Medication Errors – a challenge of pharmacovigilance – BfArM experience

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WHO - Definition of Pharmacovgilance

Pharmacovigilance

- Science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problem*
- In line with this general definition, the underlying objectives of pharmacovigilance in accordance with the applicable EU legislation are:
  - preventing harm from adverse reactions in humans arising from the use of authorised medicinal products within or outside the terms of marketing authorisation or from occupational exposure; and
  - promoting the safe and effective use of medicinal products, in particular through providing timely information about the safety of medicinal products to patients, healthcare professionals and the public.

→ **Pharmacovigilance is therefore an activity contributing to the protection of patients' and public health.**

*World Health Organization (WHO). The importance of pharmacovigilance: safety monitoring of medicinal products, Geneva: WHO; 2002

Definition of Adverse (Drug) Reaction
in Article 1 of Directive 2001/83/EC

Old:

An adverse reaction is a response to a medicinal product which is noxious and unintended.

New:

An adverse reaction is a response to a medicinal product which is noxious and unintended.
This includes adverse reactions which arise from:

- use of a medicinal product within the terms of the marketing authorisation;
- use **outside the terms of the marketing authorisation**, including overdose, misuse, abuse and **medication errors**;
- occupational exposure.

What is the meaning of **within** and **outside** the terms of marketing authorisation ??

Pharmacovigilance:

→ **within the terms of marketing authorisation:** the use of medicinal product in accordance to the product information (SmPC, Package Leaflet) → ADRs in relation to the drug/active substance itself

→ **outside the terms of marketing authorisation:** the use of medicinal product not in accordance to the product information (SmPC, Package Leaflet or ”state-of-the-art standard of care”) → ADRs in relation to abuse, misuse, off-label use and **medication errors** or occupational exposure

Definitions of Abuse, Misuse, Off-label Use and Medication Error

Good Pharmacovigilance Practices (GVP) Definitions (Rev 3) / Good practice guide on recording, coding, reporting and assessment of medication errors

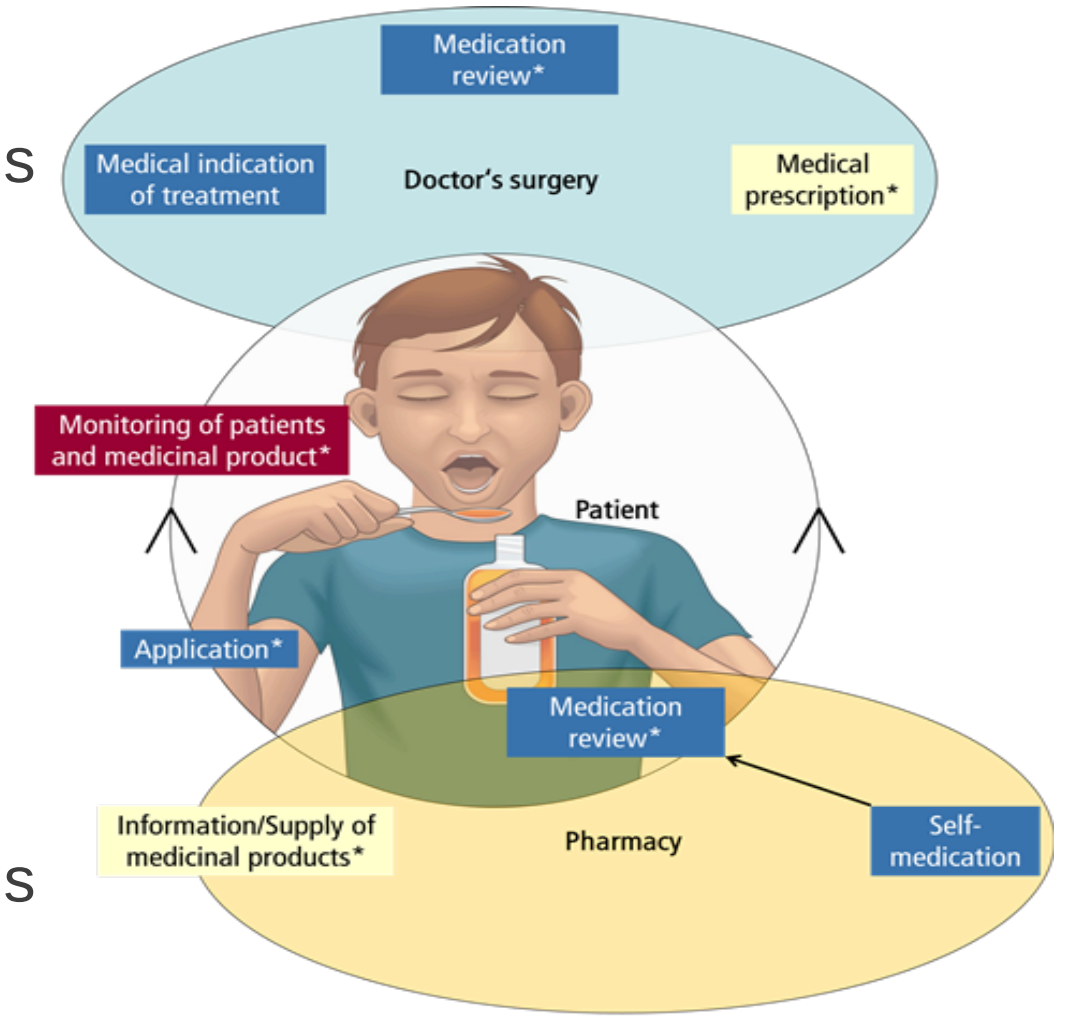
- **Abuse of a medicinal product**
  Persistent or sporadic, intentional excessive use of medicinal products which is accompanied by harmful physical or psychological effects.
- **Misuse of a medicinal product**
  Situations where the medicinal product is intentionally and inappropriately used not in accordance with the authorised product information.
- **Off-label use***
  Situations where a medicinal product is intentionally used for a medical purpose not in accordance with the authorised product information.
  *Off-label use includes use in non-authorised paediatric age categories. Unless specifically requested, it does not include use outside the EU in an indication authorised in that territory which is not authorised in the EU.
- **Medication error**
  A medication error is an unintended failure in the drug treatment process that leads to, or has the potential to lead to, harm to the patient. A failure in the drug treatment process does not refer to lack of efficacy of the drug, **rather to human or process mediated failures.**

Medication Process

Health Care Professionals

Patient and its relatives

Health Care Professionals



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Workload of Medication Errors

Assessment

Distribution

Legal Basis

10 %

Recording, coding, reporting, assessment **and prevention** of medication errors

90 %

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Definition of Medication Errors

Good practice guide on recording, coding, reporting and assessment of medication errors

A **medication error** is an unintended failure in the drug treatment process that leads to, or has the potential to lead to, harm to the patient.

and is therewith preventable!!!!

A failure in the drug treatment process does not refer to lack of efficacy of the drug, rather to human or process mediated failures.

Definition of potential Medication Errors

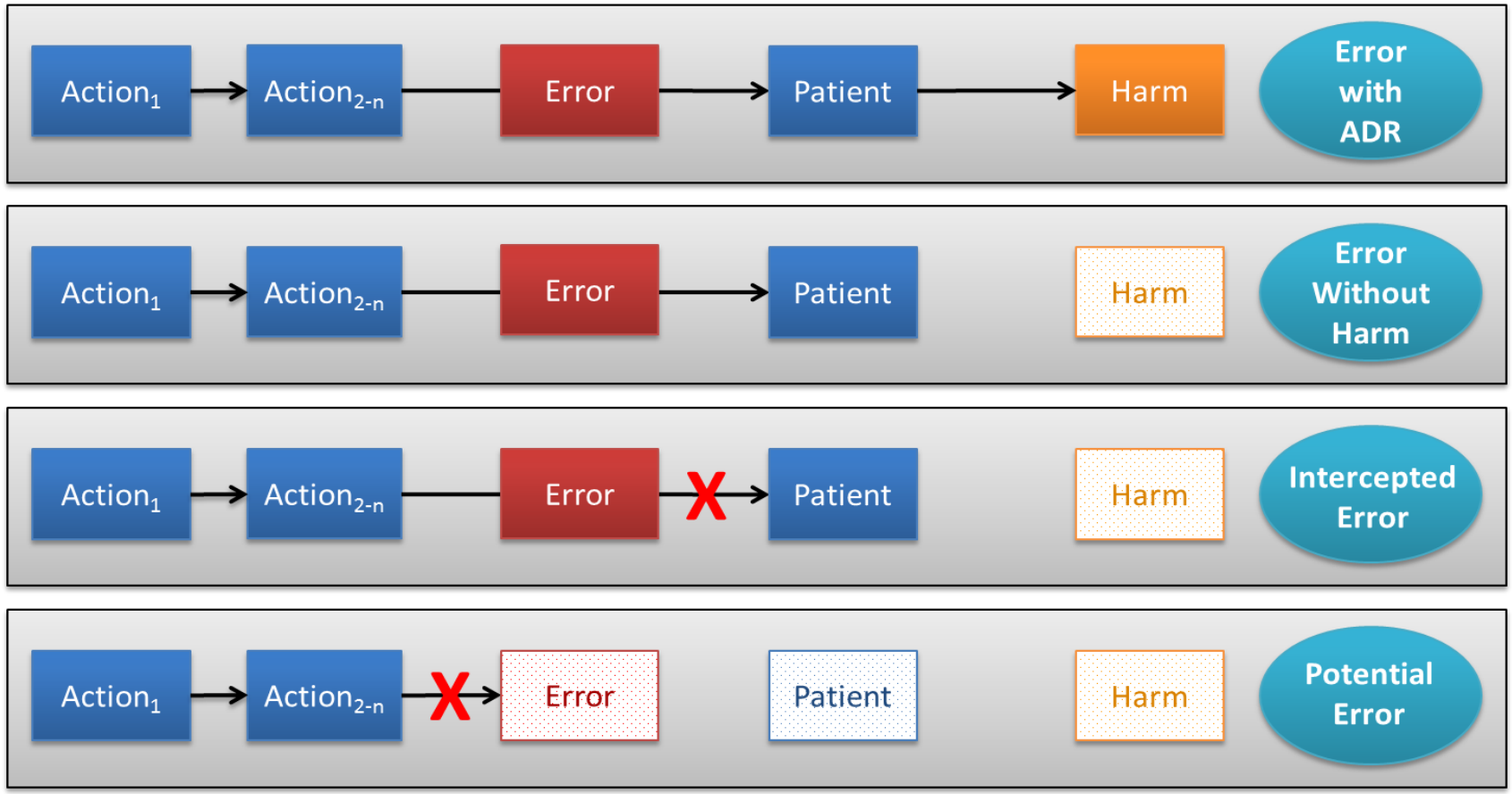
Good practice guide on recording, coding, reporting and assessment of medication errors

The term **potential medication error** refers to all possible mistakes in the prescribing, storing, dispensing, preparation for administration or administration of a medicinal product by all persons who are involved in the medication process and may lead to

a) a medication error with harm, but without knowing the actual cause,
b) a medication error without harm and without knowing the actual cause, or
c) a medication error without harm, but with the awareness of the actual cause.

Classification of Medication Errors

Good practice guide on recording, coding, reporting and assessment of medication errors



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Medication Error Reporting at BfArM

from the Medication Safety Unit at BfArM

Case Reports at BfArM:

Sources:

- spontaneous ADR case reports in German data base, where medication errors are included (656 in 2015)
- reports of ‘potential’ medication errors, especially from health care professional organisations (e.g. AMK, AkdÄ; 173 reports in 2015)

Main causes:

- dosing errors e.g. due to confusing information on strength
- sound- and look-alikes
- wrong kind/route of administration, e.g. i.v. instead of i.m.

ADRs from the German data base

from the Medication Safety Unit at BfArM

656 spontaneous case reports in 2015

with at least one term in HLGT Medication Errors

↓

(+) groups of preferred terms (PT) which meet the definition of medication errors:

(e.g. accidental overdose, drug administration error, drug dose omission, drug name confusion, expired drug administered, incorrect dose administered, incorrect route of drug administration, intercepted drug administration error, labeled drug-drug interaction medication errror, medication error, overdose, underdose, wrong drug administered)

↓

(-) groups of Standardized MedDRA Queries (SMQs) which do not meet the definition of medication errors:

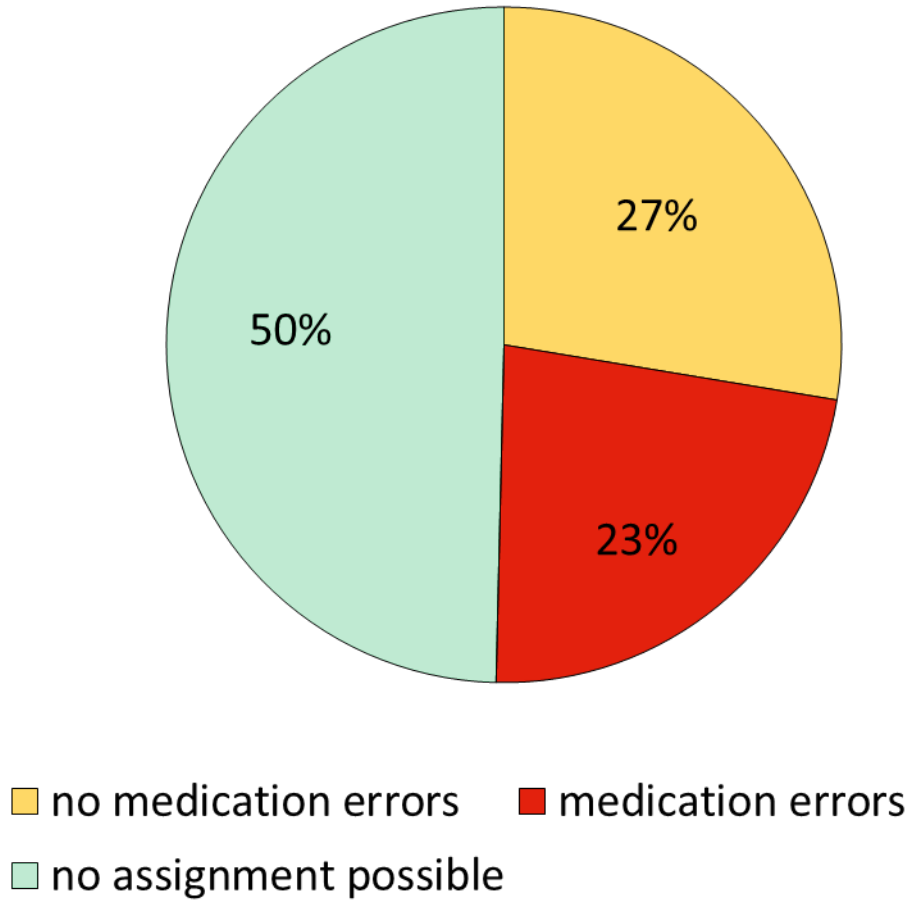
(e.g. depression and suicide and self-injury, intentional overdose, suicide attempt und off-label use, drug abuse/dependence, alcohol interaction/poisoning, intentional poisoning and accidental intake)

↓

551 case reports

Problems of the Identification of Medication Errors in ADR Reports

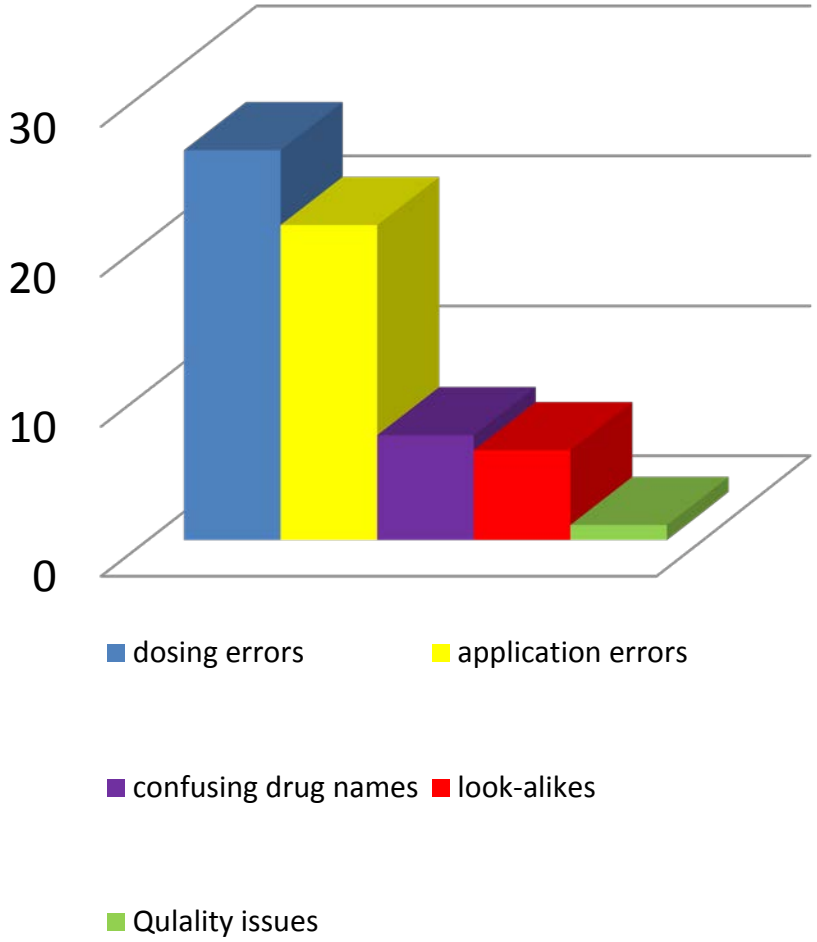
from the Medication Safety Unit at BfArM

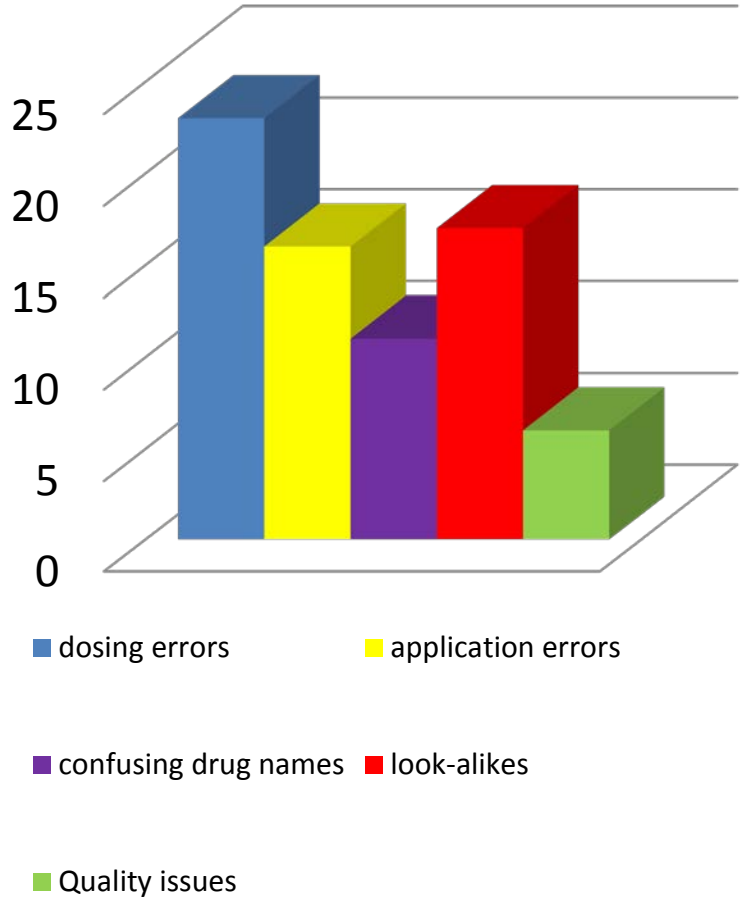


Assessment of narratives

- No clear medication process or product name with information on strength or pharmaceutical form;
- No correct PT or more than one PT;
- No causal relationship between cause and clinical consequences; often only general description of clinical symptoms;
- Mixture of administration problems and pharmaceutical nomenclature (e.g. ‘product issue‘);

61 spontaneous identified medication errors with ADR in comparison with 73 'potential' cases reported to the Medication Safety Unit in the first half of 2015





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Reports of ‘Potential’ Medication Errors

to the Medication Safety Unit at BfArM

173 (73 + 100) case reports in 2015

(+) with a close causal relationship to potential medication errors

(-) groups of terms which do not meet the definition of medication errors:

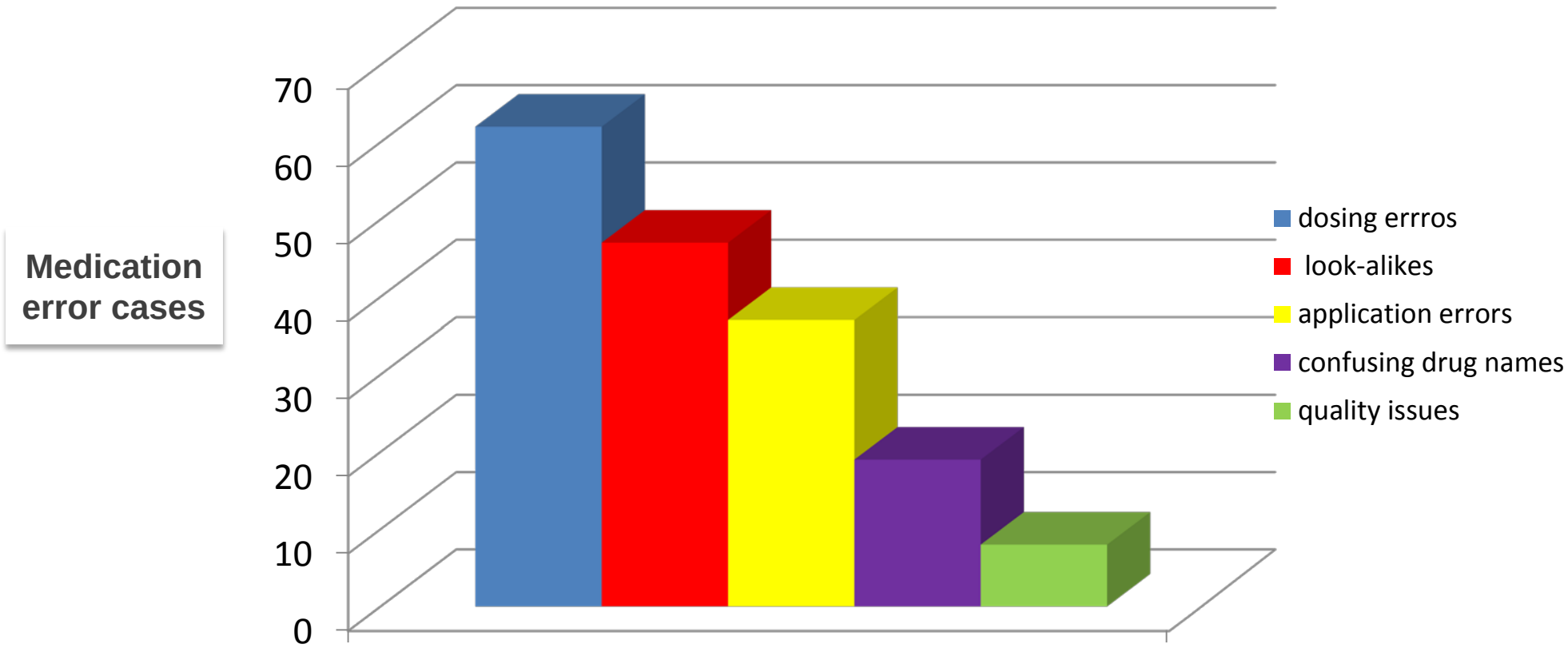
(e.g. no compliance and quality product issues)

approximately 160 case reports

Reports of ‘Potential’ Medication Errors

to the Medication Safety Unit at BfArM

173 ‘potential‘ medication errors in 2015



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Reports of 'Potential' Medication Errors
First Example
From the Medication Safety Unit at BfArM

Problem:

Imbun 1000 mg film-coated tablets were prescribed. The patient used without further advice **Imbun 800 mg prolonged-release tablets**, because these tablets were available at home and the patient thought the dose was lower than the prescribed medicinal product with 1000mg.

Afterwards the patient suffered from massive lowering of blood pressure.

What had happened?

Unintended overdose because of lack of knowledge of the real amount of active substance in the two different formulations of **Imbun** (proposed PT→ drug name confusion leads to dosing errors):

Imbun 1000mg film-coated tablets contain **585mg of ibuprofen**

Imbun 800mg prolonged-release tablets contain **800mg of Ibuprofen**

Reports of 'Potential' Medication Errors
First Example
From the Medication Safety Unit at BfArM

Solution:

After strong recommendations from the authority (BfArM), the MAH changed the names as follows:

old: Imbun 1000 mg film-coated tablets

New: Imbun IBU-Lysinat 1000mg film-coated tablets

1 film-coated tablet contains 1000mg of Ibuprofen, DL-Lysinsalt equivalent to **585,2 mg of Ibuprofen**.

old: Imbun 800 mg prolonged-release tablet

New: Imbun Ibuprofen 800mg prolonged-release tablet

1 prolonged-release tablet contains **800mg of ibuprofen**.

Now both medicinal product names are comparable with regard to strength and dose calculation is much easier for health care professionals and the patients.

Reports of ‘Potential’ Medication Errors
Second Example
From the Medication Safety Unit at BfArM

Problem:

Patients in an intensive care unit received **Nepresol Inject** for hypertension, but there was no clinical effect and the patients received other medicinal products for lowering the blood pressure.

What had happened?

The health care professionals had used only the solution for injection, namely **water for injection**, because the pack included two kinds of ampoules with the same product name:

Nepresol Inject

Reports of 'Potential' Medication Errors
Second Example
From the Medication Safety Unit at BfArM

Solution:

After strong recommendations from the authority (BfArM), the MAH changed the name of the ampoules as follows:

First (powder) Ampoule:

old: Nepresol Inject

New: Nepresol Inject ; Powder for solution for injection

Second (solution) Ampoule:

old: Nepresol Inject

New: Water for injection of Nepresol Inject

Through new and different names for the ampoules in one medicinal product (= Nepresol Inject), their content is now better identifiable and the correct use of the ampoules is much easier for health care professionals.

Spontaneous Case of Medication Error in the German ADR Database
Third example

From the Medication Safety Unit at BfArM

Problem/Narrative (PT = incorrect drug administration rate):

This report concerns a 68 year old female. … The patient's medical history included … .
The patient's weight was 120 kilograms. On 21-DEC-2005, the patient developed hypotension and cold sweats after an accidental injection of 6 ml haloperidol on 17-DEC-05. The patient was then hospitalised from 22-DEC-05 until 03-JAN-06. On 22-DEC-05 … . The patient recovered from hypotension and cold sweating on 21-DEC-2005, from hypertension on 03-JAN-2006, and from urinary tract infection on an unknown date. **Treatment with haloperidol decanoate was withdrawn.** Causality per reporter regarding hypertension: probable!

What was happened?

How did the female patient get accidentally 6ml haloperidol and why this preferred term is chosen?

Spontaneous Case of Medication Error in the German ADR Database
Third example

From the Medication Safety Unit at BfArM

What was happened?

How did the female patient get accidentally 6ml of haloperidol and why this preferred term is chosen (PT = incorrect drug administration rate)?

Drug name misinterpretation leads to application errors with the result of overdosing:

Haldol-Janssen Decanoat 3 ml **(=150mg of Haloperidol in 3 ml)**
→1x in four weeks

Haldol-Janssen Decanoat **(= 50mg of Haloperidol in 1 ml)**
→1x in four weeks

Haldol-Janssen solution for injection 5 mg/ml **(= 5mg of Haloperidol in 1 ml)**
→ 1 - 3x daily

The health care professional did confuse the formulation Haldol-Janssen solution for injection 5 mg/ml with Haldol-Janssen Decanoat (=50 mg or 150 mg Haloperidol in 1ml).

Therefore the female patient was given the slow release formulation with severe ADRs due to massive overdosing.

Spontaneous Case of Medication Error in the German ADR Database
Third example

From the Medication Safety Unit at BfArM

Solution:

After recommendation from the authority (BfArM), the MAH changed the names of the slow release formulations as follows:

old: Haldol-Janssen Decanoat 3 ml

New: **Haldol-Janssen Decanoat Depot 3 ml**

old: Haldol-Janssen Decanoat

New: **Haldol-Janssen Decanoat Depot 1 ml**

Now both new medicinal product names are better identifiable as slow release formulations with a higher content of active substance and dose calculation is done much easier for the health care professionals.

Conclusions Following the Comparison of Reports

From the Medication Safety Unit at BfArM

- In contrast to spontaneous ADR reports, in case reports of potential medication errors the causes are described in more detail;
- Many of the ADR reports with the HLGT term medication error are not medication errors in accordance with the definition (e.g. intentional poisoning, off-label use, interactions, quality issues, irrelevant exposure terms, information of incompatibility etc.);
- The coding is not consistent and PTs are mentioned twice or they are not sufficient for the cause analysis;
- The full name (with information on strength and pharmaceutical form) is necessary for the cause analysis;
- For coding purposes more specific PTs are needed (e.g. look- or sound-alikes or confusing strength data).

Proposals for improving documentation requirements

From the Medication Safety Unit at BfArM

- Categorization of all ADR reports in accordance to the EU requirements and best practice guide in within and outside the MA:
  – intentional overdosing, e.g. in context of off-label use
  – misuse
  – abuse
  – **medication error** (including unintentional overdosing)
  – occupational exposure (including accidental exposure)

- Specification of PTs in dosing and handling problems below the medication error level

- Description of the causal link between causes and clinical consequences also through the creation of new PT, like:
  - Look-alikes,
  - Sound-alikes,
  - Confusing strength data

Thank you very much for your attention!

Ask

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