



Drug Interaction Advisory Service for Clinical Decision Support of Multimorbidity Patient Centric Care Plans in the C3-Cloud System

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DRUG INTERACTIONS IN C3-CLOUD



The screenshot displays the C3-Cloud interface for a patient named Anna Svensson. The top navigation bar includes 'Home', 'My Patients', 'Schedule', and 'Messages'. Below this, there are tabs for 'All', 'BP Management', 'Glucose Management', 'HF Management', 'Renal Management', and 'Depression Management'. The main content area shows a 'Diuretics' medication entry with the following details:

- Product:** Diuretics
- Route:** Orally
- Dose:** 5
- From:** 01 Oct 2018
- To:** 01 Mar 2019
- Frequency:** 1
- Period:** 1 day
- Reason(s):** No condition selected

A warning popup is displayed over the medication details, containing the following text:

Indapamide, Venlafaxine	Indapamide is predicted to cause hypokalaemia (potentially increasing the risk of torsade de pointes) when given with venlafaxine. Manufacturer makes no recommendation.
Metolazone, Venlafaxine	Metolazone is predicted to cause hypokalaemia (potentially increasing the risk of torsade de pointes) when given with venlafaxine. Manufacturer makes no recommendation.

At the bottom of the popup are 'Modify' and 'Save Anyway' buttons. The background interface also shows a 'Goals' section on the left and a table of 'Display Inactive Activities' on the right.

DRUG – DRUG INTERACTION (BNF)

GR COSMOTE 0 K/s 71% 09:08

Warfarin

The interactions content in BNF publications has changed.
[Find out more.](#)

Aceclofenac

Alcohol (beverage)

Alteplase

Amiodarone

Amoxicillin

Ampicillin

Anagrelide

Apalutamide

GR COSMOTE 53 B/s 72% 09:05

Cimetidine

Cimetidine increases the anticoagulant effect of warfarin. Manufacturer makes no recommendation.

Severity of interaction:

Severe

Evidence for interaction:

Study

Ciprofibrate

Ciprofibrate is predicted to increase the anticoagulant effect of warfarin. Manufacturer advises monitor INR and adjust dose.

Severity of interaction:

Severe

Evidence for interaction:

Study

GR COSMOTE 27 B/s 70% 09:12

Paracetamol

Paracetamol increases the anticoagulant effect of warfarin. Manufacturer advises monitor INR.

Severity of interaction:

Moderate

Evidence for interaction:

Study

Parecoxib

Warfarin is predicted to increase the risk of bleeding events when given with parecoxib. Manufacturer advises use with caution or avoid.

Severity of interaction:

Severe

Evidence for interaction:

Theoretical



ANATOMIC THERAPEUTIC CHEMICAL (ATC)

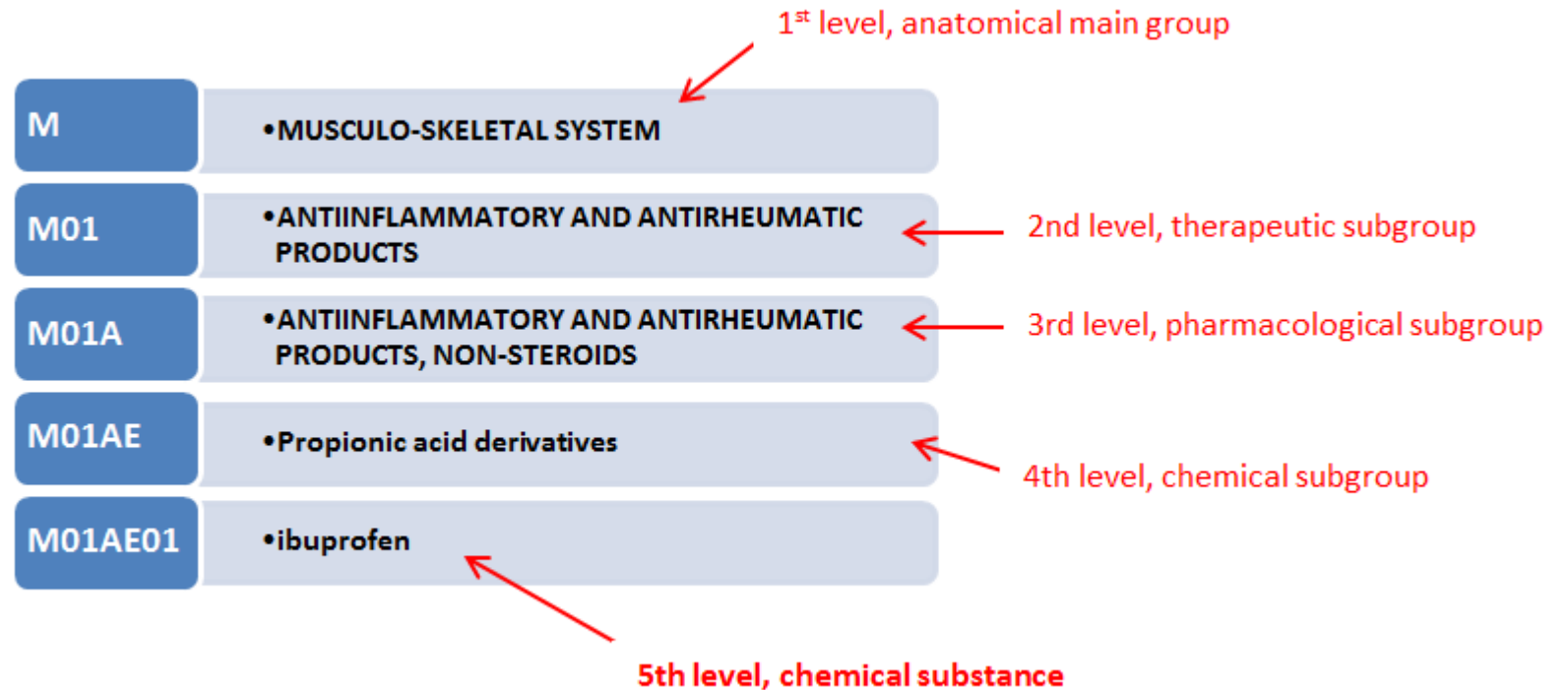
➤ Chemical's classification system

➤ Structure basis on anatomy

- E.g. Ibuprofen
- M01AE01

➤ Unambiguous classification

➤ Allows computer interpretation





European Commission > Live, work, travel in the EU >

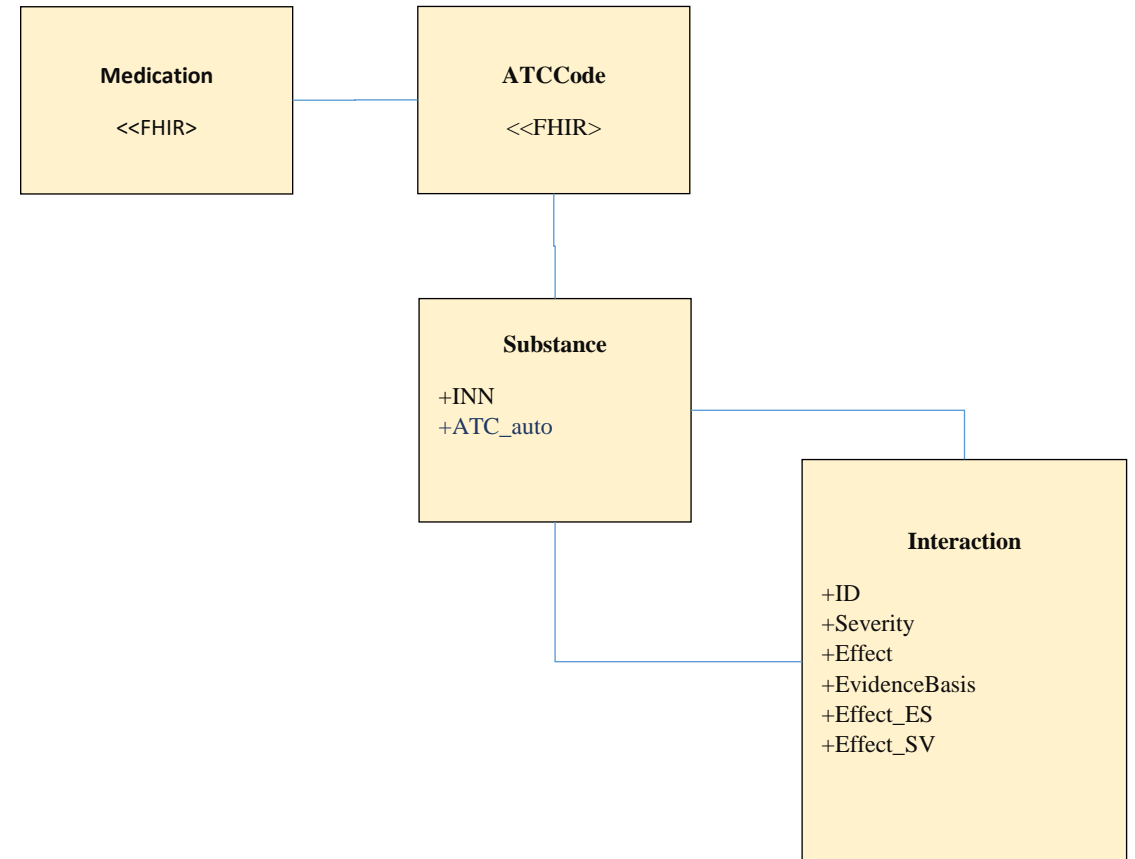
Public Health - Union Register of medicinal products

Centralised medicinal products for human use by ATC code



- ▶ A - Alimentary tract and metabolism
- ▶ B - Blood and blood forming organs
- ▶ C - Cardiovascular system
- ▶ D - Dermatologicals
- ▶ G - Genito urinary system and sex hormones
- ▶ H - Systemic hormonal prep, excluding sex hormones
- ▲ J - General antiinfectives for systemic use
 - ▲ J01 - Antibacterials for systemic use
 - ▶ J01A - Tetracyclines
 - ▲ J01C - Beta-lactam antibacterials, penicillins
 - ▶ J01CA - Penicillins with extended spectrum
 - ▶ J01CE - Beta-lactamase sensitive penicillins
 - ▲ J01CR - Combinations of penicillins, including beta-lactamase inhibitors
 - ▲ J01CR02 - amoxicillin and enzyme inhibitor
 - 📄 Augmentin (referral)
 - ▶ J01CR05 - piperacillin and enzyme inhibitor
 - ▶ J01D - Other beta-lactam antibacterials
 - ▶ J01F - Macrolides and lincosamides
 - ▶ J01G - Aminoglycoside antibacterials
 - ▶ J01M - Quinolone antibacterials
 - ▶ J01X - Other antibacterials
 - ▶ J02 - Antimycotics for systemic use

- The ontology allows modelling of all drug interaction relevant concepts
 - ...for implementation as IT infrastructure
- Ontological approach allows structured approach to designing the database
 - i.e. tables represent real-life concept data entries



```
{  
  "DIAS_id": 101762,  
  "chemical": "Warfarin",  
  "chemical_ATC_code": "B01AA03 ",  
  "interactant": "Amoxicillin",  
  "interactant_ATC_code": "J01CA04 ",  
  "interaction_criticality": "Severe",  
  "interaction_effect": "Amoxicillin potentially alters the anticoagulant effect of warfarin. Manufacturer advises monitor INR and adjust dose.",  
  "interaction_effect_ES_auto": "La amoxicilina altera potencialmente el efecto anticoagulante de la warfarina. El fabricante aconseja monitorizar el INR y ajustar la dosis.",  
  "interaction_effect_SV_auto": "Amoxicillin förändrar potentiellt warfarins antikoagulerande effekt. Tillverkaren rekommenderar att INR kontrolleras och dosen justeras.",  
  "interaction_evidence_basis": "Anecdotal"  
},
```

- Appx 105,000 interactions of over 1000 substances
- Translated in all pilot site languages
- Information presented at C3DP by criticality
 - Output in JSON/XML

```
{
  "B01AA03": [
    { ... }, // 10 items
    { ... } // 10 items
  ],
  "G03XA01": [ ... ], // 1 item
  "J01CA04": [ ... ], // 1 item
  "TEST": [ ... ], // 1 item
  "number_of_interactions_found": 4,
  "number_of_severe_interactions_found": 4
}

{
  "B01": [ ... ], // 8 items
  "G03": [ ... ], // 5 items
  "J01CA04": [ ... ], // 3 items
  "TEST": [ ... ], // 1 item
  "number_of_interactions_found": 16,
  "number_of_severe_interactions_found": 10
}

{
  "B01": [ ... ], // 68 items
  "G03": [ ... ], // 9 items
  "J01": [ ... ], // 67 items
  "TEST": [ ... ], // 1 item
  "number_of_interactions_found": 144,
  "number_of_severe_interactions_found": 104
}
```

➤ ATC allows comparison at various levels

➤ Substance vs substance

- 4 interactions

➤ Substance vs anatomical group

- 16 interactions

➤ Anatomical group vs group

- 144 interactions

THANK YOU



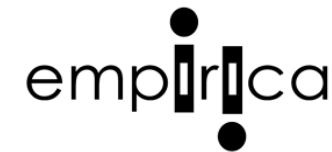
- C3-Cloud is an ICT infrastructure applied for multi-morbidity
- Clinical Decision Support provides continuous automated oversight
- Drug interaction service
- 1004 chemicals
- >100,000 interactions



@idhwarwick



c3-cloud.eu



Osakidetza

