg	(amoksicilin+klav.kisl.) ??
Simvastatin Lek 40mg 1tbl. zvečer	(simvastatin)
Kornam 1 tbl. zvečer	(terazosin)
Lioresal 25mg 2x1 tbl	(baklofen)
Marevan – po shemi	(varfarin)
Tagren 2x1 tbl.	(tiklopidin) ??
Donepezilijev klorid Lek 1 tbl. zv.	(donepezil) - ex
Kvelux 2x25mg	(kvetiapin) ??
Ebixa 10mg tbl. 2tbl. 1x na dan	

Datum: 25.3.2011

Podpis:

## What was done so far in the hospital...

- Antibiotic orders reviews by a pharmacist was integrated as obligatory
- Pharmacotherapy lectures for clinicians
- Workshops on accurate drug handling and administration for nurses
- Instructions for dilution and preparation of parenteral antimicrobial therapy
- A drug formulary list, equipped with brand names, as a sources for nurses during drug administration







Tertiary clinic:  
*University Clinic Golnik*



## University Clinic Golnik

Clinical pharmacists are integrated in the treatment of:

- Patients at higher risks for adverse drug reactions
- Oncology patients
- Patients with tuberculosis
- Patients with hereditary angioedema

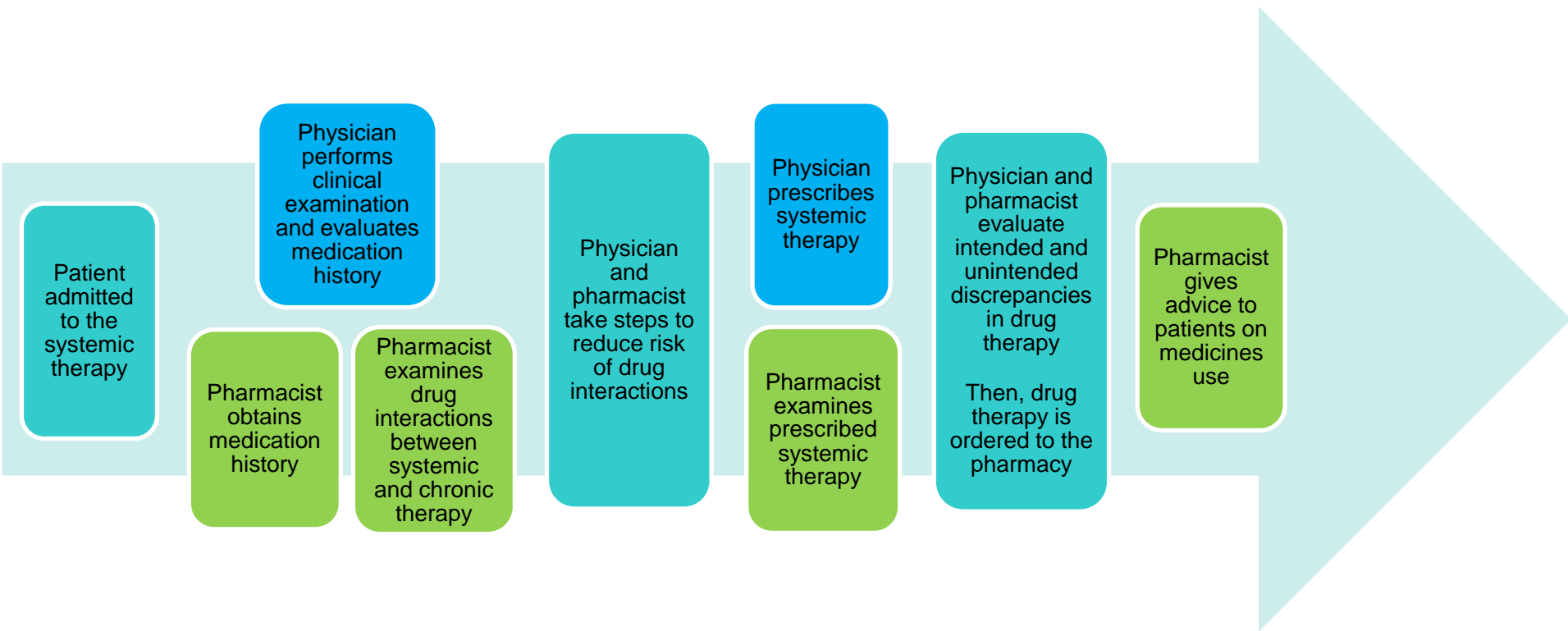



Medication review is obligatory in patients at higher risks for adverse drug reactions:

- Decreased renal function (<30 mL/min)
- Prescribed with strong inhibitors or inducers
- Prescribed with strong opioids
- Prescribed with drugs where TDM is performed
- Prescribed drugs with a feeding tube
- Prescribed medicines with restrictions in their use

# Clinical pharmacist's role in oncology

## Implementation of medication reconciliation model






The way forward: to integrate good clinical pharmacy service in routine clinical practice

Pharmacists at University Clinic Golnik daily:


- Review drug treatment in all above mentioned patients
- Document drug therapy suggestions in patient's medical documentation and discuss them with the treating clinician.





*University Medical Centre Maribor:*  
Moving from the pharmacy to the  
ward






## UMC Maribor, in year 2010

- 1.300 hospital beds
- 50.000 patients per year
- 30 hospital wards
- 6 pharmacists (2 specialised in clinical pharmacy)
  
- 10 pharmacists (4 specialised in clinical pharmacy in the year 2014)

Challenge: how to provide clinical pharmacy service for patients at highest risk?

- 
- pharmacists prepared a protocol for Vancomycin TDM based on international guidelines
  - discussed it with clinicians and laboratory staff
  - identified and tested a pharmacokinetic program, now used for dosing recommendations
  - provided lectures to clinicians and nurses

since 30. 9. 2010 clinical pharmacists review vancomycin TDM for each patient in daily practice!

- roughly, 2/3 of patients need dosage regimen adjustments

The number of medicines is expanding

- TDM of gentamicin – July 2012
- TDM of digoxin – March 2014



- Pharmacy's TDM service is well accepted
- Pharmacists are recognised as experts in the field of medicines
- App. 250 patients annually are offered pharmacists' service



# Pharmacy consultants in primary health care

# Cooperation and harmonisation of two complementary disciplines

Pharmacist consultant



General Practitioners

Work together to improve medicine prescribing,  
**The project is coordinated by  
the Health Insurance Institute of Slovenia.**

# Pharmacist consultant

- Is a special service offered to patients at risk of DRP (as identified by GP)
- The pharmacist consultant meets patients and sees their documentation in an independent specialised clinic, ran weekly in the health center and nursing homes
- The pharmacist presents its advice in written form, discusses identified problems and suggests solutions to patient's GP

The outcome: pharmacotherapy is optimised!

# Pharmacist consultant

- 1. step: 5 pharmacist consultants in January 2012
  - In 16 months period: 233 clinics and 878 pharmacotherapy reviews
  - very good results in Pomurska region (the north-east part of Slovenia) as polypharmacy is in decline
- 2. step: clinics are expanding in April 2014 with 15 pharmacist consultants
  - currently, 16 clinics running in Pomurska region and Ljubljana







## A look into the future...

- to review the drug therapy of all hospitalised patients
- to implement a mandatory drug review in patients with feeding tube or with difficulties taking medicines orally
- to expand pharmacist consultant clinics across the whole country (estimated to 50 - 60 clinics)
- to connect and cooperate with clinical pharmacists worldwide – mutual transfer of knowledge and experience