Pharmacovigilance key points

Information for Distributors 2022

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PV legislation in the EU

- Regulation (EU) 1235/2010 amending Regulation (EC) 726/2004
- Directive 2010/84/EC amending Directive 2001/83/EC
- Comission Implementing Regulation (EU) No 520/2012/EU (19 June 2012)
- New legislation applies since July 2012
- Good Pharmacovigilance Practice (GVP) Modules

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Pharmacovigilance definition

- According to the World Health Organization:

''**Pharmacovigilance (PV)** is defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem.''

- According to EU GVP Annex I- Definitions

'' Science and activities relating to the detection, assessment, understanding and prevention of adverse effect or any other medicine-related problem.
In line with this general definition, underlying objectives of pharmacovigilance in accordance with the applicable EU legislation for are:

- Preventing harm from adverse reactions in humans arising from the use of auhtorised 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.''

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Pharmacovigilance requirements

- A continuous monitoring and evaluation of the benefit/Risk balance
- Ensure the correct use according to the SmPC
- Ensure patient safety

✓Through pharmacovigilance cases and periodic reports

✓This activity can be audited and inspected at any time

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Adverse event reporting – general rules

It is the legal obligation of the Marketing Authorisation Holder that to collect, evaluate and report the adverse events and the pharmacovigilance information!

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Pharmacovigilance case identification

Adverse Event

Any untoward medical occurence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a casual relationship with this treatment.

An adverse event (AE) can therefore be any:

- Sign (including an abnormal laboratory finding), or
- Symptom, or
- Disease

Temporally associated,

Whether or not related to the use of a medicinal (investigational) product.

Special situation

Associated or not with an adverse event and mainly when not using a medical product as indicated in the SmPC

- Off label use
- Misuse
- Medication error
- Drug abuse
- Overdose
- Exposure in pregnancy, lactation or childhood <18 years old
- Exposure to counterfeits products
- Lack of drug effect/lack of efficacy
- Unexpected benefit effect
- Transmiision of infectious agent
- Occupational exposure
- Interaction

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Adverse event reporting – general rules

REPORTABLE:

Adverse event/Unexpected event:

- **Medication error:** This is an unintended failure in the drug treatment process that leads to, or has the potential to lead to harm to the patient.
- **Off label use:** the medicinal product is intentionally used for a medical purpose not in accordance with the terms of the marketing authorisation.
- **Overdose:** administration of a quantity of a medicinal product given per administration or cumulatively, which is above the maximum recommended dose according to the authorised product information.
- **Incorrect use:** the medicinal product is not used in the way as it mentionned in the SPC or package leaflet. Moreover, if somebody does not forgive the doctor's advice in connection with the use of drug, it also can be considered as an incorrect use.
- **Abuse:** This corresponds to the persistent or sporadic, intentional excessive use of a medicinal product, which is accompanied by harmful physical or psychological effects.
- **Accidents at work:** during medicinal product administering the personnel touch with it. It can leads to such as allergic reaction or it can change the organic function.

Adverse event reporting – general rules

Validation of a spontaneous report – ICSR (Individual case safety report):

Spontaneous report is only valid if it contains at least 4 information below (Basic information):

- **Identifiable reporter** (profession, name, initials, or address)
- **Identifiable patient** (initials, patient identify number, date of birth, age, age group or gender)
- **One or more suspected medicine**,
- **Suspected adverse event**

For the purpose of reporting an adverse reaction, the unexpected event is also considered as an adverse reaction!

The batch is also an important information!

Adverse event reporting – general rules

Non-valid cases:

- If all the 4 basic information are not available, it shall be attempted to get these information.
- The non-valid cases are also should be notified in the company's safety database and these shall be considered.

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Adverse event reporting – general rules

1. Tasks related to the 4 basic information:

- Record incoming information
- Attempt to make it valid, if it is not validated
- Get availability Send to company contact

2. Additional measures:

- Help with follow-up

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Why is the follow-up important?

At case reporting, it is not sure, that outcome of the event and continuation of the therapy is known.

How long should be continoued the follow-up?

- Until the side effect is resolved
- In the event of worsening if the previous state until it is restored to its original level
- death may occur, in which case the autopsy report may also be important follow-up information
- In case of pregnancym follow-up may also be important after childbirth
- Continuation of the use of the product: the patient stops taking it or starts taking it again

Adverse event reporting – general rules

Reporting deadlines:

- For the purpose of reporting a valid ICSR report, the day 0 is the first calendar day which on the minimal required information are available.
- Serious cases: urgent report obligation: 15 days
- Not serious cases: 90 days

Necessary information:

- For the marketing authorisation shall attempt to collect at least the information necessary for validation and in optimal case, as much information as possible on the adverse reaction conditions.
- In order to this, a follow-up in relation to adverse event is obligated.

When does an event become serious?

Becomes serious when:

- ✓Results in death/is life-threatening
- ✓Hospitalization or its prolongation
- ✓Disability/incapacity
- ✓Congenital/anomaly or birth defect
- ✓Medically significant

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Unexpected adverse reaction

It is an adverse event whose nature, seriousness or outcome it does not match with adverse events listed in SPC.

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Adverse event reporting – general rules

- Information from non-organised data collect (non-solicited)
  - Spontaneous report
  - Literature case
  - Other source (media)
- Information from organised data collect (solicited)
- Clinical trial
- Patient supporting programmes
- Data collection by public authorities, etc.

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How can report a pharmacovigilance case?

1. Health Care Professional /Physicians, Pharmacists, Nurses, Rheumatologists, Gynecologists etc./
2. Patients /Patient or family/friend of the patient/
3. Sales rep
4. Literature screening sources /Local performed by your Local Safety Officer, Global performed by Drug Safety Corporate Department at MAH/Licensor
5. Other sources /Via any other department, associated with a quality compliants or a medical information, via a congress, the company website... or even yourself!

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Adverse event reporting – general rules

ALSO REPORTABLE:

- Quality error

Parallel notification of qualiy assurance/production

- Pregnancy
- Ineffectiveness

If we know that the drug has proven to be ineffective: it is a difficult matter!

NOT NECESSARILY REPORTABLE, BUT NOTIFICABLE

- If we know that drug administration and drug use have been mattered during pregnancy.

Adverse event reporting – general rules

- Suspected side effects described in the medical literature should also be reported.
- These shall be validated, followed up and reported in the same way as spontaneous reports.
- To support this, marketing authorisation holders should be entitled to carry out regular monitoring of the literature, not only in relation to the product in question, but also in relation to the active substance.

How to recognise adverse events?

Check:

- Whether the medicine prescribed and the medicine in the patient are the same,
- Whether the patient takes the prescribed dose,
- Whether the suspected adverse events occured after the medicine use (not before)

It should be determined the time between the treatment and event.

Discontinuation of treatment (or decrease the dose) – monitor effects

Check SPC (whether the adverse event is performed in it)

In the case of suspense of adverse event, create a report

PV availability for adverse event reporting

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