Simposio GVP AIFA sulle ispezioni di Farmacovigilanza
Roma, 15 Novembre 2016

La gestione dei casi e dei segnali di rischio

Domenico Di Giorgio

Agenzia Italiana del Farmaco
AIFA

FARMINDUSTRIA

Dichiarazione di trasparenza/interessi*

Interessi nell'industria farmaceutica	NO	Attualmente	Da 0 a 3 anni precedenti	oltre 3 anni precedenti
INTERESSI DIRETTI:				
1.1 Impiego per una società: Ruolo esecutivo in una società farmaceutica	X	☐	☐	☐ obbligatorio
1.2 Impiego per una società: Ruolo guida nello sviluppo di un prodotto farmaceutico	X	☐	☐	☐ obbligatorio
1.3 Impiego per una società: altre attività	X	☐	☐	☐ facoltativo
2. Consulenza per una società	X	☐	☐	☐ facoltativo
3. Consulente strategico per una società	X	☐	☐	☐ facoltativo
4. Interessi finanziari	X	☐	☐	☐ facoltativo
5. Titolarità di un brevetto	X	☐	☐	☐ facoltativo
INTERESSI INDIRETTI:				
6. Sperimentatore principale	X	☐	☐	☐ facoltativo
7. Sperimentatore	X	☐	☐	☐ facoltativo
8. Sovvenzioni o altri fondi finanziari	X	☐	☐	☐ facoltativo
9. Interessi Familiari	X	☐	☐	☐ facoltativo

* Domenico Di Giorgio, secondo il regolamento sul Conflitto di Interessi approvato dal CdA AIFA in data 25.03.2015 e pubblicato sulla Gazzetta Ufficiale del 15.05.2015 in accordo con la policy EMA /626261/2014 sulla gestione del conflitto di interessi dei membri dei Comitati Scientifici e degli esperti.

N.B. Per questo intervento non ricevo compenso.

Le opinioni espresse in questa presentazione sono personali e non impegnano in alcun modo l'AIFA

Il contesto normativo

- Regolamento 1235/2010/EU
- Direttiva 2010/84/EU
- Regolamento di esecuzione (UE) 520/2012
- Direttiva 2012/26/UE
- Regolamento (UE) N. 1027/2012
- Regolamento di esecuzione (UE) N. 198/2013 (simbolo per i medicinali per uso umano sottoposti a monitoraggio addizionale)
- Regolamento (UE) N. 658/2014 (sulle tariffe pagabili all'Agenzia europea per i medicinali per lo svolgimento delle attività di farmacovigilanza relative ai medicinali per uso umano)
- D.M. 30.04.2015 - Farmacovigilanza, procedure operative e soluzioni tecniche

Regolamento di esecuzione (UE) N. 520/2012

Come riportato nei *considerando*, l'identificazione dei segnali deve seguire una metodologia riconosciuta ed è dunque necessario:

- definire il processo di gestione dei segnali
- stabilire requisiti comuni per l'identificazione dei segnali
- chiarire i ruoli di SM, EMA e MAH

Capo III *Artt. 18-24*

Definizione di segnale

Information that arises from one or multiple sources (including observations and experiments), which suggests a new potentially causal association, or a new aspect of a known association, between an intervention and an event or set of related events, either adverse or beneficial, that is judged to be of sufficient likelihood to justify verificatory action.

Report of the Council for International Organisations of Medical Sciences
Working group VIII Practical Aspects of Signal Detection in PhV
(CIOMS, Geneva 2010)

Gestione regolatoria (procedurale) dei segnali

Signals

Signals are generated from several sources, such as spontaneous reports of suspected adverse reactions, clinical studies and the scientific literature.

The evaluation of safety signals is a routine activity within pharmacovigilance to establish whether or not there is a causal relationship between the medicine and the reported adverse event. In cases where a causal relationship is confirmed or considered likely, regulatory action may be necessary.

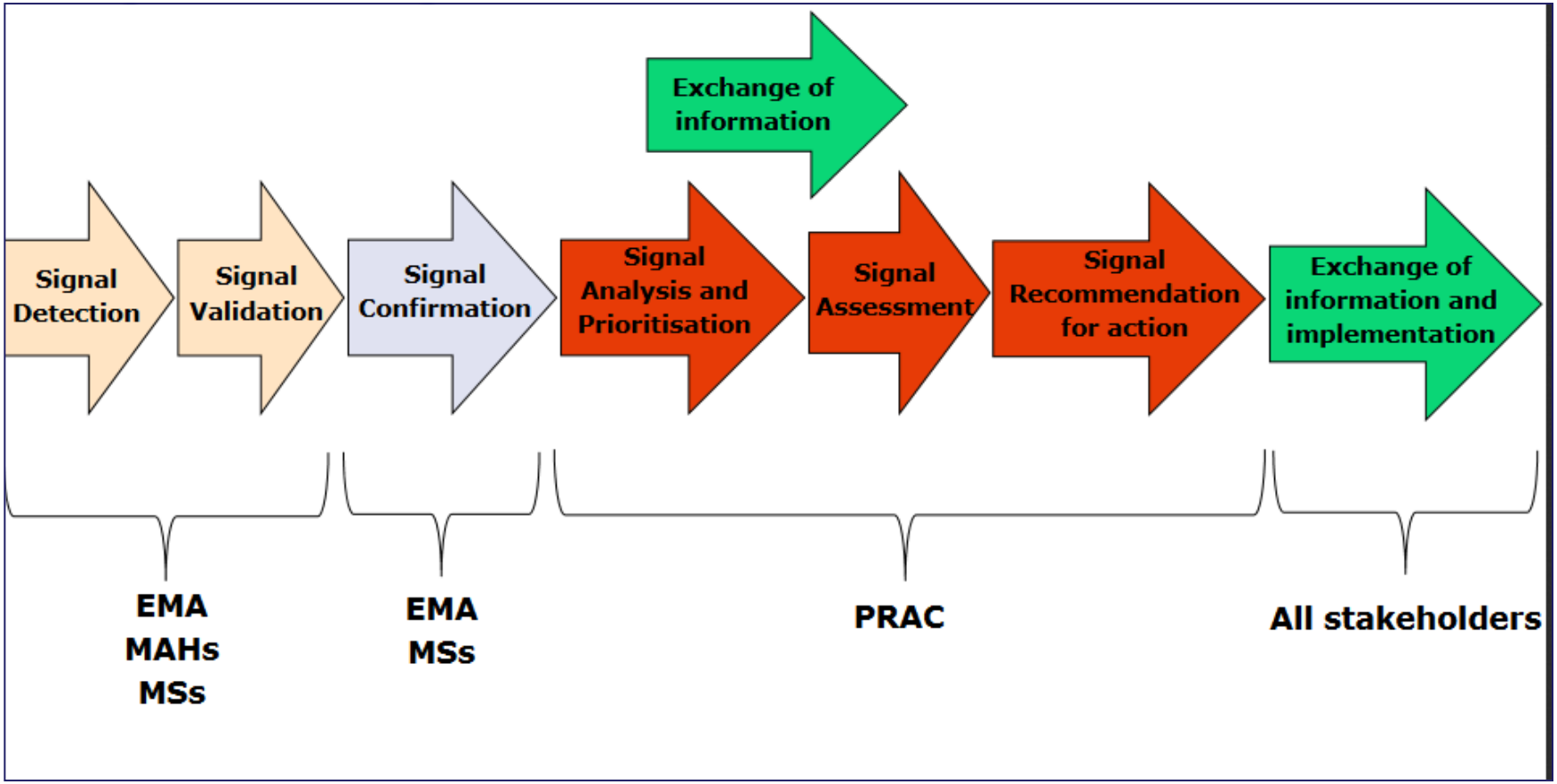
EMA's Annual Report 2015

Ruoli e responsabilità

I titolari di AIC (MAH), l'Agenzia europea dei medicinali (EMA) e le National competent authorities (NCA) sono tenuti a:

- eseguire un continuo monitoraggio dei dati
- cooperare nel monitoraggio dei dati
- informarsi reciprocamente su *emerging safety issue*

Il processo


Exchange of information
Signal Detection
Signal Validation
Signal Confirmation
Signal Analysis and Prioritisation
Signal Assessment
Signal Recommendation for action
Exchange of information and implementation
EMA
MAHs
MSs
EMA
MSs
PRAC
All stakeholders

Processi di signal management

Sui dati nazionali (Rete Nazionale di FV

- Per tutti i principi attivi
- Semestralmente

Sui dati internazionali (Eudravigilance)

- Solo per alcuni principi attivi
- Ogni 15 gg/ 30 gg

PRAC:
Pharmacovigilance Risk Assessment Committee

Il processo della segnalazione

Azienda Farmaceutica

Segnalatore

✓ 2 giorni
✓ 36 ore

Responsabile di Farmacovigilanza

7 giorni

Azienda
Regione

Rete Nazionale di FV

Gravi ogni 15 giorni
Non gravi ogni 90 giorni

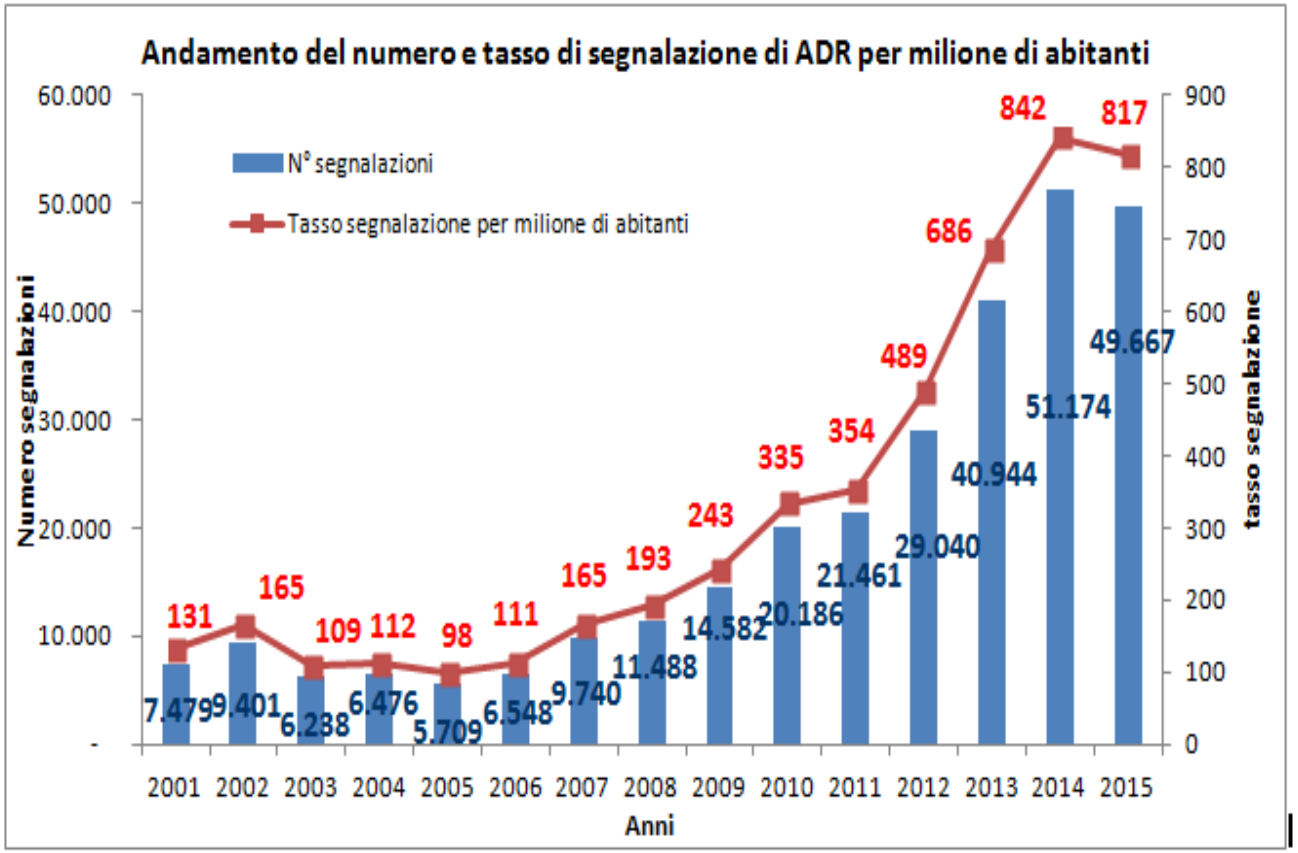
EudraVigilance

Ogni mese
tutti i casi

WHO-UMC

Segnalazioni nella Rete Nazionale di Farmacovigilanza

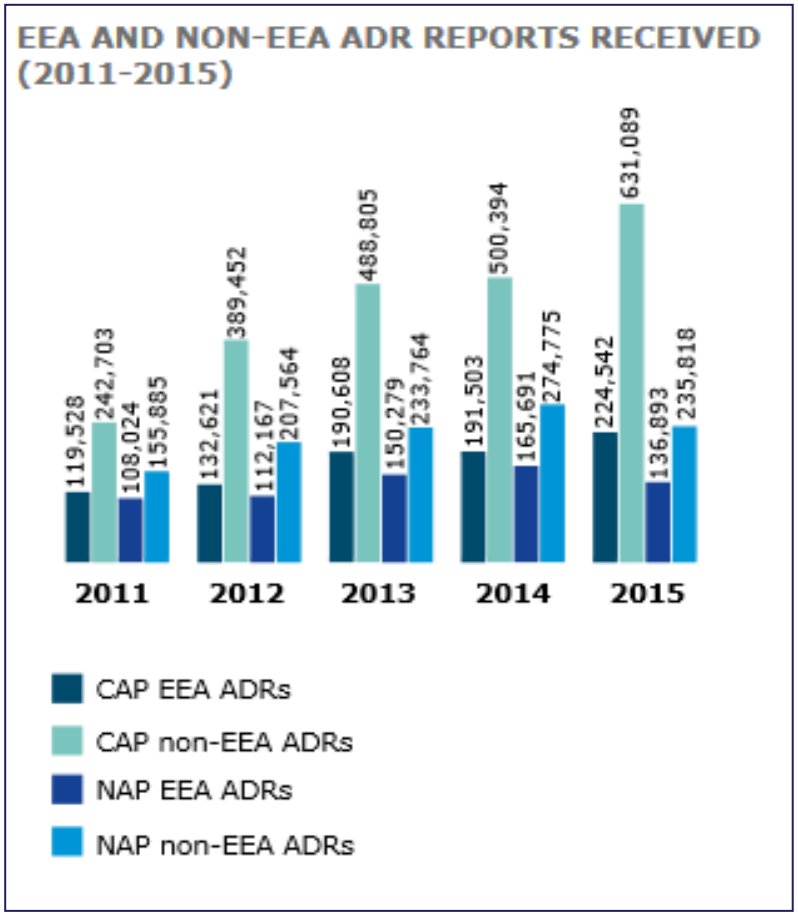
2015 vs 2014 -2.9%
Vaccini -3.7%
Farmaci -2.6%



Rapporto Osmed 2015

Eudravigilance

More than 1.2 million ADR reports were reported to EudraVigilance in 2015, an increase of 8.5%.

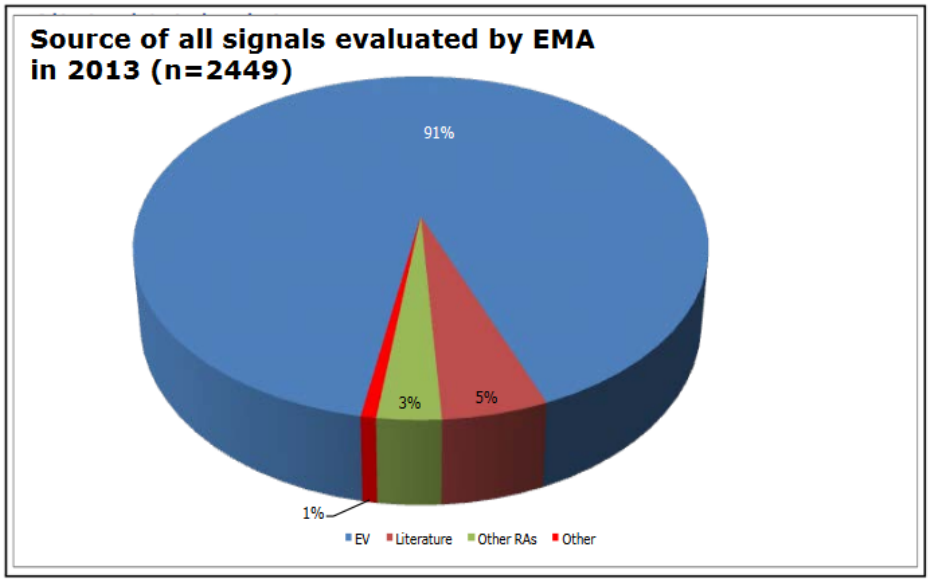


EMA's Annual Report 2015

Sources of information–Hypothesis Generating

91% of signals evaluated by EMA originate from EudraVigilance

70% of signals validated and forwarded to PRAC by EMA originate from EudraVigilance



Limitations of the spontaneous reporting

- Under reporting and reporting bias
- No drug exposure data
- No indication epidemiology (prevalence, incidence)
- Data quality and missing data
- Confounders

European Pharmacovigilance Issues Tracking Tool (EPITT)

- All validated signals are entered into EPITT by the authority who detected and validated it
- Validated signals undergo further analysis and are either:

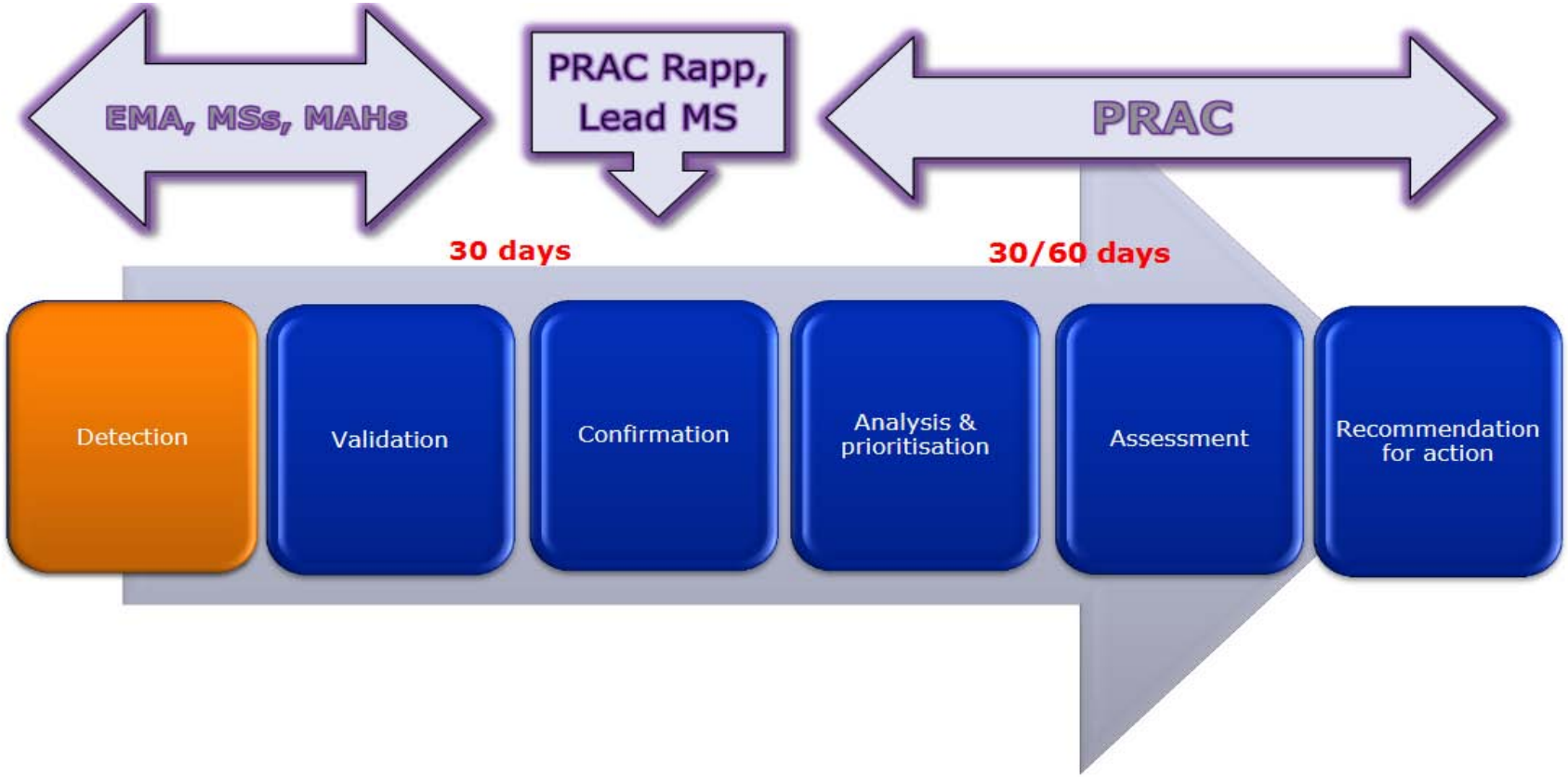
CONFIRMED

Added to agenda for the Pharmacovigilance Risk Assessment Committee (PRAC)

NOT CONFIRMED

Justification to be provided as to why signal is not confirmed

European signal process



PRAC recommendations for action

- No need for further evaluation or action at this point in time
- Request for additional data to be submitted:
  - Monitor any relevant emerging information on the signal as it becomes available
  - Address the signal in the following PSUR or submit an ad-hoc PSUR
  - Submit additional data (such as cumulative review)
  - Collect further information or perform additional analyses in EudraVigilance or other data sources
  - Conduct a post-authorisation safety study
- Need for regulatory action:
  - The product information and/or RMP should be updated through a variation
  - The Member States or the Commission, should initiate a referral procedure
  - Urgent safety restrictions should be imposed
- A Pharmacovigilance inspection should take place

Risultati conseguiti nel 2015

In 2015, 2,372 potential signals were reviewed by EMA, 88% of which originated from monitoring the EudraVigilance database.

In total, 102 confirmed signals were prioritised and analysed by the PRAC in 2015. Among these signals, 61 were validated by EMA for further evaluation and 41 signals were detected and validated by Member States.

Signal detection (2011-2015)

- 2011 – 1,586
- 2012 – 2,213
- 2013 – 2,449
- 2014 – 2,030
- 2015 – 2,372

EMA's Annual Report 2015

Example of signal analysis, prioritisation and assessment of recent signal discussed at PRAC

4. Signals assessment and prioritisation

4.1. New signals detected from EU spontaneous reporting systems

4.1.9. ***Sunitinib - SUTENT*** *(CAP)*

- *Signal of cholecystitis*

Status: *for initial discussion*

Regulatory details:

PRAC Rapporteur: Carmela Macchiarulo (IT)

Labelling change with Sections 4.4 and 4.8 of SmPC updated

Recommendation(s):

The MAH should perform a cumulative review of cases of cholecystitis and related terms associated with sunitinib with particular focus on acalculous and emphysematous cholecystitis. This review should be submitted within 2 months of adoption of these conclusions.

In case the MAH considers the need to update the product information further to this cumulative review, please be reminded of your responsibility to submit a variation in accordance with Article 16 of Regulation (EC) No 726/2004.

Esempi di alcuni segnali con Italia LMS/Rapp

- Sunitinib – SUTENT (Antineoplastic agents, protein kinase inhibitors) | Pneumatosis Intestinalis
- Aripiprazole – ABILIFY | Aggression
- Medicines containing aliskiren – Rasilamlo, Rasilez, Rasilez HCT (renin inhibitor) | Severe hyponatraemia leading to neurological symptoms
- Nicardipine (calcium ion antagonist) | Acute pulmonary oedema during off-label use in pregnancy (as tocolytic)
- Fusafungine (locabiotal) | Serious anaphylactic reactions
- Thiocolchicoside (Skeletal Muscle Relaxant) | Risk of Genotoxicity

Esempi di alcuni segnali con Italia LMS/Rapp

- Zolpidem | Risk of next-morning impairment after use of insomnia drugs; FDA requires lower recommended doses for certain drugs containing zolpidem
- Nicardipine (dihydropyridine-type calcium channel blocker) | Thrombocytopenia
- Roxithromycin (Macrolides) | Rhabdomyolysis secondary to interaction with statins
- Roxithromycin (Macrolides) | Hearing Disorders

Transparency - Publication of data on Signals

An agency of the European Union

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Text size: A A A | Site-wide search | GO
Search document library
Follow us:

Home | Find medicine | Human regulatory | Veterinary regulatory | Committees | News & events | Partners & networks | About us

- Pre-authorisation
- Post-opinion
- Post-authorisation
- What we publish
- Product information
- Scientific advice and protocol assistance
- Support for early access
- Adaptive pathways
- Scientific guidelines
- Innovation Task Force
- Supporting SMEs
- Paediatric medicine
- Geriatric medicine
- Orphan designation
- Herbal products
- Referral procedures
- Article 58 applications
- Pharmacovigilance
  - Background
  - Pharmacovigilance legislation

Home ▸ Human regulatory ▸ Pharmacovigilance ▸ Signal management ▸ PRAC recommendations

PRAC recommendations on safety signals

Email | Print | Help | Share

Each month, the European Medicines Agency publishes an overview listing all safety signals discussed during the latest Pharmacovigilance Risk Assessment Committee (PRAC) meeting and the recommendations given for each of them. The overview includes PRAC recommendations for centrally and nationally authorised medicines.

PRAC recommendations for regulatory action (i.e. amendment of the product information) are submitted to:

- the Committee for Medicinal Products for Human Use (CHMP), for endorsement, if the signal concerns a centrally authorised medicine. At the time of publication, the PRAC recommendations have been endorsed by the CHMP;
- the Coordination Group for Mutual Recognition and Decentralised Procedures - Human (CMDh), for information, if the signal concerns a nationally authorised medicine. It is the responsibility of the medicines regulatory authorities in the Member States to oversee that these PRAC recommendations are adhered to.

Marketing-authorisation holders are expected to **take action according to the recommendations**. They should monitor the information on this page regularly to keep informed about the PRAC recommendations concerning their products.

The presence of a safety signal does not mean that a medicine has caused the reported adverse event. The adverse event could be a symptom of another illness or caused by another medicine taken by the patient.

The overview of PRAC recommendations is published after each month's CHMP and CMDh meeting. The first list was published in October 2013 and lists the recommendations from the September 2013 PRAC meeting. A cumulative list of all signals discussed at the PRAC since September 2012 is also available below.

Starting from the January 2015 PRAC meeting, the Agency now publishes **recommendations for updates of product information** translated into all **official European Union (EU) languages**.

The Agency publishes these translations in all official EU languages, as well as Norwegian and Icelandic, in the table below after review of their quality by the national regulatory authorities in EU Member States.

Marketing-authorisation holders can use these translations to update their product information.

The Agency expects this initiative to accelerate the implementation of changes to product information and to ensure consistency across EU countries, thus leading to better information for patients on their medicines.

For more information on how safety signals are assessed in the EU, see:

- Signal management
- Guideline on good pharmacovigilance practices: Module IX - Signal management
- Questions and answers on signal management

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000375.jsp

Transparency - Publication of data on ADRs

http://www.adrreports.eu/it/index.html

Sviluppi in corso: draft GVP chapters and annexes for public consultation

Draft GVP chapters and annexes for public consultation

Back to top

Document(s)	Language	Status	First published	Last updated	Effective Date
Draft guideline on good pharmacovigilance practices (GVP) - Module VI – Management and reporting of adverse reactions to medicinal products (Rev. 2)	(English only)	draft: consultation open	08/08/2016		
Draft guideline on good pharmacovigilance practices (GVP) - Module IX – Signal management (Rev. 1)	(English only)	draft: consultation open	08/08/2016		
Draft guideline on good pharmacovigilance practices (GVP) - Module IX Addendum I – Methodological aspects of signal detection from spontaneous reports of suspected adverse reactions	(English only)	draft: consultation open	08/08/2016		

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000345.jsp

HMA
Heads of Medicines Agencies

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

4 August 2016
EMA/827661/2011 Rev 1* DRAFT for public consultation

Guideline on good pharmacovigilance practices (GVP)

Module IX – Signal management (Rev 1)

Date of coming into effect of first version	2 July 2012
Draft Revision 1* finalised by the Agency in collaboration with Member States	30 June 2016
Draft Revision 1 agreed by the European Risk Management Facilitation Group (ERMS FG)	18 July 2016
Draft Revision 1 adopted by Executive Director	4 August 2016
Release for public consultation	8 August 2016
End of consultation (deadline for comments)	14 October 2016
Anticipated date for coming into effect of Revision 1	Q1 2017

Monitoring of EudraVigilance data

National competent authorities and the Agency shall cooperate in the monitoring of the data available in the EudraVigilance database.

Marketing authorisation holders shall monitor the data available in the EudraVigilance database to the extent that they have access to the database.

Such monitoring should be performed to determine whether there are new risks or whether risks have changed and whether those risks have an adverse impact on the risk-benefit balance of the medicinal product (s).

Emerging Safety Issue

IX.C.3. Notifications and procedural options for signals validated by the marketing authorisation holder in the EU

This section outlines the options marketing authorisation holders have to inform competent authorities of signals they have validated. These options are also illustrated in Figure IX.1. in IX. Appendix 1. These options are without prejudice to the obligation of the marketing authorisation holder to update their marketing authorisation throughout the lifecycle of the product by variation applications.

IX.C.3.1. Emerging safety issue

When a marketing authorisation holder becomes aware of an emerging safety issue (see IX.A.), they should notify it in writing to the relevant competent authority(ies) of Member State(s) and to the Agency to the mailbox "P-PV-emerging-safety-issue@ema.europa.eu". This should be done within 2 working days of becoming aware of the issue.

When notifying an emerging safety issue, the marketing authorisation holder should describe the safety concern, the source(s) of information, any planned or taken actions, and should provide any relevant documentation. In such instances, a standalone signal notification (see IX.C.3.4.) is not required.

Emerging Safety Issue

When a marketing authorisation holder becomes aware of an emerging safety issue (see IX.A.), they should notify it in writing to the relevant competent authority(ies) of Member State(s) and to the Agency to the mailbox "P-PV-emerging-safety-issue@ema.europa.eu". This should be done within 2 working days of becoming aware of the issue.

When notifying an emerging safety issue, the marketing authorisation holder should describe the safety concern, the source(s) of information, any planned or taken actions, and should provide any relevant documentation. In such instances, a standalone signal notification (see IX.C.3.4.) is not required.

LE VERIFICHE ISPETTIVE AIFA

ICSR e gestione dei casi

- DAY 0
- Gestione della valutazione medica
- Gestione dei follow-up
- Gestione del upgrade dei casi
- Gestione dei casi riferiti a principio attivo
- Gestione di casi particolari/speciali
- Casi aperti/chiusi
- Invio/notifica dei casi
- Monitoraggio su internet o supporti digitali

Excel line listing di tutti i casi contenuti nel global safety database

Foglio1 Case

Case Id	Case type	Seriousness	Country of Reporter	Date(s) Received by Company	Date(s) Received by PV Dept	All Suspect Drugs (generic name)	Events (Serious & non-serious; MedDRA PT)	All report sources	Is the case HCP confirmed?	Patient / subject sex	Patient / subject age	Is there an identifiable patient?	Outcome	Reporter Causality	Company Causality	Expectedness (case level against EU SPC)	Expectedness (case level against IT SPC)	Expectedness (case level against CCSI)	Dates reported to AIFA	Dates reported to EMA	Last edit date	Last editor
123451	CT	Serious	United Kingdom	24Jan2005, 27Jan2005, 16May2006	25Jan2005, 27Jan2005, 23May2006	codeine; frusemide; paracetamol	Pleural effusion, Pericardial effusion	HCP	Yes	M	45	Yes	Unresolved	Unrelated	Possible				30Jan2005, 31Jan2005, 30May2006		01Aug2009	Giovanni Rossi
123462	Registry	Serious	Japan	19Jan2005, 08Apr2005, 16May2006	20Jan2005, 08Apr2005, 23May2006	heparin	Myocardial infarction	Consumer, HCP	Yes	F	34	Yes	Resolved	Related	Unrelated	Unexpected		Unexpected		29Jan2005, 18Apr2005, 26May2006	11Aug2009	Giovanni Rossi
123473	Spont	Non-serious	United Kingdom	19Jan2005, 08Apr2005	20Jan2005, 08Apr2005	codeine	Lower limb pain	Consumer, literature	Yes			No	Resolved	Related	Related		Expected	Expected			06Jun2009	Giovanni Rossi
123475	PMS	Serious	USA	01Mar2009	02Mar2009	heparin	Respiratory failure	Consumer	No	F	67	Yes	Resolved	Possible	Unrelated	Expected		Expected			01Jun2009	Giovanni Rossi
123484	Spont	Serious	United Kingdom	01Apr2009	02Apr2009	paracetamol ; ibuprofen	Chest infection	HCP	Yes	F	47	Yes	Fatal	Related	Related	Unexpected		Expected	15Apr2009		15Apr2009	Giovanni Rossi

Note: Si raccomanda l'utilizzo di una metodologia che possa permettere di identificare se il caso è stato ricevuto dall'Autorità Regolatoria

Si invita a fornire una spiegazione di come vengono definiti i diversi "Case type"

Se esistono campi separati utilizzati per identificare i casi di gravidanza o casi mortali si prega di inserire ulteriori colonne per inserire nella tabella queste informazioni

Excel line listing d i tutti i casi contenuti nel global safety database

Foglio2 Drug-event

Case Id (MCN)	Case type	Seriousness	Country of Reporter	Suspect Drug (generic name)	Is suspect drug a Company X product?	Event term as reported	Event (Serious & non-serious; MedDRA PT)	Indication	Seriousness (event level)	Expectedness (drug-event level against EU SPC)	Expectedness (drug-event level against IT SPC)	Expectedness drug-event level against IB)	Expectedness (drug-event level against CCSI)	All report sources	Is the case HCP confirmed?	Patient / subject sex	Patient / subject age	Is there an identifiable patient?	Outcome (event level)	Reporter Causality	Company Causality (case level)	Protocol ID	Subject ID	Dates reported to AIFA	Dates reported to EMA
123451	CT	Serious	United Kingdom	codeine	Yes		Pleural effusion	Facial pain	Serious			Unexpected		HCP	Yes	45	Yes	Yes	Unresolved	Unrelated	Possible	DOM123	1234	30Jan2005, 31Jan2005, 30May2006	
123451	CT	Serious	United Kingdom	frusemide	Yes		Pleural effusion	Cardiac failure congestive	Serious			Unexpected		HCP	Yes	45	Yes	Yes	Unresolved	Unrelated	Possible	DOM123	1234	30Jan2005, 31Jan2005, 30May2006	
123451	CT	Serious	United Kingdom	paracetamol	No		Pleural effusion	Facial pain	Serious					HCP	Yes	45	Yes	Yes	Unresolved	Unrelated	Possible	DOM123	1234	30Jan2005, 31Jan2005, 30May2006	
123451	CT	Serious	United Kingdom	codeine	Yes		Pericardial effusion	Facial pain	Non-serious			Unexpected		HCP	Yes	45	Yes	Yes	Unresolved	Unrelated	Possible	DOM123	1234	30Jan2005, 31Jan2005, 30May2006	
123451	CT	Serious	United Kingdom	frusemide	Yes		Pericardial effusion	Cardiac failure congestive	Non-serious			Unexpected		HCP	Yes	45	Yes	Yes	Unresolved	Unrelated	Possible	DOM123	1234	30Jan2005, 31Jan2005, 30May2006	
123451	CT	Serious	United Kingdom	paracetamol	No		Pericardial effusion	Facial pain	Non-serious					HCP	Yes	45	Yes	Yes	Unresolved	Unrelated	Possible	DOM123	1234	30Jan2005, 31Jan2005, 30May2006	
123462	Registry	Serious	Japan	heparin	Yes		Myocardial infarction		Serious	Unexpected			Unexpected	Consumer, HCP	Yes	34	Yes	Yes	Resolved	Related	Unrelated				29Jan2005, 18Apr2005, 26May2006
123473	Spont	Non-serious	United Kingdom	codeine	Yes	leg ache	Lower limb pain		Non-serious		Expected		Expected	Consumer, literature			No	No	Resolved	Related	Related				
123475	PMS	Serious	USA	heparin	Yes		Respiratory failure		Serious	Expected			Expected	Consumer	No	67	Yes	Yes	Resolved	Possible	Unrelated	PMS321	1897		
123484	Spont	Serious	United Kingdom	paracetamol	Yes		Chest infection		Serious	Unexpected			Expected	HCP	Yes	47	Yes	Yes	Fatal	Related	Related			15Apr2009	
123484	Spont	Serious	United Kingdom	ibuprofen	No		Chest infection		Serious					HCP	Yes	47	Yes	Yes	Fatal	Related	Related			15Apr2009	

Note: Si raccomanda l'utilizzo di una metodologia che possa permettere di identificare se il caso è stato ricevuto dall'Autorità Regolatoria
Si invita a fornire una spiegazione di come vengono definiti i diversi "Case type"
Se esistono campi separati utilizzati per identificare i casi di gravidanza o casi mortali si prega di inserire ulteriori colonne per inserire nella tabella queste informazioni

Esempi di deviazioni | 1

- Il personale non conosceva le modalità di segnalazione delle sospette reazioni avverse ai medicinali e le fonti attraverso cui possono essere ricevuti i casi;
- la raccolta di casi provenienti da altre fonti che non fosse la RNF non era organizzata (ad es. quella da centralino, fax, email, altri dipartimenti, ISF);
- le modalità di processazione dei casi non erano adeguatamente documentate;
- non era presente alcuna registrazione alla Rete Nazionale di Farmacovigilanza;
- non era presente alcuna registrazione al network internazionale Eudravigilance;

Esempi di deviazioni | 2

- i medicinali della ditta non erano stati inseriti nel dizionario XEVMPD (Extende Eudravigilance Medicinal Product Dictionary);
- non esistevano strumenti di registrazione dei casi (registri, fogli excel, database);
- non era prevista alcuna modalità di gestione di eventuali casi ricevuti in azienda da pazienti della Comunità Europea in seguito all'utilizzo di medicinali della ditta registrati con procedura centralizzata;
- sia la ditta, sia la parte terza incaricata per la gestione dei casi, non erano a conoscenza delle modalità di gestione e notifica dei casi in uno Stato Membro in cui veniva commercializzato il medicinale e per il quale svolgevano le attività di FV;
- la gestione di casi non notificabili non era organizzata e definita.

Article 57 (2) - Riassunto delle richieste

- I titolari di AIC devono:
- essere registrati in Eudravigilance all'interno della comunità XEVMPD (la sola registrazione per l'invio di ICSR non è sufficiente)
- presentare tutte le informazioni dei medicinali autorizzati in UE (CAPs, NAPs, MRPs and DCPs)
- mantenere aggiornate tutte le informazioni successive all'autorizzazione all'immissione in commercio (ad esempio variazioni, ritiri, trasferimento di titolarietà)
- garantire un livello adeguato di qualità dei dati

Esempi di deviazioni | 3

- la gestione delle segnalazioni di sospetta reazione avversa era inadeguata perché non efficientemente e chiaramente organizzata e con numerose deficienze, spesso imputabili anche alla mancanza di raccolta di tutti i casi in un unico database, allo scambio di informazioni con le parti terze e partners commerciali, a errori nel data-entry, data management, controllo di qualità, codifica (uso del Medical Dictionary for Regulatory Activities (MedDRA), classificazione, listdness ed expectedness;
- non venivano correttamente presi in gestione i casi di sospetta reazione avversa provenienti da alcune affiliate o partner commerciali. È stato notato che per medicinali presi in carico a seguito di un'acquisizione nulla era presente nel database di sicurezza e mancava persino un piano di inserimento/migrazione.

Esempi di deviazioni | 4

- a differenza di quanto veniva riportato nelle procedure, la prioritizzazione dei casi non era uguale per tutti i casi gestiti (ad es. le segnalazioni provenienti da Autorità Regolatoria (comprensive di quelle provenienti tramite la Rete Nazionale di Farmacovigilanza) erano gestite con una più bassa priorità rispetto a quelle pervenute tramite altre fonti);
- la raccolta dei casi non era ben organizzata in quanto non erano facilmente distinguibili (ad es. i casi di cui la ditta era titolare di AIC da quelli in cui la ditta non lo era, quelli EU da quelli extra EU, quelli "medically confirmed" da quelli "non medically confirmed";
- la valutazione della expectedness non veniva effettuata sulla base del relativo documento di sicurezza (Reference Safety Information o Riassunto delle Caratteristiche del Prodotto), ma sulla base di tabelle che descrivevano la distribuzione del farmaco nell'organismo;

Esempi di deviazioni | 4

- mancata evidenza che la listdness per i casi di sospette reazioni avverse da alcuni medicinali fosse stata effettuata correttamente anche perché non era presente il Company Core Safety Information (CCSI) in uso presso il partner commerciale e previsto nello SDEA;
- non era stato effettuato alcun controllo della codifica con eventuale richiesta di FU (ad es. un caso che nel narrative era riportato come lesione, era stato codificato in RNF come reazione cutanea; un caso non grave occorso in un bambino che aveva avuto febbre e macchie in seguito alla somministrazione del medicinale, era stato codificato nel database in maniera errata come febbre e rash maculare);
- non veniva effettuata alcuna valutazione del nesso di causalità tra sospetta reazione avversa e farmaco sospetto.

DAY 0

- Il titolare di AIC attraverso un'analisi retrospettiva aveva riscontrato a distanza di più di 2 anni che alcuni casi presenti nella RNF non erano stati inseriti nel safety database. Pertanto li ha inseriti successivamente, ma con una day 0 errato;
- talvolta l'attribuzione del day 0 era stata fatta erroneamente (ad es. era stato assegnato a tutti i casi lo stesso day 0 corrispondente al giorno della migrazione al nuovo database).

VI.B.7. Reporting of ICSRs

Only valid ICSRs (see VI.B.2.) should be reported. The clock for the reporting of a valid ICSR starts as soon as the information containing the minimum reporting criteria has been brought to the attention of the national or regional pharmacovigilance centre of a competent authority or of any personnel of the marketing authorisation holder, including medical representatives and contractors. This date should be considered as day zero. It is the first day when a receiver ~~is informed~~gains knowledge of a valid ICSR, irrespective of whether the information is received during a weekend or public holiday. ~~In practice this is the first business day the receiver becomes aware of the information.~~ Reporting timelines are based on calendar days.

Where the marketing authorisation holder has set up contractual arrangements with a person or an organisation, explicit procedures and detailed agreements should exist between the marketing authorisation holder and the person/organisation to ensure that the marketing authorisation holder can comply with the reporting obligations. These procedures should in particular specify the processes for exchange of safety information, including timelines and regulatory reporting responsibilities and should avoid duplicate reporting to the competent authorities.

For ICSRs described in the scientific and medical literature (see VI.B.1.1.2.), the clock starts (day zero) with awareness of a publication containing the minimum information for reporting. Where contractual arrangements are made with a person/organisation to perform literature searches and/or report valid ICSRs, detailed agreements should exist to ensure that the marketing authorisation holder can comply with the reporting obligations.

When additional significant information is received for a previously reported case, the reporting time clock starts again for the submission of a follow-up report from the date of receipt of the relevant follow-up information. For the purpose of reporting, significant follow-up information corresponds to new medical or administrative information that could impact on the assessment or management of a case or could change its seriousness criteria; non-significant information includes updated comments on the case assessment or corrections of typographical errors in the previous case version. See also VI.C.6.2.2.7. as regards the distinction between significant and non-significant follow-up information.

Gestione della valutazione medica

- Talvolta non vi era evidenza e/o prova documentale che una valutazione medica fosse stata mai effettuata;
- sia a livello di casa madre, sia di affiliate, non vi era garanzia della presenza di un medico;
- la valutazione medica non aveva tenuto conto di alcuna lista di principi attivi per i quali era previsto un monitoraggio specifico di alcuni eventi (ad es. quelli nei RMP, Referral (Art.31 Dir. 2001/83), segnali già noti);
- mancata valutazione dei casi non gravi, alcuni dei quali con eventi presenti nella IME List (follow up, eventuale upgrade e notifica all'Autorità);
- la valutazione medica dei casi, inclusi quelli da principio attivo, era superficiale e non dettagliata e le POS spesso non la prevedevano; in casi in cui veniva effettuata, non era stata documentata in maniera ordinata.

Gestione dei follow-up

- Per molti casi mancano i follow up o le attività di follow up non risultano ben documentate;
- per le segnalazioni di decessi, di casi gravi e non definiti, e per segnalazioni da principio attivo non era stato effettuato sempre un follow-up;
- non era previsto l'avvio di un follow-up specifico per i casi speciali (ad esempio per quelli indicati nel RMP);
- spesso erano assenti le richieste di follow up finalizzate a conoscere l'esito della reazione avversa;
- nonostante le attività di follow-up fossero state svolte regolarmente, non risultava definito dopo quanto tempo chiudere il caso in mancanza di una risposta da parte del segnalatore e non era stato stabilito quante richieste di follow-up dovessero essere effettuate e con quale frequenza.

VI.B.3. Follow-up of reports

When first received, the information in suspected adverse reactions reports may be incomplete. These reports should be followed-up as necessary to obtain supplementary detailed information significant for the scientific evaluation of the cases. This is particularly relevant for monitored events of special interest, prospective reports of pregnancy, cases notifying the death of a patient, cases reporting new risks or changes in the known risks. This is in addition to any effort to collect missing minimum information (see VI.B.2.). Any attempt to obtain follow-up information should be documented.

Follow-up methods should be tailored towards optimising the collection of missing information. This should be done in ways that encourage the primary source to submit new information relevant for the scientific evaluation of a particular safety concern. The use of targeted specific forms in the local language should avoid requesting the primary source to repeat information already provided in the initial report and/or to complete extensive questionnaires, which could discourage future spontaneous reporting. Therefore, consideration should be given to pre-populating some data fields in those follow-up report forms to make their completion by the primary source easy.

When information is received directly from a consumer suggesting that an adverse reaction may have occurred, if the information is incomplete, attempts should be made to obtain consent to contact a nominated healthcare professional to obtain further follow-up information. When such a case, initially reported by a consumer, has been confirmed (totally or partially) by a healthcare professional, this information should be clearly highlighted in the ICSR[13].

For suspected adverse reactions relating to biological medicinal products, the definite identification of the concerned product with regard to its manufacturing is of particular importance. Therefore, all appropriate measures should be taken to clearly identify the name of the product and the batch number. A business process map in relation to the mandatory follow-up of information for the identification of suspected biological medicinal products is presented in VI.Appendix 1..

For cases related to vaccines, the recommendations provided in the Guideline on good pharmacovigilance practices (GVP) Product- or Population-Specific Considerations I: Vaccines for prophylaxis against infectious diseases ~~Guideline on the conduct of Pharmacovigilance for Vaccines for Pre- and Post-exposure Prophylaxis against Infectious Diseases~~[14] should also be followed as appropriate.

Gestione del upgrade dei casi

- Non vi era evidenza che l'upgrade dei casi fosse stato effettuato e la possibilità di poterlo effettuare non era contemplata in alcuna procedura;

- non era previsto l'upgrade dei casi anche versus IME list, né la valutazione di casi speciali e delle situazioni riportate nei RMP.

GVP Module VI (Rev 1), VI.A.2.4 Seriousness

VI.A.2.4 Seriousness

As described in the ICH-E2A guideline, a serious adverse reaction corresponds to any untoward medical occurrence that at any dose results in death, is life-threatening, requires inpatient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, or is a congenital anomaly/birth defect.

The characteristics/consequences should be considered at the time of the reaction to determine the seriousness of a case. For example, life-threatening refers to a reaction in which the patient was at risk of death at the time of the reaction; it does not refer to a reaction that hypothetically might have caused death if more severe.

Medical judgement should be exercised in deciding whether other situations should be considered as serious reactions. Some medical events may jeopardise the patient or may require an intervention to prevent one of the above characteristics/consequences. Such important medical events should be considered as serious[4]. The EudraVigilance Expert Working Group has co-ordinated the development of an important medical event (IME) terms list based on the Medical Dictionary for Regulatory Activities (MedDRA). This IME list aims to facilitate the classification of suspected adverse reactions, the analysis of aggregated data and the assessment of the Individual Case Safety Reports (ICSRs) in the framework of the day-to-day pharmacovigilance activities. The IME list is intended for guidance

Important Medical Event Terms - IME list

EudraVigilance Human

Home

Registered users: Test • Production

Pharmacovigilance in EEA

General

- Mandatory e-reporting essentials
- Community legislation and guidance documents
- 6 steps to e-reporting
- Registration with EudraVigilance
- Template for EU risk-management plans

EudraVigilance (EV)

- Main systems components:
  - EV Organisation and User Management
  - EV Gateway
  - EV Database Management System
  - EVWEB Reporting Application
  - Extended EV Medicinal Product Dictionary
  - EV Data Analysis System
- EudraVigilance Access Policy
- EudraVigilance Technical Documents
- EudraVigilance Training Programme
- EudraVigilance Fora:
  - EV Steering Committee
  - EV Expert Working Group

The EudraVigilance Expert Working Group (EV-EWG) has co-ordinated the development of an Important Medical Event Terms (IME) list. This IME list aims to facilitate the classification of suspected adverse reactions as well as aggregated data analysis and case assessment in the frame of the day to day pharmacovigilance activities of stakeholders in the EU. The IME list is intended for guidance purposes only.

The new IME list based on MedDRA version 18.0 is now available here, together with the inclusion and exclusion criteria which have been developed to help maintain it. To obtain a copy, please click here.

Building upon the experience gained with the use of the IME list and the comments received from stakeholders, it is recognised that the distinction between Core serious and Extended serious terms is often difficult to apply, since many MedDRA Preferred Terms (PTs), with the provision of additional clinical information, may become serious. As a result of that, it has been agreed by the EV-EWG that as of version 15.0 the IME list contains Core Serious events only, e.g. events that are serious per se, independent of information on the context in which the Adverse Drug Reaction occurs.

We invite you to submit any comments you may have on those documents to MedDRAIMElist@ema.europa.eu.

▲ up | go back

Last update: Tuesday, 10 March 2015.

News

- Updated documents related to data submission for authorised medicinal products in accordance to Article 57(2) of Regulation 726/2004 available
- New IME list based on MedDRA version 18.0

Help Desk

- EudraVigilance Registration
- EudraVigilance General Queries
- Article 57 Queries
- Good pharmacovigilance practices (GVP)
- e-reporting: What to do in case of system failure
- E2B (R2) DTD conversion tool
- Volume 10 Q&As version 10 (April 2012)
- Electronic submission of Article 57(2) data Questions & Answers (Q&As)

https://eudravigilance.ema.europa.eu/human/textforIME.asp

Important Medical Event Terms

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

30 Churchill Place • Canary Wharf • London E14 5EU • United Kingdom
Telephone +44 (0)20 3660 6000 Facsimile +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

An agency of the European Union

10 March 2015
EMA/160304/2015
Inspections and Human Medicines Pharmacovigilance Division

18.0 IME list

MedDRA Code	SOC Name	PT Name	Comment	Added in 18.0
10066274	Blood and lymphatic system disorders	Cytopenia	In v17.1 this term was an LLT under the PT Pancytopenia, which was included in the 17.1 IME list. Cytopenia fulfills the inclusion criteria - Bone marrow depressions and cytopenias are included and thus this term merits inclusion as a CS term in the IME list.	X
10014472	Blood and lymphatic system disorders	Elephantiasis	In v17.1 this term was an LLT under the PT Filariasis, which was included in the 17.1 IME list.	X
10075738	Blood and lymphatic system disorders	Splenic artery perforation	PT Splenic artery perforation fulfills the inclusion criteria for inclusion as a CS event - immediately life-threatening or result in death or hospitalization and may jeopardize the patient or may require intervention to prevent" death.	X
10076419	Cardiac disorders	Anginal equivalent	New PT in v18.0. This term fits the inclusion criteria for ischaemic conditions. Anginal equivalents are considered to be symptoms of myocardial ischaemia.	X
10076040	Cardiac disorders	Atrial flutter with 1:1 atrioventricular conduction	New PT in v18.0. This term fits the inclusion criteria for relevant terms for cardiac arrythmias. This is an uncommon arrhythmia which may be associated with certain anti-arrhythmic drugs. Although it starts as atrial flutter, the 1:1 conduction may result in ventricular rates of over 300 beats per minute, causing syncope, heart failure, loss of consciousness etc.	X
10075846	Cardiac disorders	Degenerative aortic valve disease	This term fits the inclusion criteria for relevant terms for cardiac valve disorders. Similar aortic valve terms are already included.	X
10075847	Cardiac disorders	Degenerative mitral valve disease	This term fits the inclusion criteria for relevant terms for cardiac valve disorders. Similar mitral valve terms are already included.	X
10075889	Cardiac disorders	Sinus node dysfunction	This term fits the inclusion criteria for relevant terms for cardiac arrhythmias. Previously included PT Sick sinus syndrome was demoted under this new PT.	X
10075721	Congenital, familial and genetic disorders	Acardia	This PT was added to V18.0. It represents a condition which results in death or is life-threatening. It fits the criteria for inclusion on the IME list.	X
10076367	Congenital, familial and genetic disorders	Ash leaf macule	PT Ash leaf macule was added to MedDRA V18.0. It is a dermatological lesions associated with tuberous sclerosis. Tuberous sclerosis is a condition associated with impairments such as seizures, intellectual disability and major organ dysfunction and, for this reason, is already on the IME List. As the ash leaf macule lesion is often the earliest recognizable sign of tuberous sclerosis, it is appropriate to add this term to the IME List.	X

https://eudravigilance.ema.europa.eu/human/textforIME.asp

Important Medical Event Terms

MedDRA Code	Term	SOC	Comment
10040639	Sick sinus syndrome	Cardiac disorders	Demoted under PT Sinus node dysfunction, which is included in the IME list.
10022557	Intermediate uveitis	Eye disorders	Demoted under PT Autoimmune uveitis, which is included in the IME list.
10051401	Small bowel angioedema	Gastrointestinal disorders	Demoted under PT Intestinal angioedema, which is included in the IME list.
10048440	HIV infection CDC category A1	Infections and infestations	Demoted under PT HIV infection CDC category A, which is included in the IME list.
10048443	HIV infection CDC category A2	Infections and infestations	Demoted under PT HIV infection CDC category A, which is included in the IME list.
10048446	HIV infection CDC category A3	Infections and infestations	Demoted under PT HIV infection CDC category A, which is included in the IME list.
10048441	HIV infection CDC category B1	Infections and infestations	Demoted under PT HIV infection CDC category B, which is included in the IME list.
10048444	HIV infection CDC category B2	Infections and infestations	Demoted under PT HIV infection CDC category B, which is included in the IME list.
10048447	HIV infection CDC category B3	Infections and infestations	Demoted under PT HIV infection CDC category B, which is included in the IME list.
10048442	HIV infection CDC category C1	Infections and infestations	Demoted under PT HIV infection CDC category C, which is included in the IME list.
10048445	HIV infection CDC category C2	Infections and infestations	Demoted under PT HIV infection CDC category C, which is included in the IME list.
10048448	HIV infection CDC category C3	Infections and infestations	Demoted under PT HIV infection CDC category C, which is included in the IME list.
10022813	Intraspinal abscess	Infections and infestations	Demoted under PT Spinal cord abscess, which is included in the IME list.
10028517	Mycotic aneurysm	Infections and infestations	Demoted under PT Infective aneurysm, which is included in the IME list.
10038173	Red blood cells CSF positive	Investigations	Demoted under PT CSF red blood cell count positive, which is included in the IME list.
10063554	Hyperglycaemic hyperosmolar nonketotic syndrome	Metabolism and nutrition disorders	Demoted under PT Hyperosmolar hyperglycaemic state, which is included in the IME list.
10054784	Contralateral breast cancer	Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Demoted under PT Breast cancer, which is included in the IME list.
10010904	Convulsion	Nervous system disorders	Demoted under PT Seizure, which is included in the IME list.
10048464	Spinal haematoma	Nervous system disorders	Demoted under PT Spinal cord haematoma, which is included in the IME list.
10038436	Renal failure acute	Renal and urinary disorders	Demoted under PT Acute kidney injury, which is included in the IME list.
10038444	Renal failure chronic	Renal and urinary disorders	Demoted under PT Chronic kidney disease, which is included in the IME list.
10068854	Artificial bladder implantation	Surgical and medical procedures	Demoted under PT Neobladder surgery, which is included in the IME list.
10015076	Epiphyseal stapling	Surgical and medical procedures	Demoted under PT Epiphysiodesis, which is included in the IME list.
10075373	Implant site dehiscence	General disorders and administration site conditions	Previously on IME list. This term does not meet revised inclusion criteria for administration and other "site" terms in one of the five following categories: ischaemia, joint infection, necrosis, thrombosis and and other site conditions that have the potential to spread systematically and result in immediate clinical consequences with the loss or compromise of arteriovenous fistula/arteriovenous graft function.
10053995	Implant site haemorrhage	General disorders and administration site conditions	Previously on IME list. This term does not meet revised inclusion criteria for administration and other "site" terms in one of the five following categories: ischaemia, joint infection, necrosis, thrombosis and and other site conditions that have the potential to spread systematically and result in immediate clinical consequences with the loss or compromise of arteriovenous fistula/arteriovenous graft function.
10065479	Infusion site nerve damage	General disorders and administration site conditions	Previously on IME list. This term does not meet revised inclusion criteria for administration and other "site" terms in one of the five following categories: ischaemia, joint infection, necrosis, thrombosis and and other site conditions that have the potential to spread systematically and result in immediate clinical consequences with the loss or compromise of arteriovenous fistula/arteriovenous graft function.
10022083	Injection site nerve damage	General disorders and administration site conditions	Previously on IME list. This term does not meet revised inclusion criteria for administration and other "site" terms in one of the five following categories: ischaemia, joint infection, necrosis, thrombosis and and other site conditions that have the potential to spread systematically and result in immediate clinical consequences with the loss or compromise of arteriovenous fistula/arteriovenous graft function.

https://eudravigilance.ema.europa.eu/human/textforIME.asp

Gestione dei casi riferiti a principio attivo

- Non si era tenuto conto di segnalazioni di sospette reazioni avverse insorte in seguito all'utilizzo del principio attivo e pertanto non era stata avviata nessuna attività di registrazione, controllo della qualità, codifica, classificazione, valutazione medica e follow-up;
- per i casi da principio attivo non vi era una valutazione documentata che permettesse di escludere quelli che ad es. erano stati somministrati attraverso forme farmaceutiche e vie di somministrazione diversi da quelli dei medicinali della ditta.

Gestione dei casi riferiti a principio attivo

- Le modalità di gestione di casi particolari, quali l'esposizione a farmaci in gravidanza, i casi di sospetta mancanza di efficacia e la gestione di reclami non erano ben strutturate e proceduralizzate. Inoltre la possibilità di effettuare un upgrade dei casi non era prevista;

- non era previsto che le segnalazioni di mancanza di efficacia relative a medicinali salvavita, o utilizzati in situazioni speciali, dovevano essere notificati all'autorità competente;

- per i casi di mancanza d'efficacia non vi erano garanzie che nel passato fossero stati presi in carico eventuali segnalazioni pervenute dall'officina della ditta;

- spesso non era prevista alcuna riconciliazione periodica e documentata con i reclami che erano pervenuti al QA dell'officina;

Gestione di casi particolari/speciali 2/2

- non erano previste attività specifiche per la gestione dei casi speciali e di esposizione al medicinale in corso di gravidanza;

- le segnalazioni di esposizione al medicinale in corso di gravidanza erano gestite in maniera inadeguata (era previsto esclusivamente un registro cartaceo senza che esistesse alcun sistema di avviso per ricordare di effettuare i necessari follow-up dopo il parto);

- lo scambio di informazioni relativamente a casi provenienti da segnalazione spontanea, mancanza di efficacia e reclami, ricevuti dai vari dipartimenti aziendali non era documentato né contemplato nelle POS in uso nei rispettivi dipartimenti.

Casi aperti/chiusi

- Gli ICSR rimanevano “aperti” e non venivano chiusi dopo un adeguato periodo di tempo dalla richiesta di follow-up;

- molti casi non venivano “chiusi” e nel database di farmacovigilanza ne risultavano tantissimi ancora “aperti” (2000); tale situazione, relativa a più medicinali, ha determinato l’esclusione di questi casi dalle elaborazioni effettuate sul database, essendo queste effettuate esclusivamente sui casi “chiusi”.

Invio/notifica dei casi 1/2

- Alcuni casi italiani provenienti da diverse fonti (Clinical Study, post marketed study, Health Professional, Regulatory Agency e Third Party, Other) erano stati erroneamente inviati alla RNF tramite Eudravigilance (Minisal02);
- nella sezione CIOMS della RNF erano stati inseriti casi extra UE che pertanto non risultavano presenti in Eudravigilance;
- tutti i casi che erano stati notificati dalla ditta via Eudravigilance come casi provenienti da segnalazioni spontanee, studi clinici o altro, per lo più extra EU, erano invece riferiti a casi provenienti dalla letteratura;

Invio/notifica dei casi 1/2

- casi gravi ricevuti da AIFA/RNF erano stati inviati a Eudravigilance (EVHUMAN) generando duplicati;
- casi segnalati alla ditta da pazienti di più sospette reazioni avverse associate a difetti di qualità e valutati dalla ditta come gravi, non risultavano essere stati inviati né a Eudravigilance né all'autorità regolatoria.

Monitoraggio su internet o supporti digitali

Non era previsto alcun monitoraggio su internet o supporti digitali (siti, pagine web, blog, social network, forum internet, portali sulla salute/sanità) e non era stata considerata la possibilità di ricevere casi di sospette reazioni avverse tramite il sito web della ditta.

Sistemi IT: normativa

- Directive 2001/83/EC, as amended by Directive 2010/84/EU
- Article 11(1c)(1d), 12(1) Implementing Regulation (EU) no. 520/2012
- Guideline on good pharmacovigilance practices (GVP)
- EudraLex Volume 4, Annex 11: Computerised Systems
- Code of Federal Regulations 21 (CFR 21) Part 11: Guidelines on Electronic Records and Electronic Signatures
- Good Automated Manufacturing Practice (GAMP 5)

Computerised system

- MS-Word© Documents

- MS-Excel© Spreadsheets

- Computerised Databases

- Custom software (self-developed software)

- Modified off-the-shelf (MOTS) software (ARGUS©, Clintrace©, ARISg©)

System Validation

Quale sistema dovrebbe essere validato?

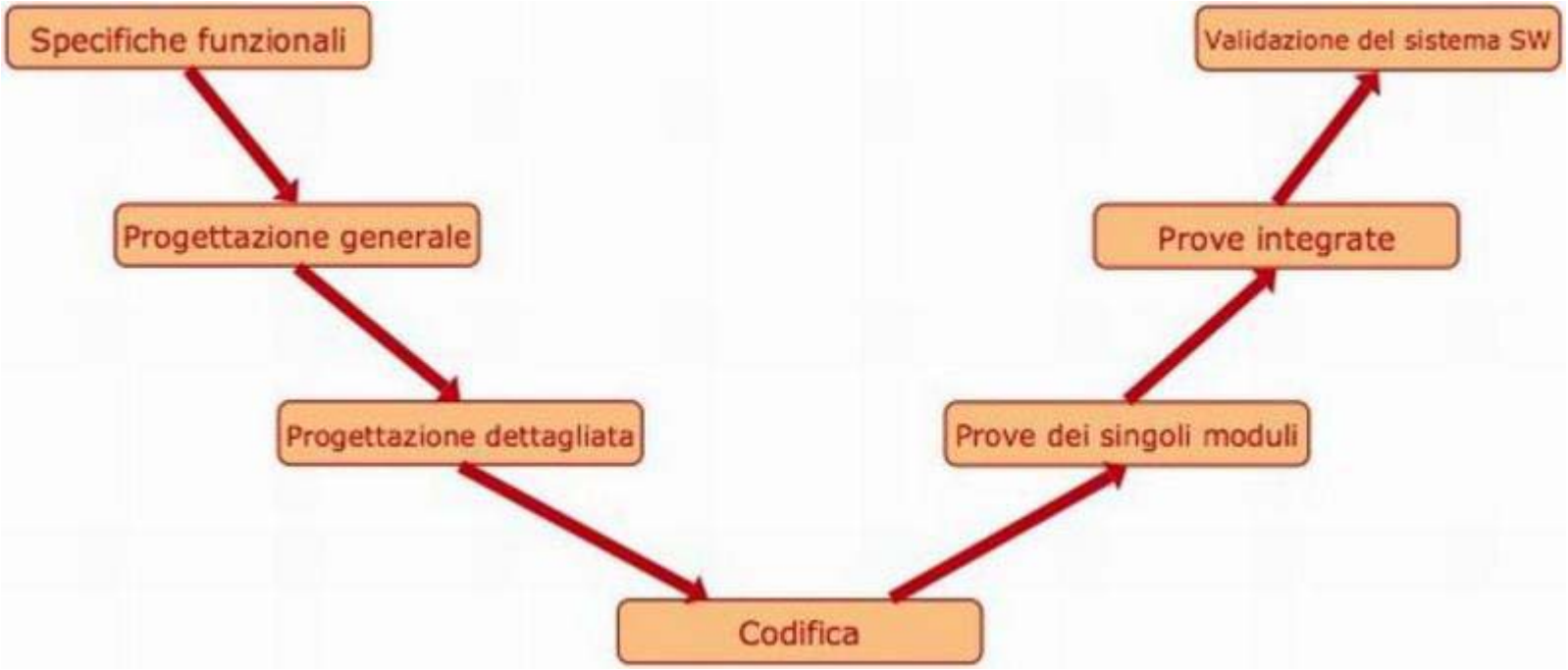
- PhV data: MS Excel, Word, ARGUS, ...
- Database Medical Information, Q-complaints,...

Indipendente dalla loro origine, i sistemi elettronici che generano dati (in modo automatico) che vengono utilizzati per soddisfare dei requisiti di legge, devono essere validati

- Oracle® *ARGUS*, Oracle® *AERS, ARISg*™ e *ARISj*™, *SafetyDrugs*® .....→ SI

- MS Excel, Word, Q-complaints → dipende

Ciclo di sviluppo del software applicativo: Ciclo “a V” dello sviluppo del software



Migrazione dei dati di farmacovigilanza (Data Migration)

- EU Regulation 726/2004 as amended by EU Regulation 1235/2010
- Consolidated Directive 2001/83/EC, as amended by Directive 2010/84/EU
- Commission Implementing Regulation (EU) No. 520/2012, Chapter II
- GVP Module VI – Management and reporting of adverse reactions to medicinal products
- GVP Module II – Pharmacovigilance Systems and their quality systems

Migrazione dei dati di farmacovigilanza (Data Migration)

GVP Module VI

"Competent authorities and marketing authorisation holders should have a quality management system in place to ensure compliance with the necessary quality standards at every stage of case documentation, such as data collection, data transfer, data management, data coding, case validation, case evaluation, case follow-up, ICSR reporting and case archiving".

Bisogna cercare di stabilire quali processi saranno utilizzati in ogni fase della migrazione dei dati, il personale responsabile dei vari compiti, i controlli che verranno eseguiti dopo la migrazione al fine di fornire garanzie circa l'integrità e la completezza dei dati nel database di sicurezza, e come verranno documentate queste attività.

Migrazione dei dati di farmacovigilanza (Data Migration)

In quali situazioni si potrebbe verificare la migrazione dei dati di sicurezza

- Implementazione di un nuovo database di sicurezza
- Acquisizione di una ditta, fusioni aziendali o acquisizione di autorizzazioni

Perché è necessaria la migrazione dei dati?

- dati cumulativi sugli ICSRs sono richiesti per l'analisi del segnale e per la valutazione del rischio / beneficio
- PSURs (dove previsto) devono contenere "summary tabulations" cumulative delle reazioni avverse
- le autorità competenti possono richiedere revisioni cumulative per tipi di evento specifici
- di tanto in tanto per i casi precedentemente segnalati informazioni di follow-up potrebbero essere ricevute in un secondo momento (ad es. ad esempio, per i di gravidanza)

Oltre ai database di sicurezza, quali altri database devono essere considerati/riportati nel PSMF?

Qualsiasi sistema del MAH utilizzato per ricevere, raccogliere, registrare e riportare le informazioni di sicurezza

Potrebbero essere inclusi

- sistemi dell'informazione medica
- sistemi usati per la formazione online e per la gestione della formazione
- banche dati dei difetti di qualità
- sistemi per le sperimentazioni cliniche qualsiasi sistema importante per la raccolta dei dati di sicurezza
- sistemi per l'archiviazione

Contatti

Domenico Di Giorgio
Dirigente Area Vigilanza Post-Marketing
AIFA – Agenzia Italiana del Farmaco

d.digiorgio@aifa.gov.it

www.aifa.gov.it