Drug Saf
DOI 10.1007/s40264-016-0410-4

LEADING ARTICLE

Medication Errors: New EU Good Practice Guide on Risk Minimisation and Error Prevention

Thomas Goedecke[1] · Kathryn Ord[2] · Victoria Newbould[1] · Sabine Brosch[1] · Peter Arlett[1]

Abstract 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. Reducing the risk of medication errors is a shared responsibility between patients, healthcare professionals, regulators and the pharmaceutical industry at all levels of healthcare delivery. In 2015, the EU regulatory network released a two-part good practice guide on medication errors to support both the pharmaceutical industry and regulators in the implementation of the changes introduced with the EU pharmacovigilance legislation. These changes included a modification of the 'adverse reaction' definition to include events associated with medication errors, and the requirement for national competent authorities responsible for pharmacovigilance in EU Member States to collaborate and exchange information on medication errors resulting in harm with national patient safety organisations. To facilitate reporting and learning from medication errors, a clear distinction has been made in the guidance between medication errors resulting in adverse reactions, medication errors without harm, intercepted medication errors and potential errors. This distinction is supported by an enhanced MedDRA® terminology that allows for coding all stages of the medication use process where the error occurred in addition to any clinical consequences. To better understand the causes and contributing factors, individual case safety reports involving an error should be followed-up with the primary reporter to gather information relevant for the conduct of root cause analysis where this may be appropriate. Such reports should also be summarised in periodic safety update reports and addressed in risk management plans. Any risk minimisation and prevention strategy for medication errors should consider all stages of a medicinal product's life-cycle, particularly the main sources and types of medication errors during product development. This article describes the key concepts of the EU good practice guidance for defining, classifying, coding, reporting, evaluating and preventing medication errors. This guidance should contribute to the safe and effective use of medicines for the benefit of patients and public health.

Key Points

Medication errors are the most common preventable cause of undesired adverse events in medication practice and present a major public health burden.

EU legislation requires information on medication errors to be collected and reported through national pharmacovigilance systems for evaluation and assessment.

Use of common definitions and collaboration with patient safety organisations underpin error prevention through the product life-cycle.

The views expressed in this article are the personal views of the authors and may not be understood or quoted as being made on behalf of or reflecting the position of the EMA or one of its committees or working parties. Figures 1 and 4 are reproduced with the permission of the EMA.

✉ Thomas Goedecke
thomas.goedecke@ema.europa.eu

[1] Pharmacovigilance Department, Inspections and Human Medicines Pharmacovigilance Division, European Medicines Agency (EMA), 30 Churchill Place, London E14 5EU, UK

[2] Benefit Risk Management Group, Vigilance and Risk Management of Medicines, Medicines and Healthcare products Regulatory Agency (MHRA), 151 Buckingham Palace Road, London SW1W 9SZ, UK

Published online: 03 March 2016

1 Introduction

Medication errors may occur at any stage of the drug treatment process during prescribing, storing, dispensing, preparing for administration or administering medicinal products and may lead to, or may have the potential to, lead to harm. Medication errors are the most common single preventable cause of adverse events in medication practice, with annual costs for European healthcare systems between €4.5 and 21.8 billion [1]. A systematic review of hospital admissions in several EU and non-EU countries showed a median of 3.7 % (range 1.4–15.4) of admissions were drug-related (i.e. due to adverse reactions, over- or under-treatment or treatment non-adherence) and preventable [2]. In the EU, estimates of medication-error rates in ambulatory care were 7.5 % at prescription and 0.08 % at dispensing, whereas in hospital care the rates were higher at between 0.3–9.1 and 1.6–2.1 %, respectively [3–7]. Since 2012, the EU pharmacovigilance legislation [8] includes medication errors in the definition of an adverse reaction and requires national competent authorities (NCAs) and marketing authorisation holders (MAHs) to report medication errors associated with suspected serious and non-serious adverse reactions to EudraVigilance, the EU system for collecting safety reports for post-authorisation safety monitoring of medicines [9]. Following the recommendations of an international stakeholder workshop in 2013 [10], the heads of Medicines Agencies agreed an action plan to support the implementation of these legal provisions with the good practice guide on medication errors as key deliverable [11]. The guidance was developed through a collaborative inter-stakeholder approach, launching new initiatives for cooperation amongst NCAs and patient safety organisations (PSOs) in Member States, represented at EU level by the European Commission's Patient Safety and Quality of Care Expert Group [12], which provides recommendations on patient incident reporting and learning systems [13]. This article explains the underlying concepts of the two-part good practice guide on medication errors [14, 15] released in 2015, which is complementary to the guideline on Good Pharmacovigilance Practices (GVP) [16] and other scientific guidelines on quality, safety and efficacy of medicines published by the European Medicines Agency (EMA).

2 Definition and Classification of Medication Errors

To facilitate compliance with pharmacovigilance obligations and to encourage patient and healthcare professional reporting for regulatory purposes, a new definition of medication error is proposed as "an unintended failure in the drug treatment process that leads to, or has the potential to lead to, harm to the patient." With this definition, failure is interpreted as a human- or process-mediated error rather than the lack of efficacy of a medicine, and for pharmacovigilance recording and reporting purposes the concepts of intentional overdose, off-label use, misuse and abuse need to be clearly distinguished from medication errors. In the classification proposed in Fig. 1, it can be seen that a

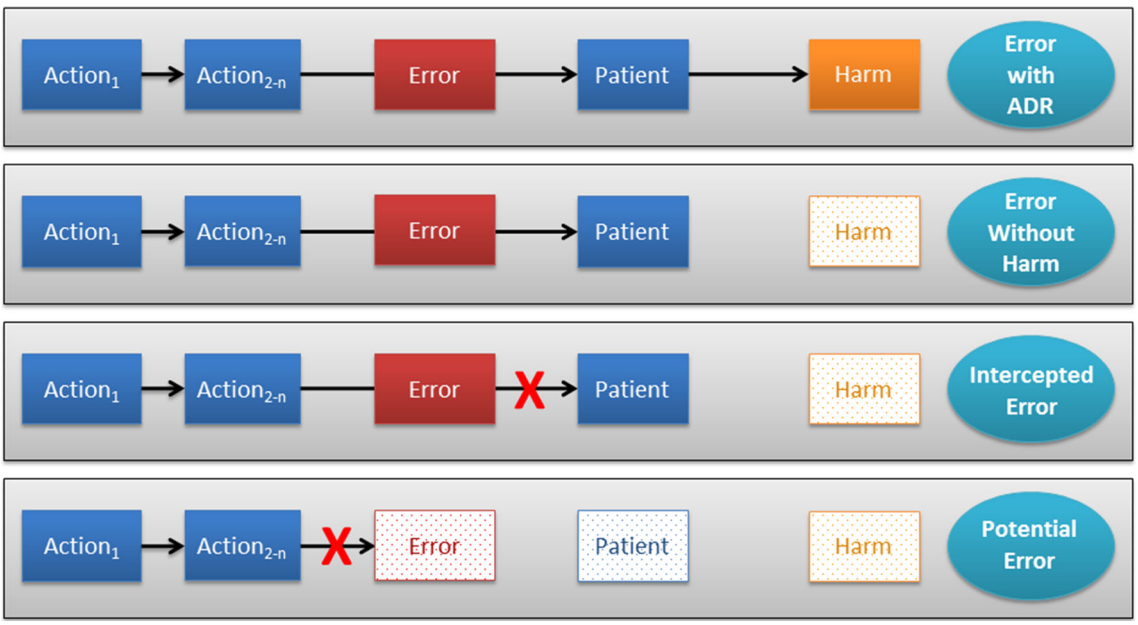

Fig. 1 Classification of medication error reports for pharmacovigilance purposes. Depending on the break in the chain of events (represented by *X*), medication errors may be classified as error with ADR, error without harm, intercepted error and potential error [14]. *ADR* adverse drug reaction

medication error may be associated with an adverse drug reaction (ADR) or may occur without causing harm to the patient. Furthermore, an error may occur but be intercepted before it reaches the patient. The classification includes the recognition of circumstances that could potentially lead to a medication error and may or may not involve a patient as a potential error [14].

3 Recording and Reporting Medication Errors in the EU

Recording and reporting medication errors are important public health processes providing the opportunity to gain knowledge on their causes and strengthen risk minimisation. Since the new EU legislation made it clear that medication errors that result in harm are reportable within the EU pharmacovigilance system, the number of cases of medication errors reported to EudraVigilance has dramatically increased (Fig. 2). By November 2015, 1.74 % of the total number of (serious and non-serious) cases in EudraVigilance with European Economic Area (EEA) origin and 3.36 % of non-EEA cases include terms that describe a medication error (Fig. 1 inset).

Equally important is the implementation of an exchange mechanism between NCAs responsible for the regulation of medicines and patient safety organisations. Through access to more and better information, these new rules for collaboration aim to further improve the learning from errors in daily medication practice. Experience from the UK has shown that collaboration between the National Health Service (NHS) in England and the Medicines and Healthcare products Regulatory Agency (MHRA) in sharing medication incident data has improved the quality of reports and optimised learning from errors [17]. To effectively reduce the burden of harm from medication errors will require an understanding not only of whether errors occur with a certain pattern or at increased frequencies but also of the causes, contributing factors and clinical consequences of the error, including any mitigating actions that could prevent the error from occurring again.

4 Terminology to Support Good Coding Practice

MedDRA®[1] is the terminology used internationally by regulatory authorities, pharmaceutical companies, and clinical research organisations to share regulatory

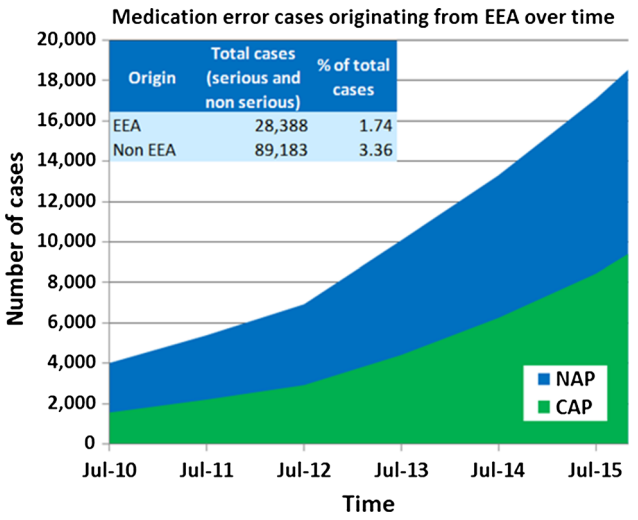

Fig. 2 Reporting of medication errors to EudraVigilance. Number of individual cases with EEA origin where a medication error has been reported for nationally authorised (NAP) and centrally authorised (CAP) medicinal products between 2010 and 2015. The inset shows the total number of serious and non-serious EEA and non-EEA cases in EudraVigilance where a medication error has been reported, including the percentage of the total number of cases (cut-off date: 15 November 2015). *CAP* centrally authorised medicinal product, *EEA* European Economic Area, *NAP* nationally authorised medicinal product

information on medicinal products. Good coding practice is fundamental for efficient data retrieval, analysis and learning from medication error reports. Based on real-life examples, MedDRA® provides the terminology for coding medication errors as reported, including the ability to code the parameters essential for the conduct of root cause analysis (RCA) referred to in Table 1 and the (potential) clinical consequences regardless of whether the error was associated with adverse reaction(s). The most commonly reported terms describing a medication error in individual cases reported spontaneously to EudraVigilance are shown in Fig. 3.

MedDRA® version 18.0 includes changes to the hierarchy with additional granularity to facilitate a precise description of the error. The Higher Level Group Term (HLGT) 'Medication Errors' has been reorganised and an additional HLGT 'Product use issues' created to encourage distinction between unintentional/accidental events and intentional acts (off-label use or misuse). Work is ongoing for future enhancement of the hierarchy as further experience is gained. The MedDRA® Term Selection Points to Consider (MTS:PTC) documents [18] have also been updated and expanded accordingly. To further support retrieval of cases from pharmacovigilance databases, a

[1] MedDRA®, the Medical Dictionary for Regulatory Activities, is the international medical terminology developed under the auspices of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). The MedDRA® trademark is owned by the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) on behalf of ICH.

Table 1 Follow-up parameters relevant for medication error reporting in pharmacovigilance

Parameter	Example
Setting	• Inpatient (hospital, nursing home, care home)
	• Outpatient (general practitioner, specialist, ambulatory)
	• Pharmacy, drug store, private home, etc.
Stage of medication process	• Prescribing
	• Storage in clinical practice
	• Dispensing
	• Preparation for administration
	• Administration
Contributing factors	• Human factors, e.g. communication issues
	• Organisational issues, e.g. transition of patient care
	• System or work-process related, e.g. staffing
	• External factors, e.g. IT system issues
Risk factors defining the treated population	• Special populations, e.g. paediatric population, elderly
	• Disease (severity, co-morbidities)
	• Medical history, e.g. alcohol use, tobacco use, concomitant therapies/treatment
	• Pharmacology, e.g. pharmacodynamic, pharmacokinetic or pharmacogenetic factors

Standardised MedDRA® Query (SMQ) [19] for medication errors has been developed by the Council for International Organisations of Medical Sciences (CIOMS). Further tools are required to support the detection of signals of medication errors in pharmacovigilance databases, acknowledging that commonly applied statistical methodologies based on proportional reporting rates cannot be applied to medication errors given the lack of a causal association between the occurrence of a human- or system-related error and the use of a medicine.

5 Reporting Requirements

In line with EU pharmacovigilance legislation applicable to MAHs and NCAs, reports of medication errors associated with an adverse reaction are reportable to EudraVigilance in the same way as any other suspected adverse reaction. Within regulatory pharmacovigilance, medication errors may be reported spontaneously either by healthcare professionals (HCPs) or consumers to MAHs and/or NCAs through national pharmacovigilance reporting systems in Member States. Additionally, suspected adverse reactions related to medication errors may be described in the scientific or medical literature or reported in the context of non-interventional studies and compassionate use programmes (solicited reports). The EU reporting requirements are presented in Fig. 4. Medication error reports not associated with suspected serious adverse reactions brought to the attention of MAHs are outside the scope of EU expedited (15-day) reporting requirements and should therefore not be submitted as individual case safety reports (ICSRs). However, such reports should be included as summary tabulations in periodic safety update reports (PSURs) and risk management plans (RMPs). From a public health perspective, in addition to NCAs informing PSOs of medication errors reported to them, it is considered good practice that NCAs in Member States are also informed of adverse reactions associated with medication errors that have been brought to the attention of a PSO in the respective EU Member State.

To facilitate the establishment of collaborative relationships between regulatory bodies and PSOs in Member States, the good practice guide provides a model for collaboration [14]. The primary purpose of this model is to support the exchange of information and make available to PSOs medication error reports associated with adverse reaction(s). To date, not all EU Member States have established national patient safety reporting systems or independent PSOs; therefore, the EU regulatory network's initiative on medication errors is a step towards raising awareness of the new legal provisions, to address underreporting of medication errors from both a pharmacovigilance and a patient safety perspective and ultimately to strengthen the knowledge base for regulatory decision making through efficient collaboration [14].

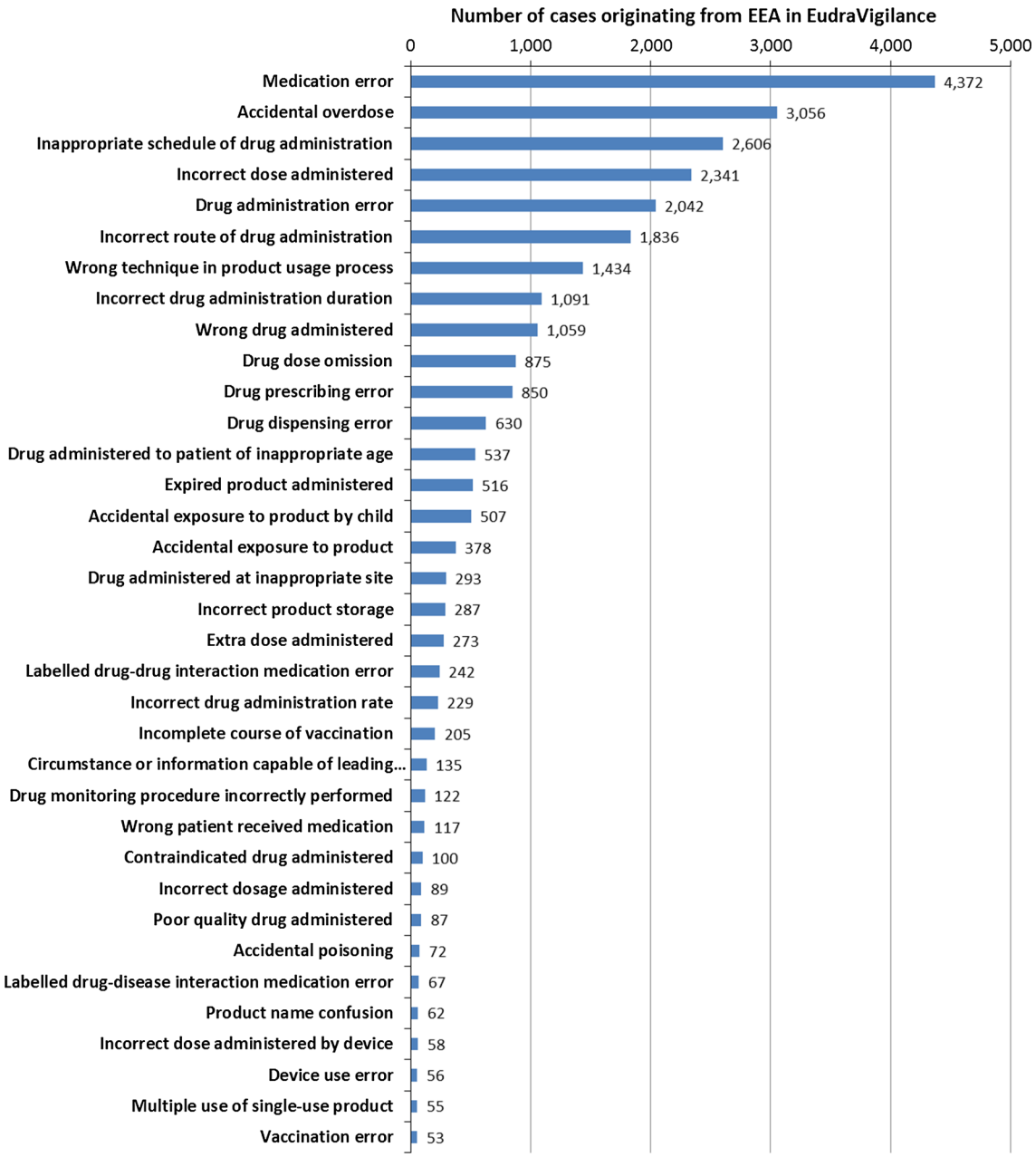

Fig. 3 Most common MedDRA® preferred terms describing a medication error in individual cases with European Economic Area (EEA) origin spontaneously reported to EudraVigilance (cut-off date: 15 November 2015)

6 Life-Cycle Approach to Prevent Errors

The documentation of the risk of medication errors at all stages of a medicinal product's life-cycle is a key principle of risk management planning and a prerequisite to choosing the right tools for error prevention as required for a medicinal product's risk management system [15]. Risk management planning in relation to medication errors is a continuous, pro-active endeavour that ideally starts at the early stages in product development and continues with the development of new products in the same therapeutic class, and as the use of authorised medicines changes with increasing experience in clinical practice. For example, the US FDA has issued draft guidance, which is also widely applied by EU manufacturers, on safety considerations for product design and for container and carton label design to minimise the risk of medication errors [20, 21]. The risk management process involves the systematic collection of pharmacovigilance data, analysing and evaluating new and known risks, selecting and implementing appropriate risk

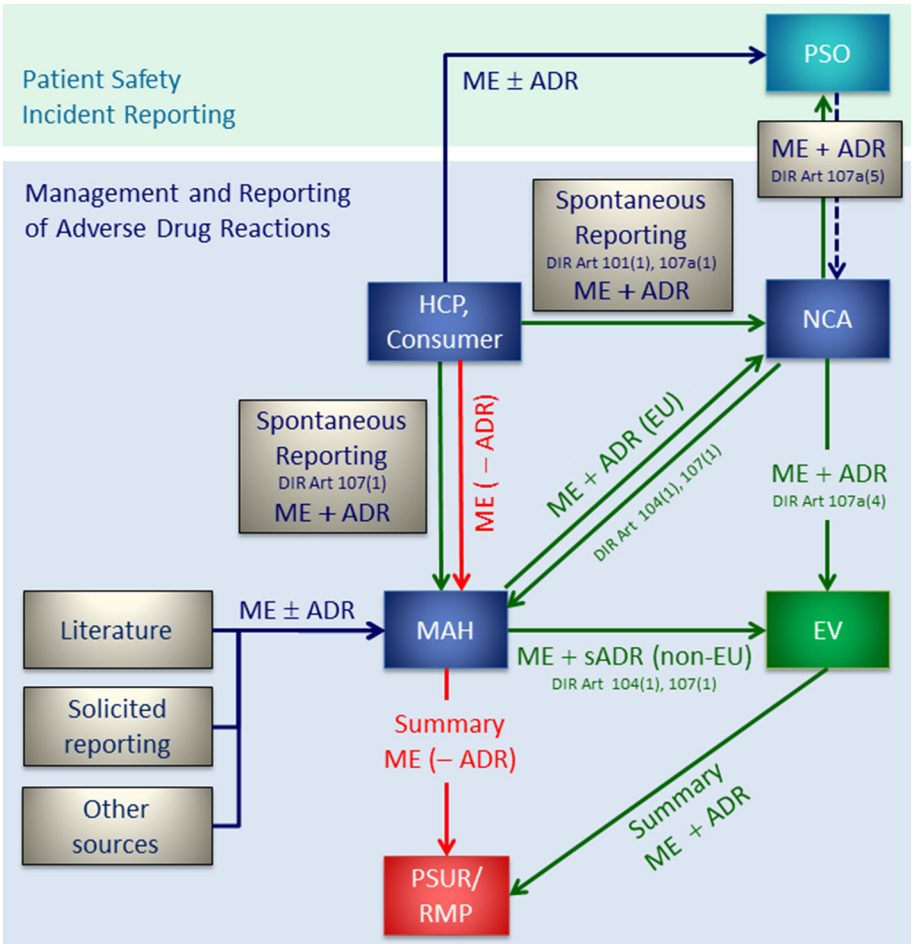

Fig. 4 EU reporting requirements for medication errors (MEs) (*solid blue arrows*) and the stakeholders involved: marketing authorisation holders (MAHs), national competent authorities (NCAs), healthcare professionals (HCPs) and consumers, and authorities, bodies, organisations and/or institutions responsible for patient safety (PSOs) where they exist in EU Member States in accordance with Article 107a (5) of Directive 2001/83/EC [14]. *Green arrows* refer to medication error reports associated with (serious and non-serious) suspected adverse drug reaction(s) (+ADR), including non-EU suspected serious ADR(s) (+sADR), which MAHs must report to EudraVigilance. *Red arrows* represent medication error reports not associated with suspected adverse reactions (− ADR). The *blue dotted arrow* represents adverse reactions associated with medication errors brought to the attention of a PSO. *PSUR* periodic safety update report, *RMP* risk management plan

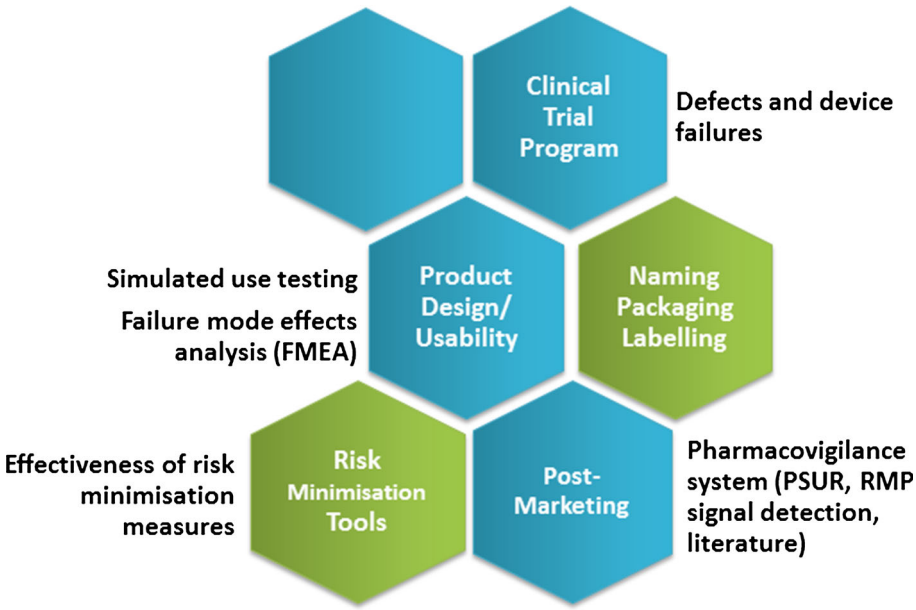

Fig. 5 The management of the risk of medication errors involves evidence from all stages of the product life-cycle. *PSUR* periodic safety update report, *RMP* risk management plan

minimisation tools and monitoring the effectiveness under real-life conditions through process indicators and health outcome measures. Because the actual harm arising from medication errors is difficult to quantify in public health and economic terms, the prevalence of hospital admissions due to preventable adverse reactions before and after such

interventions may be compared as a measure of effectiveness, as described in research on the UK NHS [22].

Any significant changes to the marketing authorisation of existing medicinal products or the introduction of new medicinal products with marked differences in product name, pharmaceutical form, strength, method of preparation, route of administration or target population compared with existing medicines has the potential to change the risk of medication errors. Therefore, such changes to product use should be accompanied by consideration of additional risk management.

Figure 5 presents the different stages of a product's lifecycle, and all these stages can generate evidence to be considered in risk management planning. Typical errors during the clinical trial programme include defects and device failures that may be related to the product design being tested, i.e. the pharmaceutical form, posology, preparation steps for administration or the use of an administration device. Other sources of errors include the naming, packaging and labelling of the investigational medicinal product, which often involves multi-language labelling and multiple dosages or dosage forms in the same package. The risk analysis of use-related errors during the clinical trial programme should take into account the potential for confusion and mix-up with alternative treatment options focussing on similarities in posology, appearance, method of administration, strength and packaging.

Pharmaceutical quality systems apply RCA to investigate any deviations or product defects. RCA is commonly applied to analyse the causes and lessons learnt from medication errors in patient safety incidents and not a classical pharmacovigilance activity as it is performed on an individual case level within the healthcare setting. In pharmacovigilance systems, RCA may be undertaken on a case-by-case basis to better inform error-prevention measures proportionate to the clinical consequences, based on appropriate case follow-up to obtain accurate information on the facts and circumstances contributing to the adverse reaction. Table 1 includes follow-up parameters for recording and reporting cases of medication errors for pharmacovigilance purposes, providing essential information for the conduct of RCA, in addition to information routinely followed up in adverse reaction reports.

Failure mode and effects analysis (FMEA), often used during product development, involves the analysis of processes leading to potential failures in the drug-treatment process and of medication errors before they occur, including possible causes, the effects on patients, the probability for error and actions to reduce the occurrence of failures. The assessment for the potential for medication errors will also take into account the results of human factor testing methods (e.g. simulated use testing), if this has been performed to provide supporting evidence for new marketing authorisation applications or line extensions, as to whether user instructions are adequately understood by healthcare professionals, patients and consumers. A complementary method to FMEA is the Fault Tree Analysis (FTA) method, widely used to assess system safety and reliability, which may be equally effective to manage the risk of medication errors. For medicinal products supplied with an administration device, EU harmonised standards such as ISO 14971[2] and IEC62366[3] may be applied to identify hazards, to estimate and evaluate associated risks and to monitor the effectiveness of controls.

Learning from medication errors during the early post-marketing period is particularly relevant for effective risk management, and activities should focus on each stage of the drug treatment process, taking into account all available data generated by the pharmacovigilance system, including a review of data in periodic safety update reports, RMPs, and the scientific literature. Typical errors during prescribing may be related to unclear or illegible instructions regarding the patient, medicinal product, pharmaceutical form (e.g. immediate or modified release), strength, dosing and length of treatment. Dispensing errors due to mix-ups of similar product names and/or packaging or pharmaceutical forms are common at community and hospital pharmacy level, and the quality of a medicine may be compromised by incorrect storage conditions, leading to a medication error. Product quality issues are abnormalities that could also be introduced during manufacturing, labelling, packaging, shipping or otherwise handling the product, and should be clearly distinguished from medication errors. Further sources for errors with marketed products include parenteral formulations requiring complex dilution or reconstitution steps for preparation for administration and potential incompatibilities with diluents. Errors related to the use of complex drug-delivery devices (e.g. pre-filled injector devices) are a concern, particularly if devices are not used in line with user instructions or if instructions are unclear or not supported by appropriate illustrations.

7 Common Errors in Paediatric Patients

Due to the variation in age, body surface area, body weight and size depending on the degree of development, the risk of medication errors is particularly high in paediatric

[2] ISO 14971—medical devices—application of risk management http://www.iso.org/iso/iso_catalogue/catalogue_ics/catalogue_detail_ics.htm?csnumber=38193.

[3] IEC62366—medical devices—application of usability engineering to medical devices http://www.iso.org/iso/catalogue_detail.htm?csnumber=38594.

patients, with both overdosing [23] and under-dosing [24] commonly reported in the literature as a result of paediatric medication errors. Errors may be due to the prescribing of medicines based on patient weight or body surface area, which is not routinely measured in clinical practice at each prescription, or due to the lack of adequate paediatric formulations, increasing the risk of dose miscalculations when adult-strength formulations are used instead. Marked differences in the pharmacokinetic profile of neonates compared with older children and adults mean that careful dose adjustment is required if other than paediatric formulations are used. Specific dosing devices such as oral syringes for liquid oral formulations have been shown to reduce dosing errors in paediatric patients [25], and the risk of mix-ups of different strengths should be minimised by adequate naming, labelling and packaging distinct from similar medicines used in children and/or adults.

8 Common Errors in the Elderly

Polypharmacy in elderly patients is a common cause for mix-ups and confusion of medicines, with a high propensity for errors. Physical and/or cognitive impairment in elderly patients adds to difficulties in taking medication according to the instructions for use, i.e. opening child-resistant containers, pushing tablets or capsules through aluminium blisters, counting drops, etc. Dexterity problems and impaired eyesight should be taken into account in the design of medicines intended for use in older patients to avoid difficulties in reading labels, dialling units on an insulin pen, etc. The pharmaceutical development of medicines used in these special populations should consider the potential for medication errors in the product design. Post-authorisation experience has demonstrated that novel high-strength insulin products (i.e. higher than the EU-wide standard 100 units/ml concentration) should ideally be manufactured in pre-filled insulin pen devices that automatically adjust for strength without the need for dose conversion or re-calculation [26].

9 Minimising the Risk of Medication Errors

Based on the product-specific past experience of the EMA's Pharmacovigilance Risk Assessment Committee (PRAC), the potential sources of medication errors in medicinal product design have been reviewed, and an overview of design features that have been proven to reduce the risk of medication errors for common pharmaceutical formulations is provided in the annex of the good practice guide [15]. The potential for medication errors is an integral part of a medicine's RMP in line with GVP Module V [16], taking into account user-tested product design and routine risk minimisation with a focus on the naming, labelling and packaging of the medicinal product. The invented name of a medicinal product should avoid orthographic or phonetic similarity with other invented names to avoid confusion in print, speech and handwriting, and should not include international non-proprietary names (INNs). In line with the EMA's guideline on the acceptability of invented names for medicinal products processed through the centralised procedure [27], the risk of cognitive errors due to similarity with approved invented names is routinely assessed by the CHMP's (Invented) Name Review Group [28]. User instructions for patients, carers and healthcare professionals in the patient information leaflet (PIL) and summary of product characteristics (SmPC) should be clear, understandable and tailored to the target population, explaining (and illustrating with pictures or pictograms if necessary) how the product is used safely under normal conditions of use. Good labelling ensures that a medicinal product can be clearly identified to reduce the risk of confusion with other products when selecting a medicine, and the minimum information is provided on the outer packaging (or immediate packaging when there is no outer packaging) for the safe storage, selection, preparation, dispensing, administration and tracking of medicines in line with the labelling requirements of Directive 2001/83/EC, outlined in Articles 54–57 and 61–63 [9]. The packaging should be designed in a way that the critical information necessary for the safe use of medicine is legible and easy to assimilate. Colour coding products from the same MAH and to match multi-constituent components of a medicinal product (e.g. concentrate and solvent) may help to distinguish and identify products correctly. Use of colour is also recommended to highlight the name, strength or warnings on the primary packaging.

If all options towards optimising the product design, naming, packaging and labelling to prevent medication errors have been sufficiently explored, in exceptional circumstances and after evaluation by the responsible EMA Scientific Committee, additional risk minimisation such as patient and/or healthcare professional educational material may be implemented as a condition of marketing authorisation to manage the risk of medication errors. Any additional risk minimisation measures designed to tackle medication errors must be agreed with NCAs and measures of their effectiveness in daily practice included in the RMP. To promote the safe use of medicines, the EMA has recently launched a new webpage to highlight the specific measures recommended by the EMA's Scientific Committees to prevent medication errors, with clear and easy-to-understand information to patients and healthcare professionals [29]. The EU funded Joint Action on 'Strengthening Collaboration for Operating Pharmacovigilance in Europe

(SCOPE)' [30] will deliver tools for the media on scientific risk communication, one of the key regulatory outputs for medication error prevention.

10 Conclusion

For more than 15 years, EU pharmacovigilance has provided a robust system for the proactive monitoring of the risk of medication errors, which feeds into the continuous evaluation of the benefits and risks of medicinal products. To further enlarge the evidence base for regulators and health authorities to take preventive actions against medication errors, close collaboration between various stakeholders is important, including between NCAs and PSOs at EU Member State level as has been required by the pharmacovigilance legislation since 2012. The exchange of data between national pharmacovigilance and patient incident reporting and learning systems should also include errors that did not result in harm to the patient. The assessment and evaluation of data from both systems not only provides a tool to regulators to more quickly detect and communicate safety issues related to medication errors but also opens opportunities for quality of care improvement and error prevention through changes in policy and practices that improve safety. To further improve healthcare professionals' engagement in reporting and learning from medication errors, the role of medication safety officers introduced by the UK NHS in 2014 is a model to be further explored more widely across Europe [31]. Beyond the data exchange and communication aspects, there is a need for new methodologies to support the detection of safety signals[4] associated with medication errors in pharmacovigilance databases. The EU pharmacovigilance legislation requirement for reporting medication errors does not formally apply to clinical trials, which are therefore outside the scope of the EU good practice guide on medication errors. Nevertheless, clinical trials provide an opportunity to monitor errors in a controlled setting where the therapeutic margin of a product may be less understood, but learning from those errors provides a significant contribution to the development of risk minimisation and error-prevention strategies for the marketed product.

Acknowledgments The authors thank the members of the PRAC for their active support throughout the development of the EU good practice guide on medication errors and the members of the European Commission's Patient Safety and Quality of Care Expert Group for their useful contribution to the guidance.

Compliance with Ethical Standards

Funding No sources of funding were used to assist in the preparation of this article.

Conflict of interest Thomas Goedecke, Kathryn Ord, Victoria Newbould, Sabine Brosch and Peter Arlett have no conflicts of interest that are directly relevant to the content of this article.

[4] A safety signal is information on a new or known adverse event that is potentially caused by a medicine and that warrants further investigation. Signals are generated from several sources, such as spontaneous reports, clinical studies and the scientific literature.

References

1. World Health Organization. Reporting and learning systems for medication errors: the role of pharmacovigilance centres. 2014. Available from: http://www.who.int/medicines/areas/quality_safety/safety_efficacy/emp_mes/en. Accessed 27 Nov 2015.
2. Howard R, Avery A, Slavenburg S, Royal S, Pipe G, Lucassen P, Pirmohamed M. Which drugs cause preventable admissions to hospital? A systematic review. Br J Clin Pharmacol. 2007;63(2):136–47.
3. Dean B, Schachter M, Vincent C, Barber N. Prescribing errors in hospital inpatients: their incidence and clinical significance. Qual Saf Health Care. 2002;11(4):340–4.
4. Shah S, Aslam M, Avery A. A survey of prescription errors in general practice. Pharm J. 2001;267:860–2.
5. Recio Blázquez M, López Ruiz M, Arias Fernández L, Zamora Barrios M. Analysis of medication errors detected in the dispensing process by the unit dose system in a Spanish hospital. Eur J Hosp Pharm. 2004;1:20–5.
6. Beso A, Franklin B, Barber N. The frequency and potential causes of dispending errors in a hospital pharmacy. Pharm World Sci. 2005;27(3):182–90.
7. Chua S, Wong I, Edmondson H, Allen C, Chow J, Peacham J, et al. A feasibility study for recording of dispensing errors and near misses in four UK primary care pharmacies. Drug Saf. 2003;26(11):803–13.
8. Union European. Directive 2010/84/EU of the European Parliament and of the council of 15 December 2010 amending, as regards pharmacovigilance, Directive 2001/83/EC on the Community code relating to medicinal products for human use. OJ. 2010;53(L348):74–99.
9. Union European. Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use. OJ. 2001;44(L311):67–128.
10. European Medicines Agency. Medication-errors workshop report (EMA/144458/2013). 2013. Available from: http://www.ema.europa.eu/docs/en_GB/document_library/Report/2013/05/WC500143163.pdf. Accessed 27 Nov 2015.
11. European Medicines Agency. Medication errors—follow-up actions from workshop (EMA/20791/2014). 2014. Available from: http://www.ema.europa.eu/docs/en_GB/document_library/Other/2014/04/WC500165496.pdf. Accessed 27 Nov 2015.
12. European Commission. Patient Safety Policy: EU Patient Safety and Quality of Care Expert Group. 2016. Available from: http://ec.europa.eu/health/patient_safety/policy/index_en.htm. Accessed 27 Jan 2016.
13. Reporting and learning subgroup of the European Commission Patient Safety Quality of Care Working Group. Key findings and recommendations on reporting and learning systems for patient safety incidents across Europe. 2014. Available from: http://ec.europa.eu/health/patient_safety/docs/guidelines_psqcwg_reporting_learningsystems_en.pdf. Accessed 27 Nov 2015.

14. Pharmacovigilance Risk Assessment Committee. Good practice guide on recording, coding, reporting and assessment of medication errors (EMA/762563/2014). 2015. Available from: http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2015/11/WC500196979.pdf. Accessed 27 Nov 2015.
15. Pharmacovigilance Risk Assessment Committee. Good practice guide on risk minimisation and prevention of medication errors (EMA/606103/2014). 2015. Available from: http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2015/11/WC500196981.pdf. Accessed 27 Jan 2016.
16. European Medicines Agency. Good pharmacovigilance practices. 2016. Available from: http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000345.jsp&mid=WC0b01ac058058f32c. Accessed 27 Jan 2016.
17. Cousins D, Gerrett D, Richards N, Jadeja M. Initiatives to identify and mitigate medication errors in England. Drug Saf. 2015;38(4):349–57.
18. International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). Medical Dictionary for Regulatory Activities (MedDRA). 2016. Available from: http://www.meddra.org. Accessed 27 Jan 2016.
19. Council for International Organisations of Medical Sciences. CIOMS Working Group on Standardised MedDRA Queries (SMQs). 2016. Available from: http://www.cioms.ch/index.php/2012-06-10-08-47-53/working-groups/meddra-smqs. Accessed 27 Jan 2016.
20. US Food and Drug Administration Center for Drug Evaluation and Research (CDER). Safety considerations for product design to minimize medication errors. 2012. Available from: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM331810.pdf. Accessed 27 Jan 2016.
21. US Food and Drug Administration Center for Drug Evaluation and Research (CDER). Safety considerations for container labels and carton labeling design to minimize medication errors. 2012. Available from: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM349009.pdf. Accessed 27 Jan 2016.
22. Pirmohamed M, James S, Meakin S, Green C, Scott A, Walley T, et al. Adverse drug reactions as cause of admissions to hospital: prospective analysis of 18,820 patients. BMJ. 2004;329(7456):15–9.
23. Manias E, Kinney S, Cranswick N, Williams A. Medication errors in hospitalised children. J Paediatr Child Health. 2014;50(1):71–7.
24. Bolt R, Yates J, Mahon J, Bakri I. Evidence of frequent dosing errors in paediatrics and intervention to reduce such prescribing errors. J Clin Pharm Ther. 2014;39(1):78–83.
25. Padden Elliot J, McConaha J, Bunk E, Hilton L, Modany A, Bucker I. Influence of viscosity and consumer use on accuracy of oral medication dosing devices. J Pharm Tech. 2014;30(4):111–7.
26. Pharmacovigilance Risk Assessment Committee. Risk minimisation strategy for high-strength and fixed-combination insulin products. Addendum to the good practice guide on risk minimisation and prevention of medication errors (EMA/686009/2014). 2015. Available from: http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2015/11/WC500196980.pdf. Accessed 18 Dec 2015.
27. Committee for Medicinal Products for Human Use. Guideline on the acceptability of names for human medicinal products processed through the centralised procedure (EMA/CHMP/287710/2014 - Rev. 6). 2014. Available from: http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2014/06/WC500167844.pdf. Accessed 27 Nov 2015.
28. Committee for Human Medicinal Products. Mandate, objectives and rules of procedure for the Name Review Group (NRG) (EMA/411943/2014). 2014. Available from: http://www.ema.europa.eu/docs/en_GB/document_library/Other/2014/07/WC500169642.pdf. Accessed 27 Nov 2015.
29. European Medicines Agency. Recommendations on medication errors. 2016. Available from: http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000398.jsp&mid=WC0b01ac058098f1c0. Accessed 27 Jan 2016.
30. Medicines and Healthcare products Regulatory Agency. The strengthening collaboration for operating pharmacovigilance in Europe (SCOPE) joint action. 2016. Available from: http://www.scopejointaction.eu. Accessed 27 Nov 2015.
31. NHS England. Patient Safety Alert (NHS/PSA/D/2014/005): Improving medication error incident reporting and learning. 2014. Available from: http://www.england.nhs.uk/wp-content/uploads/2014/03/psa-med-error.pdf. Accessed 28 Jan 2016.