EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Pharmacovigilance in the European Union

Role of the European Medicines Agency

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Disclaimer

The views presented are those of the individual and may not be understood or quoted as being made on behalf of EMA or reflecting the position of EMA

I have no conflict of interests

Presentation overview

- About the Agency
- Pharmacovigilance
- EudraVigilance
- Signal Detection
- ENCEPP, Protect
- Recent issues

European Medicines Agency

- A decentralised body of the European Union, located in London
- Main responsibility is the protection and promotion of public and animal health, through the evaluation and supervision of medicines for human and veterinary use
- Hub of 41 authorities from 31 EU and EEA-EFTA countries, EC, EP

European Medicines Agency

- A secretariat of approx. 600 full-time staff
- Governed by Management Board
- Works with a network of over 4,500 European experts as members of committees, working parties or assessment teams
- 7 scientific committees composed of members of EU and EEA-EFTA states, some including patients' and doctors' representatives, conduct the main scientific work of the Agency

European Medicines Agency

- Scientific evaluation of applications for marketing authorisation for both human and veterinary medicines via ‘centralised procedure’ – one authorisation valid in the EEA
- Obligatory for biotechnology products, ATMPs, medicines for treatment of HIV/AIDS, diabetes mellitus, cancer, neurodegenerative diseases, immune disorders, viral diseases, orphan diseases (designation process)
- Additionally, if a medicine constitutes a significant therapeutic, scientific or technical innovation, or is in any other respect in the interest of patient health

European Medicines Agency

- Stimulation of innovation and research in the pharmaceuticals
- Scientific advice and other assistance to companies for the development of new medicines, guidelines
- A dedicated SME Office, established in 2005, provides special assistance to small and medium-sized enterprises
- International cooperation with WHO, non-European authorities, international harmonization/standardization
- Providing information to patients and HCPs
- Arbitrations (referrals)
- Safety monitoring

Adverse Drug Reactions – Public Health Burden

- ADR is response to a medicinal product which is noxious and unintended (Dir. 2010/84/EU)
- 5% of all hospital admissions are due to an ADR
- 5% of all hospital patients suffer an ADR
- ADRs are the 5th most common cause of hospital death
- It is estimated that 197,000 deaths per year in the EU are caused by ADRs
- Average costs of 1 ADR treatment estimated at €2250 (DE)
- The total cost to society of ADRs in the EU is €79 billion

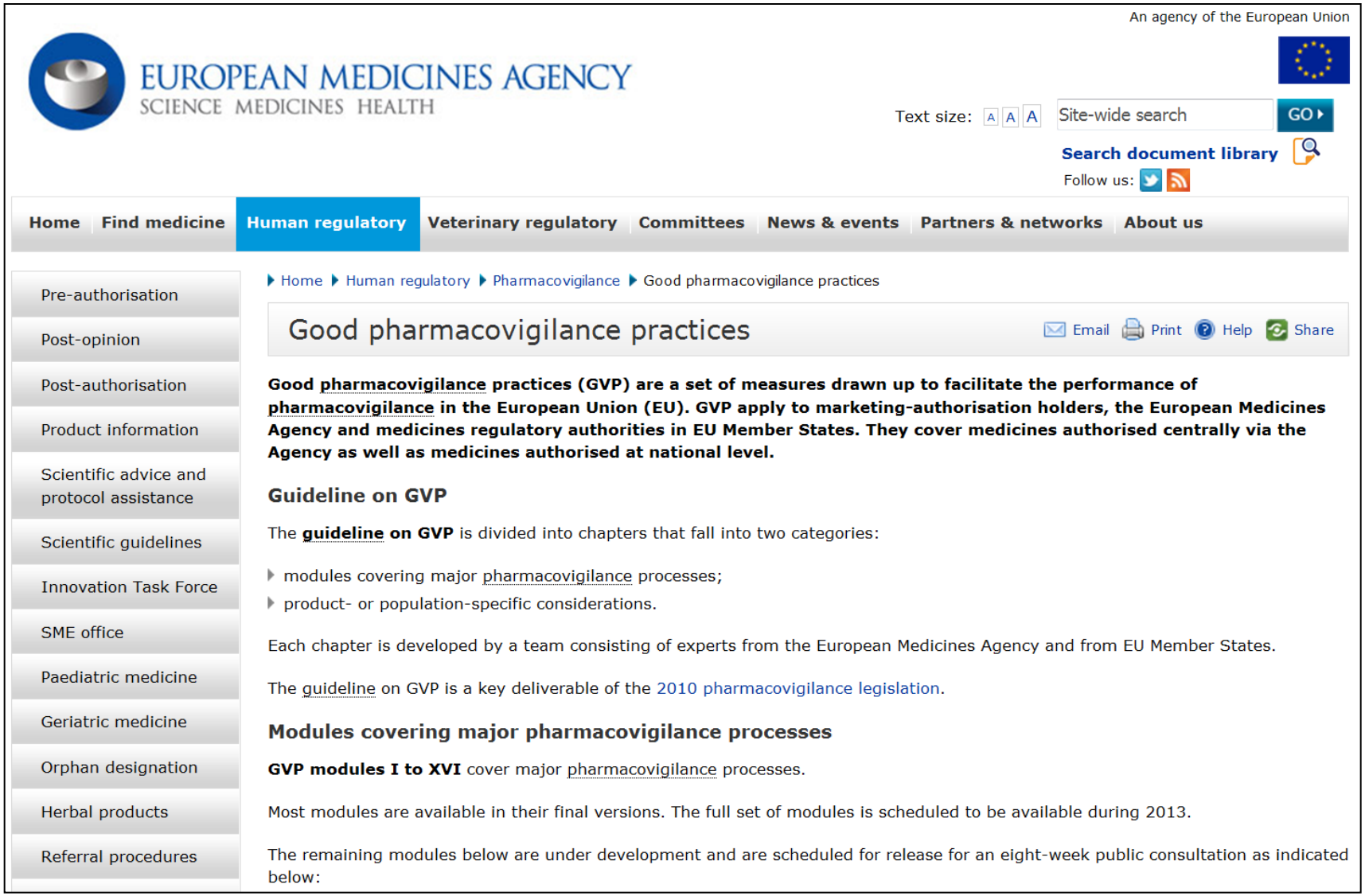
Even small improvements in the pharmacovigilance system will have a major impact on public health and society

Pharmacovigilance (Preamble, Paragraph 2, Regulation 1235/2010)

Pharmacovigilance rules are necessary for the protection of public health in order to prevent, detect and assess adverse reactions to medicinal products for human use placed on the Union market, as the full safety profile of medicinal products for human use can be known only after they have been placed on the market.

Pharmacovigilance

- Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency as amended
- 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 as amended
- Good pharmacovigilance practices (GVP) – modules I-XVI cover major PhV processes



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Good pharmacovigilance practices

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Good pharmacovigilance practices (GVP) are a set of measures drawn up to facilitate the performance of pharmacovigilance in the European Union (EU). GVP apply to marketing-authorisation holders, the European Medicines Agency and medicines regulatory authorities in EU Member States. They cover medicines authorised centrally via the Agency as well as medicines authorised at national level.

Guideline on GVP

The **guideline on GVP** is divided into chapters that fall into two categories:

- modules covering major pharmacovigilance processes;
- product- or population-specific considerations.

Each chapter is developed by a team consisting of experts from the European Medicines Agency and from EU Member States.

The guideline on GVP is a key deliverable of the 2010 pharmacovigilance legislation.

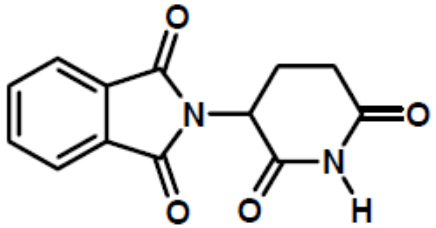
Modules covering major pharmacovigilance processes

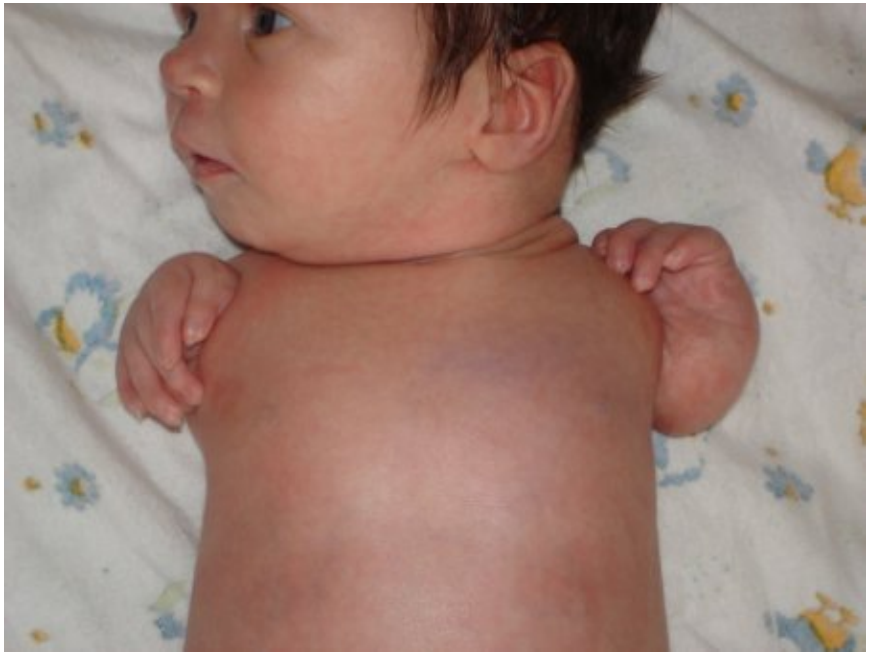
GVP modules I to XVI cover major pharmacovigilance processes.

Most modules are available in their final versions. The full set of modules is scheduled to be available during 2013.

The remaining modules below are under development and are scheduled for release for an eight-week public consultation as indicated below:

Pharmacovigilance





- Thalidomide introduced in 1957 as a sedative ‘wonder drug’ for insomnia, plus anti-emetic effect for morning sickness, resulting in exposure of thousands of pregnant women
- Approx. 10 000 children affected with congenital anomalies e.g. phocomelia during late 50s and 60s leading to its withdrawal (1961) and laws being introduced

Pharmacovigilance

- Regulatory action will depend on risk-benefit balance
- Thalidomide currently authorised in the EU in combination with prednisone and melphalan as first line treatment of patients with untreated multiple myeloma, aged ≥ 65 years or ineligible for high dose chemotherapy
- Procedure started in Feb 2007 and Patients' and victims' organisations were consulted on RMP and labelling; positive CHMP opinion in Jan 2008 and CD in Apr 2008
- RMP includes multiple risk minimization activities

Pharmacovigilance – ADR reporting

National Competent Authorities (NCAs)

ICSRs within the EEA

Marketing Authorisation Holders (MAHs)

ICSRs outside the EEA

EudraVigilance

- The first operating version was launched in Dec 2001
- Electronic exchange of suspected adverse reaction reports (Individual Case Safety Reports, ICSRs) between the Agency, NCAs, MAHs, and sponsors of clinical trials in EEA
- Early detection of possible safety signals associated with medicinal products for Human Use
- Continuous monitoring and evaluation of potential safety issues in relation to reported adverse reactions
- Decision making process, based on a broader knowledge of the adverse reaction profile of medicinal products especially in the frame of Risk Management

EudraVigilance

- 15.7 million transactions during 2013
- >450,000 product presentations in xEVMPD
- over 1 million adverse reaction reports received and processed in 2013
- 52% increase in patient reporting (EEA)
- In total >7 million reports (approx 4.6 million cases)
- EudraVigilance among 3 largest databases of ADRs in the world
- Signal detection, best evidence/decision making, transparency

Signal detection

A signal is an information that arises from one or multiple sources (including observations and experiments), which suggest 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

Practical Aspects of Signal Detection in Pharmacovigilance
Report of CIOMS Working Group VIII, Geneva 2010

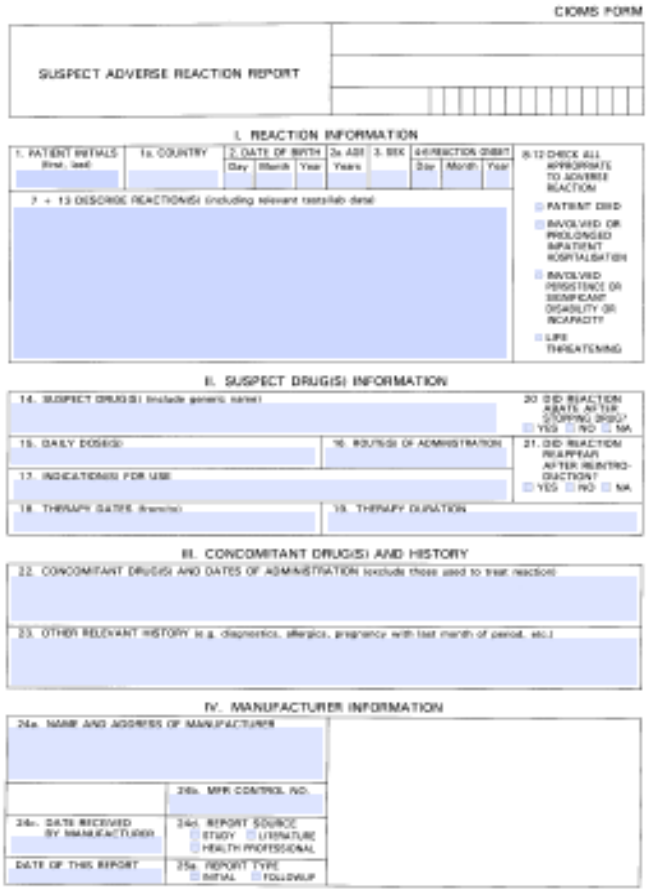
Signal detection

- Part of Signal management process (GVP module IX)
- Performed at the EMA in cooperation with EU Rapporteurs for CAPs
- Performed at NCAs for non-CAPs (lead MSs for monitoring in EV) – here the Agency has a support role – provision of reports, training etc.

Signal detection

EV output (eRMRs/ Line listings/ CIOMs/ Special searches) reviewed in the context of relevant additional information:

- SPCs
- PSURs
- RMP
- Previous evaluation
- Literature articles


CIOMS FORM

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last) | 1a. COUNTRY | 2. DATE OF BIRTH (Day, Month, Year) | 2a. AGE (Years) | 3. SEX | 4/5. REACTION ONSET (Day, Month, Year)

6. (1-2) CHECK ALL APPROPRIATE TO ADVERSE REACTION
- PATIENT DIED
- INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- INVOLVED PERSISTENCE OR SIGNIFICANT DISABILITY OR INCAPACITY
- LIFE THREATENING

7. + 13. DESCRIBE REACTION(S) (including relevant tests/lab data)

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)

20. DID REACTION ABATE AFTER STOPPING DRUG? YES NO NA

15. DAILY DOSE(S)

16. ROUTE(S) OF ADMINISTRATION

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? YES NO NA

17. INDICATION(S) FOR USE

18. THERAPY DATES (from/to)

19. THERAPY DURATION

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER

24b. MFR CONTROL NO.

24c. DATE RECEIVED BY MANUFACTURER

24d. REPORT SOURCE: STUDY, LITERATURE, HEALTH PROFESSIONAL

DATE OF THIS REPORT

25a. REPORT TYPE: INITIAL, FOLLOW-UP

Signal detection
Electronic Reaction Monitoring Report

Active substances

C	D	E	F	G
SOCs	HLGTs	HLTs	SMQ Narrow	PTs
Blood	Haematological Disorders	Haematological Disorders		Haemoconcentration
Blood	Anaemias nonhaemolytic and marrow depression	Marrow Depression And Hypoplastic Anaemias	Agranulocytosis, Haematopoietic Cytopenias	Aplastic Anaemia
Blood	White blood cell disorders	Neutropenias	Haematopoietic Cytopenias	Neutropenia
Blood	Platelet disorders	Thrombocytopenias		Idiopathic Thrombocytopenic Purpura
Card	Heart failures	Heart Failures Nec	Cardiac Failure	Cardiac Failure
Card	Heart failures	Heart Failures Nec	Cardiac Failure	Cardiac Failure Congestive
Card	Myocardial disorders	Myocardial Disorders Nec		Ventricular Hypertrophy
Card	Myocardial disorders	Noninfectious Myocarditis		Myocarditis

Signal detection
Electronic Reaction Monitoring Report

New EV	Tot EV	New Fatal	Tot Fatal	New Med Err/Abus	Tot Med Err/Abus	New Paed	Tot Paed	New Geriatr	Tot Geriatr	New EEA	Tot EEA	New HCP	Tot HCP	New Serious	Tot Serious	New Spontaneou	Tot Spontaneou	PRR (-)	New Lit	Tot Lit	New Obs	Tot Obs	New CT	Tot CT
2	24	0	2	0	2	0	0	1	2	0	1	2	22	2	21	2	**24**	3.01	0	0	0	0	0	0
1	2	0	0	0	0	0	0	1	1	0	0	1	2	1	2	1	**2**	0.50	0	0	0	0	0	0
6	119	0	7	0	3	0	1	1	10	3	27	2	106	6	115	6	**102**	1.73	0	1	0	4	0	13
1	113	0	1	0	2	0	0	1	38	1	27	1	71	1	87	1	**102**	0.14	0	2	0	11	0	0
1	8	0	2	0	0	0	0	1	4	0	0	0	2	1	8	1	**6**	0.12	0	0	0	2	0	0
1	253	0	22	0	7	0	0	1	144	0	132	1	233	1	248	1	**244**	0.83	1	25	0	8	0	1
2	188	0	46	0	4	0	0	1	57	0	39	1	111	2	188	2	**150**	0.19	0	0	0	33	0	5
2	104	0	1	0	3	0	0	2	32	0	61	1	71	2	81	2	**102**	0.42	0	0	0	2	0	0
2	58	0	0	0	4	0	2	1	20	0	9	1	43	2	57	2	**53**	0.53	0	0	0	5	0	0
2	207	0	2	1	4	0	0	1	50	0	67	1	104	2	89	1	**200**	1.51	0	0	1	7	0	0
2	103	0	0	1	3	0	0	2	31	0	24	0	56	2	103	2	**80**	0.71	0	0	0	23	0	0

Signal detection

After validation of potential signals, actions is:

- Close
- To investigate further
- Monitor
- Communicate to Rapporteur – via European Pharmacovigilance Issues Tracking Tool, EPITT
- Confirmed signals are brought to the PRAC for prioritisation and for assessment

Pharmacovigilance Risk Assessment Committee

- Responsible for assessing all aspects of the risk management of medicines for human use
- This includes the detection, assessment, minimisation and communication relating to the risk of adverse reactions, while taking the therapeutic effect of the medicine into account
- Recommendations on any questions relating to pharmacovigilance activities related to a medicine for human use and on risk-management systems, including the monitoring of the effectiveness of those risk-management systems
- Transparency: Agendas, minutes, signal recommendations published

Public access to EV

- www.adrreports.eu
- Summarised tabular and graphic information from spontaneous reports
- Currently done for CAPs (>700 products)
- Updated once monthly
- To be expanded to WS non-CAPs in 2014

EUROPEAN MEDICINES AGENCY

European database of suspected adverse drug reaction reports

Contacts | FAQ | Glossary

English (en)

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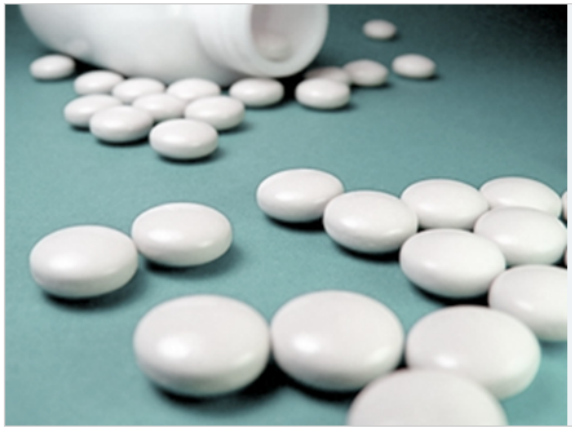
Online access to suspected side-effect reports



On this website you can view data on **suspected side-effects** also known as suspected adverse drug reactions for authorised medicines in the European Economic Area (EEA).

This data is presented in a format called a **web report**. Currently the data only relates to medicines approved through the **centralised authorisation procedure**.

Search for a report

Search here for suspected adverse drug reaction reports

News

31/05/2012 European Medicines Agency boosts EU transparency with online publication of suspected side effect reports.

Key information

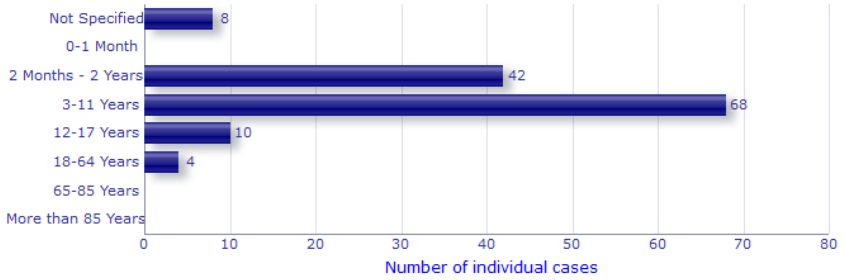
The information on this website relates to ***suspected* side effects**, i.e. medical events that have been observed following the use of a medicine, but which are **not necessarily related to or caused by the medicine**.

Number of Individual Cases | Number of Individual Cases By Reaction Groups | Number of Individual Cases for a selected Reaction Group | Number of Individual Cases for a selected Reaction

The number of individual cases identified in EudraVigilance for **FLUENZ** is **132** (up to May 2014)

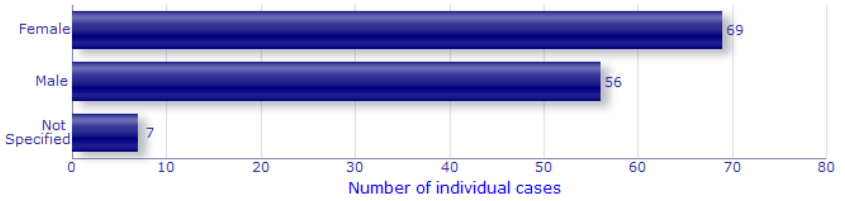
Number of individual cases by Age Group

Age Group	Cases	%
Not Specified	8	6.1%
0-1 Month	0	
2 Months - 2 Years	42	31.8%
3-11 Years	68	51.5%
12-17 Years	10	7.6%
18-64 Years	4	3.0%
65-85 Years	0	
More than 85 Years	0	
Total	**132**	**100.0%**



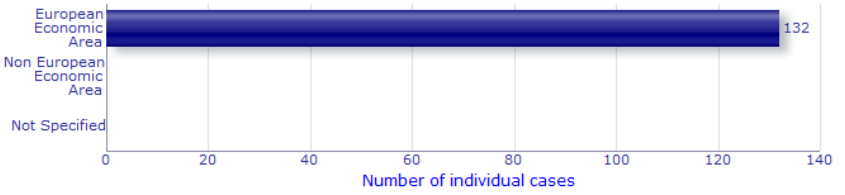
Number of individual cases by Sex

Sex	Cases	%
Female	69	52.3%
Male	56	42.4%
Not Specified	7	5.3%
Total	**132**	**100.0%**



Number of individual cases by Geographic Origin (EEA/Non-EEA)

Occurrence Country EEA/Non EEA	Cases	%
European Economic Area	132	100.0%
Non European Economic Area	0	
Not Specified	0	
Total	**132**	**100.0%**



ENCePP: The European Network of Centres for Pharmacoepidemiology and Pharmacovigilance

- Project led by the EMA intended to further strengthen the postauthorisation monitoring by facilitating the conduct of multi-centre, independent, post-authorisation studies focusing on safety and on benefit-risk
- Using available expertise and research experience in the fields of PhEpi and PhV across Europe, comprising relevant research centres, medical-care centres, healthcare databases, electronic registries and existing European networks covering certain rare diseases, therapeutic fields and adverse drug events of interest
- ENCePP complements the existing tools of the European Union's pharmacovigilance system, such as RMP and EV

ENCePP partners (as of 16 June 2014)

- **137 centres**
  - 103 public (university, hospital, government, charities)
  - 34 other (CROs, consultants)
- **22 networks**
  - 15 International, 7 National (France, Italy, Spain, Belgium, Austria, Sweden)

  Special interests: Psychiatry, rheumatology, respiratory, teratology, pharmacogenetics, congenital abnormalities, women's health, paediatrics, psoriasis, SCARs
- **49 data sources**

ENCePP

www.encepp.eu

- Code of Conduct
- Checklist of Methodological Standards for ENCePP Study Protocols
- ENCePP Guide on Methodological Standards in Pharmacoepidemiology
- Public online databases
  - ✓ Inventory of research resources
  - ✓ E-Register of studies: 311 so far

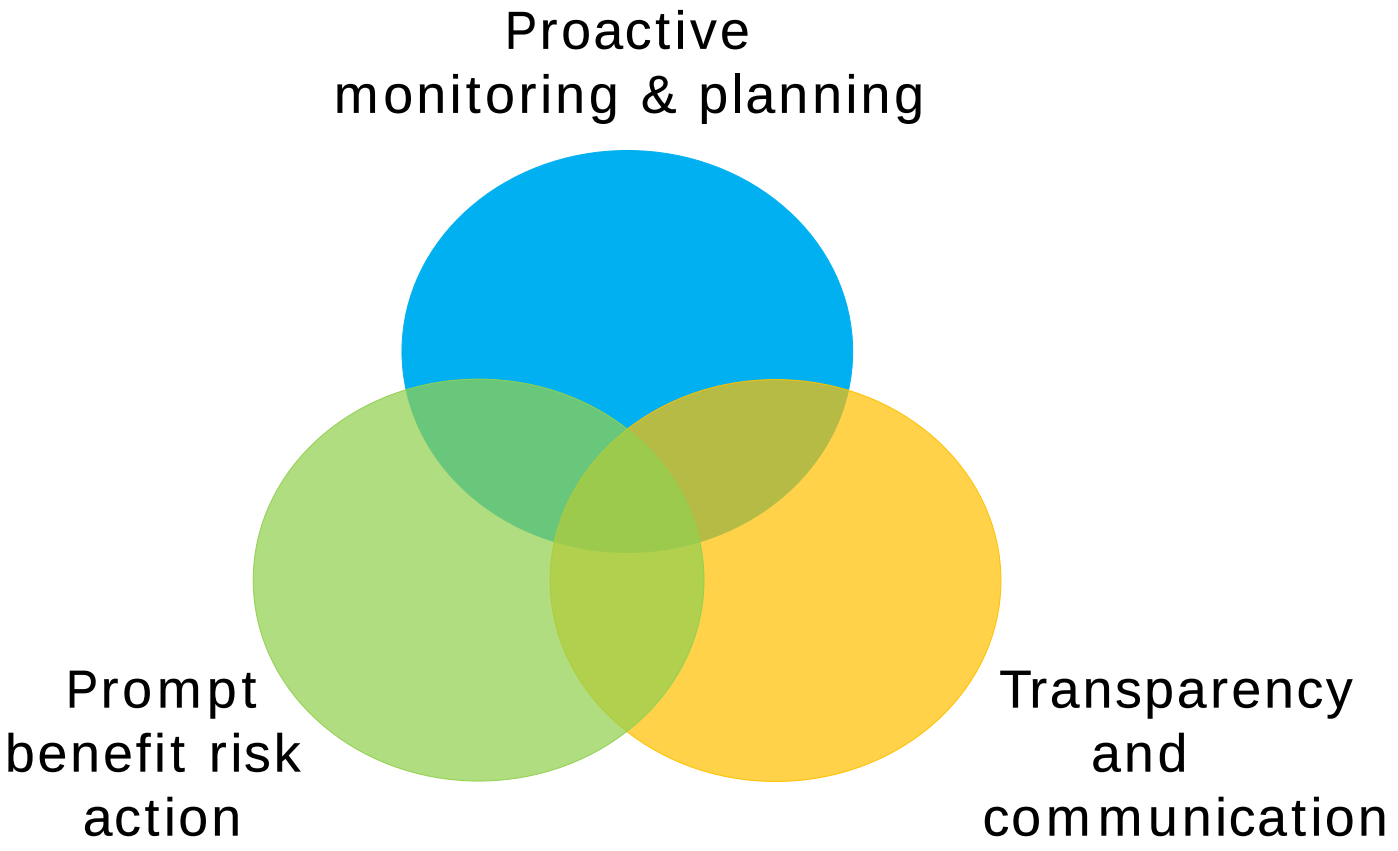
Protect

- Pharmacoepidemiological Research on Outcomes of Therapeutics by a European Consortium
- Collaborative European project that comprises a programme to address limitations of current methods in the field of pharmacoepidemiology and pharmacovigilance, strengthen the monitoring of the benefit-risk
- The EMA is the coordinator of PROTECT and GSK is the deputy co-ordinator
- They manage a multi-national consortium of 29 partners including academics, regulators, SMEs and EFPIA companies

Protect

- Data collection directly from consumers of medicines in their natural language in EU using modern tools of communication
- Early and proactive signal detection from spontaneous reports, electronic health records and clinical trials
- Methodological standards for pharmacoepidemiological studies applicable to different safety issues and using different data sources
- Methods for continuous benefit-risk monitoring of medicines, by integrating data on benefits and risks (clinical trials, observational studies and spontaneous reports)
- Test and validate various methods developed in PROTECT using a large variety of different sources in the European Union

Better post-authorisation supervision



Future outlook

- EV to be further enhanced ('EudraVigilance functionalities to be audited')
- PSUR repository
- Literature monitoring
- Structured product information - Art 57(2) data to be updated and validated
- EV Audit
- EU webportal

Recent issues

A rare but serious reaction: two contexts

Raptiva (efalizumab) – powder and solvent for solution for injection

-Indicated in moderate to severe plaque psoriasis in patients who failed or don't tolerate other systemic therapies (methotrexate, cyclosporin, PUVA)

-Efficacy - as 75% improvement is symptoms after 12 weeks – achieved in 26% vs 4% (placebo) and 31% vs 4% in studies

-Common side effects were mild – flu-like symptoms, headache, fever, chills, nausea, myalgia, leucocytosis

-Benefit-risk positive, authorized in Sep 2004

A rare but serious reaction: two contexts

- Four (three confirmed and one suspected) cases of progressive multifocal leukoencephalopathy (PML) in psoriatic patients under long-term treatment with efalizumab have been
- re-evaluation of the benefit-risk. Two confirmed cases were fatal and the one suspected case as well.
- Other serious reactions since authorisation: aseptic meningitis, immune mediated haemolytic anaemia, antibody development with vaccinations, interstitial pneumonitis, arthritis, erythema multiforme, inflammatory polyradiculoneuropathy Miller Fisher syndrome, facial palsy and Bells palsy and severe infections, malignancies during long-term use, including serious (fatal) events such as opportunistic infections and Guillain Barré syndrome (GBS), encephalitis, encephalopathy.

A rare but serious reaction: two contexts

Considering that moderate to severe psoriasis is not a life threatening disease, the efficacy of efalizumab is modest, the safety profile is of concern and includes fatal reports of PML, encephalopathy, encephalitis and the availability of alternative treatments, the CHMP recommends a suspension of the marketing authorisation of Raptiva (efalizumab) for the treatment of adult patients with moderate to severe chronic plaque psoriasis.

No sub-group with positive risk-benefit could be found and product was voluntarily withdrawn by MAH in May 2009.

Tysabri (natalizumab)

concentrate for solution for infusion

- Indicated in highly-active relapsing-remitting multiple sclerosis for patients with high disease activity (failed interferon beta treatment, relapses etc.)
- In trials, approx. 66% decrease of MS attacks after 1 year; and approx. 42% decrease in disability progression over 2 years
- Risk of infections incl. PML known [monitoring envisaged]. Most common side effects included urinary tract infection, nasopharyngitis, urticaria, headache, dizziness, vomiting, nausea, arthralgia, rigors, pyrexia and fatigue.
- Authorised Jun 2006 with RMP

Tysabri

Aug 2008: 2 reports of PML in patients treated beyond 12 months

Sep 2008: benefits continue to outweigh risks in the treatment of relapsing-remitting MS, but existing warning on the risk of PML should be strengthened to heighten awareness about this rare but serious side effect; also physician guide (risk minimization plan) to be updated

Tysabri

Jan 2010: Art.20 CHMP review of 23 cases concludes that

- risk for PML increases after 2 years of treatment but remains low; approx. 1 PML in 1000 patients/2 years
- B-R still positive due to few therapeutic options for highly active RRMS – but risk minimization activities needed
- Update of SPC to highlight risk beyond 2 years and advice on management of patients who show PML symptoms
- Forms to be signed at initiation of treatment and at 2 years after detailed discussion of PML risk with physician

Antidiabetics – glitazones/thiazolidinediones

- agonists at the PPARγ (peroxisomal proliferator activated receptor gamma) nuclear receptor, reduce glycaemia by reducing insulin resistance at adipose tissue, skeletal muscle and liver
- Incidence of DM increases fast worldwide
- 1 in 10 US adults has DM – expected to rise to approx. 50 milion DM patients in 2050
- Troglitazone: withdrawn in the 1990s due to idiosyncratic liver failure

Antidiabetics – glitazones/thiazolidinediones

- Thiazolidinediones can cause fluid retention which may exacerbate or precipitate signs or symptoms of congestive heart failure. Rosiglitazone can cause dose-dependent fluid retention
- Rosiglitazone: CV risk monitored since MA, and being 2nd line; in 2010 EC initiated an Art 20 procedure (726/2004) – marketing authorisation suspended due to increased CV risk (ischaemic heart disease)
- Pioglitazone: PhEpi studies (Kaiser Permanente Northern California cohort study, French CNAMTS cohort study, GPRD case control study) suggest small increase of risk of bladder cancer (RR 1.12-1.33), in particular at long duration and with high cumulative dose

Weight loss medicines: obesity

- USA: 111,909 - 365,000 deaths per year; EU: 1 milion (7.7%) deaths attributed to obesity; huge associated morbidity
- Life expectancy is lowered with increasing BMI: BMI 30–35: 2-4 yrs, BMI >40: 10 years
- EU: 2008/09 women: 8% (Romania) and 24% (UK); men: 7.6% (Romania) and 24.7% (Malta)
- USA: 2007 33% men and 36% women (50% Afro-American); 6% at BMI >40; overall 65% are obese or overweight
- 2030 forecast: 51% population obese; 11% morbidly (BMI >40), healthcare cost estimate: USD 550 billion Am J Prev Med. 2012 Jun;42(6):563-70.

Weight loss medicines: obesity

Acomplia (rimonabant) - a cannabinoid receptor antagonist (CB1), that affects energy balance, glucose and lipid metabolism and body weight, and in neurons of the mesolimbic system modulates the intake of highly palatable, sweet or fatty foods; CTs showed weight loss (Jun 2006)

- New data showed 2-fold risk of psychiatric ADRs (depression, anxiety, aggression, sleep disorders, suicide) vs placebo
- Risk minimisation options limited
- Marketing authorisation suspended; withdrawn Jan 2009

Weight loss medicines: obesity

•Reductil (sibutramine): SNRI related to amphetamines (1999); CV risk to be better characterised – SCOUT study - 10,000 patients

- showed an increased risk of serious, non-fatal cardiovascular events, such as stroke or heart attack vs placebo – Art 107 procedure (2001/83/EC); benefits were discreet: 2-4 kg vs placebo

  •MA suspended Aug 2010

•Xenical, Alli (orlistat): blocks GI lipase (1998; 2007 OTC)

- Very rare reports of liver injury – in context of huge exposure and inconclusive causality: risk minimisation (SmPC, symptoms in PL)

Weight loss medicines: obesity

Other options:

- Belviq (lorcaserin): MA withdrawn
- Qsiva (phentermine/topiramate): MA refused

- Concerns over efficacy and safety

Statins

- Simvastatin is the 2nd most prescribed drug in the USA; atorvastatin among best selling (sales volume, USA)
- Established role in CV disease prevention
- Risk of myopathy known: myalgia – rhabdomyolysis
- Huge exposure: even small increase in risk will have an impact
- Studies suggested increased risk of new onset DM, OR 1.09 (95% CI 1.02-1.17); 1 extra DM case in 255 patients treated for 4 years
- Treatment benefit – risk of death, MI/stroke in the same population decreased: approx 9:1 benefit over risks. Risk highest in patients with risk factors (SmPC updates 4.4. a 4.8)

MMR vaccine – forged risk of autism: risk perception very damaging

- Vaccine against measles, mumps and rubella (live attenuated)
- 1998: Wakefield et al paper suggests a link between MMR and an autism disorder, enterocolitis (12 patients, questionable method, conflict of interests) Lancet. 1998;351(9103):637-41
- Epi studies consistently found no evidence of a link between the MMR vaccine and autism
- The study was retracted – Wakefield's licence revoked; in 2011 BMJ labelled the research as fraud *BMJ* 2011;342:c7452
- Vaccine scare as a result – lower vaccine coverage (80%, UK 2003-4) epidemics of these viral diseases with morbidity and fatalities

Drug shortages

- Manufacturing/GMP problems, highly specialised technology
- Suppliers outside the EEA
- Market consolidation/1 manufacturer, cancelled production, commercial reasons
- USA: 267 medicines (2011); 123 (Aug 2012)
- Mostly cytostatics (methotrexate, leucovorine, doxorubicin), anaesthetics (propofol, benzodiazepins, fentanyl)
- Treatment efficacy (dosing); ADRs due to use of alternatives; drug administration errors; underdosing (enzyme replacement); risks due to keeping products on the market

And when you think you've seen it all

- Vials of Herceptin (trastuzumab), Alimta (pemetrexed), Remicade (infliximab), Avastin (bevacizumab), MabThera (rituximab) have been stolen in Italy
- Some Herceptin vials have been tampered with and reintroduced into supply chain – found in Britain, Finland and Germany
- Possible risks to patients (sterility, efficacy)
- Urgent communication to HCPs
- Implicated batches quarantined, investigations ongoing

Take home message

- Pharmacovigilance is crucial for timely detection and subsequent management of ADRs
- The role of the Agency is in authorisation and supervision of human medicinal products based on benefit-risk balance, operation of EV and coordination of the EU PhV network
- Involvement of patients, healthcare professionals, pharmaceutical companies, national authorities and the Agency is necessary
- EU PhV system is protecting public health whilst providing timely access to efficacious innovative therapies

Thank you!

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