Pharmacovigilance

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Agenda

- Pharmacovigilance
- Definitions
- Reporting details
- Local literature surveillance

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- Definitions
- Reporting details
- Local literature surveillance

Why is Pharmacovigilance important?

To identify:

- Risks and benefits of medicines to improve their safe use
- Changes in the patterns of adverse effects (frequency, severity)

Pharmacovigilance is a legal obligation for all MAH's and is subject to strict requirements under national and regional legislation.

Please let us know as soon as you become aware (within one working day) of new pharmacovigilance requirements in your country!

If we become aware of any pharmacovigilance requirements changes in your country, we will let you know and you should take action immediately.

Why is Pharmacovigilance important?

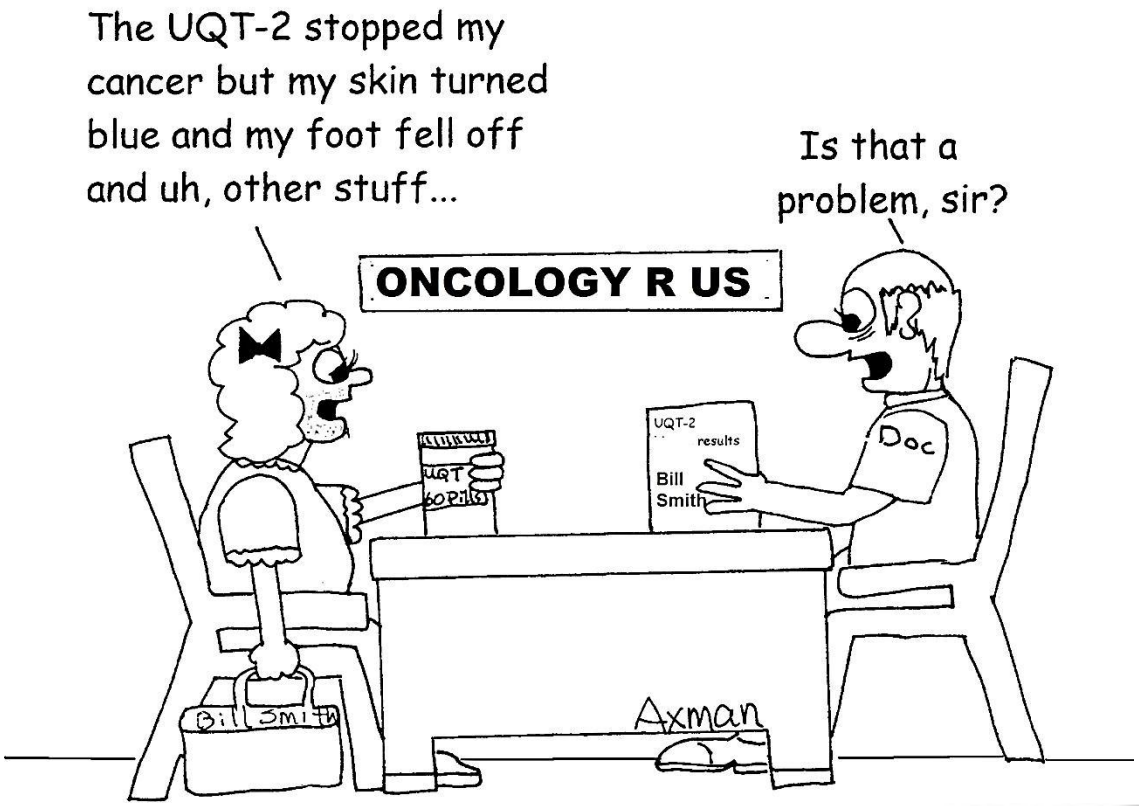
CSL has a regulatory requirement to provide an appropriate system of Pharmacovigilance (PV), in order to provide assurance for the safety and liability of its products throughout their lifecycle

Definitions

- Pharmacovigilance
- **Definitions**
- Reporting details
- Local literature surveillance

Definitions: Adverse Drug Reaction (ADR)

A response to a medicinal product which is noxious and unintended.



Definitions- Adverse Event or Adverse Experience (AE)

Is any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product which does not necessarily have to have a causal relationship with this treatment *(ICH).*

Please inform CSL as soon as you become aware of an Adverse Event

Definitions – Adverse Event Report

In addition to Adverse events, the following events should be reported to CSL:

- reports of drug exposure **via mother** (e.g. exposure during **pregnancy**, breastfeeding)
- lack of drug effect
- medication **errors**/maladministration (including wrong route or unknown route of administrations)
- **overdose** (accidental or intentional)
- off-label use
- drug abuse, Drug misuse, drug dependency
- occupational exposure
- pre-existing condition improved (unexpected therapeutic benefits were observed)

Additional guidance on medication errors

Good practice guide on recording, coding, reporting and assessment of Medication Errors

From EMA (PRAC)

V1 effective from 27 Nov 2015

Potential and Intercepted Medication Errors

Potential medication error:

Already a circumstance that may lead to a Medication Errors is an issue (to be processed)!

Intercepted medication error ('near miss'):

Even if the error does not make its way to the patient, it is an issue (to be processed)!

MEs without ADRs

"It is good practice to also record cases of medication errors not associated with adverse reaction(s) in the format of an ICSR, however these cases are not reportable as valid ICSR …"

"In line with the ICH E2C (R2) guideline and GVP Module VII.B.5.9 on PSURs, marketing authorisation holders should summarise relevant information **on patterns of medication errors and potential medication errors**, even when not associated with adverse outcomes, …"

Examples received at CSL Behring

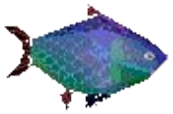
1/ Potential ME with the look alike package between AlbuRx and Privigen. Upon request from FDA, CSL revised AlbuRx package because of this issue.

2/ Potential medication error: different gynaecologists complain about the instructions of dose calculation in the SmPC of Rhophylac which already caused an intercepted ME (-> almost double dose administered)

3/ Intercepted ME: The patient was prescribed treatment with AlbuRx 25%. The pharmacist reported that due to the similarity of packaging of Albumin 25% (50 ml and 100ml) vials, this led to dispensing incorrect product. This was a near miss event caught before incorrect volume was given to patient.

4/ ME: administration of expired Rophylac

EXAMPLES



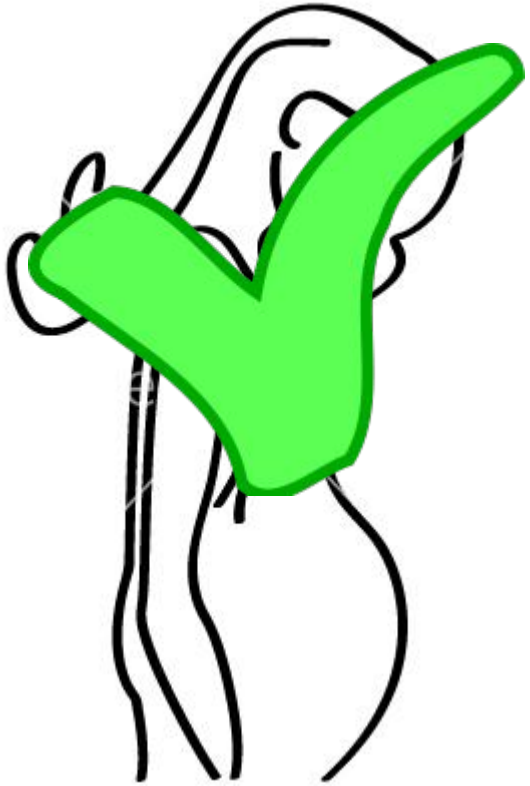
Need to be reported?

Midwife administered a dose of Rhophylac that had passed the expiry date to a patient as post partum prophylaxis.

Medication error / maladministration

Need to be reported?

Pregnant women receives Privigen



Exposure during pregnancy

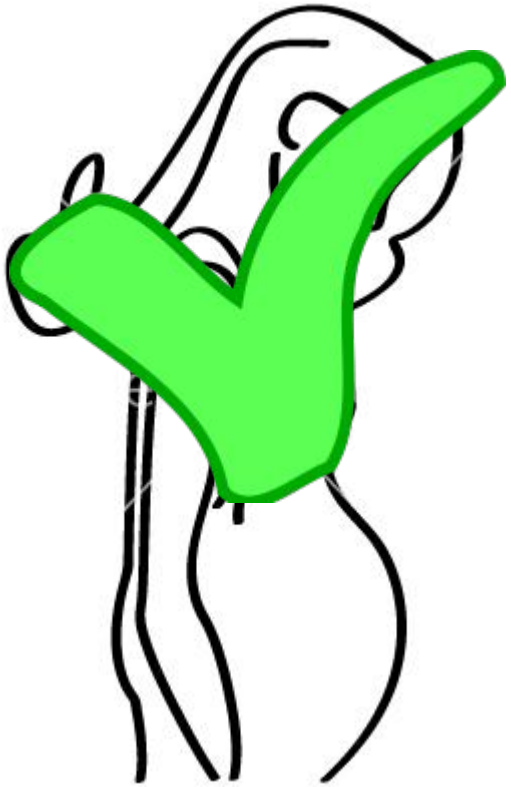
Need to be reported?

The patient had a poor response to the drug after 2 days of treatment with sandoglobulin

Lack of drug effect

Need to be reported?

- Treatment with Kybernin of preeclampsia in pregnant woman



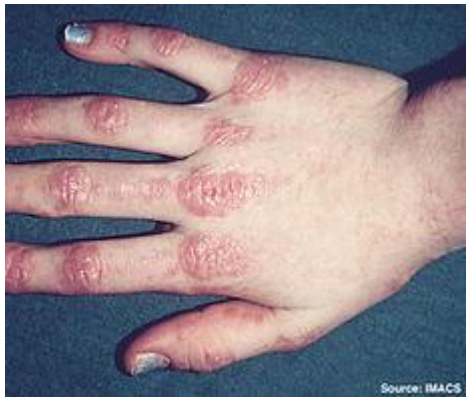
Exposure during pregnancy

+

Off-label use: treatment of preeclampsia with Kybernin is not labelled

Need to be reported?

US case: Treatment of dermatomyositis with IVIG (brand name not known)



Off-label use

Unapproved indication

Need to be reported?

Breastfeeding baby was exposed to Privigen

Drug exposure by mother

Need to be reported?

Haemate was transferred into the syringe and kept for 8 hours until it was administered to a patient

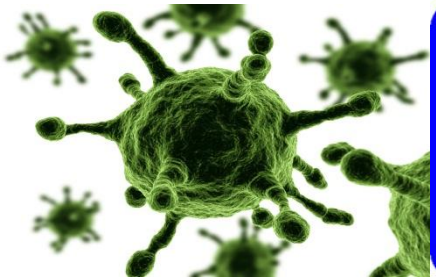
maladministration

Haemate should be used immediately after the reconstituted product has been transferred into the syringe, as storage includes the risk of bacterial contamination.

Adverse Reactions – Some examples

Non-serious – e.g. rash, headache

Serious – death, hospitalisation, virus transmission, results in persistent or significant disability or incapacity



Definitions

Unexpected / unlisted ADR

not defined in the Reference Safety Information (for licensed products) or Development Core Safety Information/Investigator Brochure (for investigational products).

*In the absence of a Global Reference Safety Information, the term refers to the defined Reference Safety Information.

Individual Case Safety Report (ICSR)

This term includes

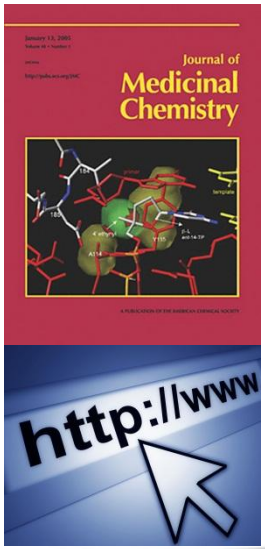
- solicited AE reports (sought by CSL, e.g. clinical trial reports)
- unsolicited AE reports („spontaneous“)
- reports of drug exposure via mother/father with/without AEs (e.g. exposure during conception, pregnancy, childbirth, breastfeeding).

Spontaneous ICSR

An unsolicited communication by a healthcare professional or consumer to a company, regulatory authority or other organization that describes an AE in a patient given one or more medicinal products, and which is not derived from a study or any organized data collection scheme.

Sources:

- Scientific literature, conference abstracts
- Internet
- HCP



Minimum Criteria for a valid ICSR

To qualify as an ICSR there must be a minimum of four criteria including:

- an identifiable patient (patient initials, gender, age, age group, or other identifier such as patient study number, etc.)
- an identifiable CSL product/study drug (INN or trade name)
- an identifiable reporting source
- Adverse Event

ICSR reporting

A report that does not contain the four minimum criteria is referred to as a „non-valid" (or invalid) case and is a report that must be forwarded to CSL Behring

Reporting details

- Pharmacovigilance
- Definitions
- **Reporting details**
- Local literature surveillance
- Reconciliation process
- Product Technical Complaints
- Setting a SharePoint alert

Pharmacovigilance – LSO/RSO Contacts

Regional Safety Officer (RSO) ECI:

Marta D. Puente Navazo (marta.puente@cslbehring.com)

Local Safety Officer Russia:

Olga Kalinina (olga.kalinina@cslbehring.com)

Please send any information to our PV e-mail address:

PhV-ECI@cslbehring.com

An Adverse Drug Reaction (ADR) – What Should I Do?

Post and faxes should be scanned and e-mailed and e-mails and phone calls forwarded to RSO

- ***PhV-ECI@cslbehring.com***

This must all be done **within one business day**

Information must be in English

Adverse Reactions – What Should I Do?

If phone calls cannot be forwarded to RSO obtain the following information :

- contact details of reporter
- Suspected drug + lot number
- Suspected adverse reaction
- Patient details (e.g.* initials, DOB, age, sex, patient no., etc.)
- Note the date of call ➔ day zero

⇨ Email details to RSO within one Business day

* Whatever detail can be obtained

Important to know:

Every information on a potential AE must be forwarded to the RSO within one business day, even if not all minimum criteria are known

RSO is then in charge of the follow up

Adverse Reactions – Reporting Timelines

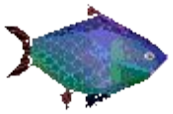
- All adverse reactions (ADR) must be reported to RSO within **one business** day

- ADRs are then reported to the Pharmacovigilance department at CSL, who then report to worldwide regulatory authorities for which there are strict timelines for compliance

Product Exposure during Pregnancy

- Pregnancy reports should be monitored until the pregnancy outcome is known
- Attempts should be made to follow-up cases
- Scope of report does not end at birth –for ICSRs of congenital anomalies, the reporter shall be asked to provide an assessment of the severity of the malformation, and a final diagnosis

An example



If you suspect an ADR…

Conference:

Patient, in therapy with Hizentra has pain at injection site after administration

Side effects, which are described in the Patient information leaflet have to be reported

Patterns of side effects might change (e.g. frequency)

“European Journal of Neurology”

Attending a conference you come across an abstract reporting an ADR or other safety relevant observation (remember earlier slides)

What do you do with this information and why?

- Pass the abstract to RSO
- CSL Behring has a duty to follow up
- May not have been picked up by regular Global Literature Search, as conference abstracts are difficult to locate by online searching

Local Literature surveillance

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- Reconciliation process
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Why local literature surveillance?

Information on safety relevant observations in local journals may not be missed

1. Search for local peer reviewed scientific journals, which are not listed in Embase

2. Screen abstracts of local journals for ADRs involving CSL Behring products

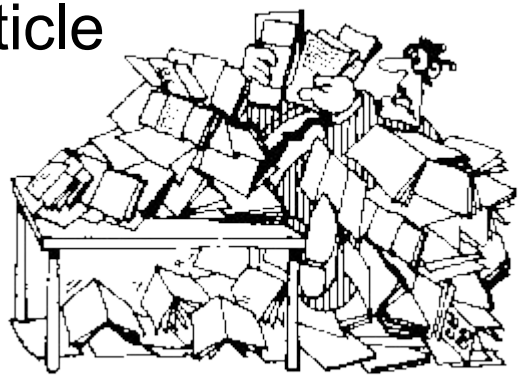
⇨Use key words (e.g. product names, active su
provided by RSO

Local literature surveillance

3. If you find an abstract mentioning a key word, read the full article

4. Pass relevant articles to RSO within **one Business day** and short summary in English if article is not in English

5. Provide English translation of the full article



⇨ Frequency of screening depends on publication frequency

Local literature surveillance Example Rhophylac:

Global literature search uses following key words:

- rhesus d antibody
- rh immune globulin
- rh d immunoglobulin
- rho d immunoglobulin
- rho d antibody
- rhesogamma
- rhophylac
- side effect
- adverse drug reaction
- drug safety
- case report

needs to be adapted to local needs