swissmedic

VIGILANCE-NEWS

EDITION NO. 11 – DECEMBER 2013

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EDITORIAL

Europe and Switzerland

Dear Reader,

This year, we are limiting ourselves to a single edition of our Vigilance-News. We have been upgrading our IT systems, which has been a very time-consuming process. In this edition, we want to focus on this year's pharmacovigilance specialist conference which was held on September 9th, 2013. The subject of the conference was "Good Pharmacovigilance Practice: the New EU Pharmacovigilance Modules and Switzerland" (please see the conference report).

Increasingly, EU decisions are playing an important role in our everyday business in Switzerland. When it comes to pharmaceutical products in particular, mutual transparency is vital for patient

well-being. For Swissmedic, this means analysing the new EU pharmacovigilance modules, considering these with specific reference to Switzerland and implementing them as appropriate. This includes, for example, converting “Periodic Safety Update Reports (PSUR)” to “Periodic Benefit-Risk Evaluation Reports (PBRER)” and the associated updates of Swissmedic forms and information sheets.

A further example is the coding of Individual Case Safety Reports (ICSR). During the first half of 2014, Swissmedic will be switching to MedDRA (Medical Dictionary for Regulatory Activities) in order to standardise medical terminology with other authorities and marketing authorisation holders (MAH).

Swissmedic also keeps abreast of the decisions made by the newly created “Pharmacovigilance Risk Assessment Committee (PRAC)” of the European Medicines Agency (EMA) in relation to pharmacovigilance signals and risk problems. Equally, the marketing authorisation holder also has an obligation to inform Swissmedic, contemporaneously and unprompted, of safety-related changes that are being planned on an international scale. Both the EU and Switzerland were affected by the signals relating to “calcitonin” and “intravenous iron medical products” described in this newsletter, but they each took action individually.

We would like to stress once more that Swissmedic does not simply adopt EU decisions; instead, the Swissmedic staff form their own independent and critical opinions about the potential risks and the resultant safety measures, evaluating and implementing these where appropriate with specific reference to Switzerland.

There are also many signals which are primarily detected, managed or updated in Switzerland, e.g. the incidence of anaphylaxis with chlorhexidine products. This is also evident from our annual statistics which, exceptionally, we are publishing in the second half of the year.

We would be pleased to receive any comments or feedback about this edition of Vigilance-News at vigilance@swissmedic.ch.

We wish all our readers enjoyable holidays and a successful start to 2014.

The Editors

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We want to thank all colleagues for their contribution to the realisation of this edition of Vigilance-News.

FLASH: SIGNALS RELATING TO THE SAFETY OF MEDICINES

Combined hormonal contraceptives and the risk of venous and arterial thromboembolism – Swissmedic's assessment confirmed by European experts

The Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has completed its review of combined hormonal contraceptives[1] and has issued its recommendations: the advantages clearly outweigh the risks, as long as the indication and contraindication and the risk factors for a venous and arterial thromboembolism (VTE and ATE) are taken into account every time these products are prescribed. The product information for these medicinal products is to be harmonised on an EU level, and completed by information material for the attention of physicians and users.

Since 2009, Swissmedic has been providing regular information on this topic, and has introduced a series of measures to improve prescribing methods for these products.

More recently, the Swiss Association for Gynaecology and Obstetrics ("SGGG") has drafted information material for physicians and users in consultation with Swissmedic. It has been available (in German and French) since July 2013 at:
http://www.swissmedic.ch/marktueberwachung/00091/00092/02462/index.html?lang=en.

The product information with regard to warnings and precautionary measures is to be harmonised in accordance with the latest evaluation.

Swissmedic provides a reminder of the current data available on the risk of thrombosis below:

- The VTE risk is increased for all users of a combined hormonal product.
- In this connection, products containing the gestagen levonorgestrel are the safest among combined hormonal products with regard to the risk of venous thrombosis and embolisms of the lungs. The risk of VTE is 1.5 to 2 times higher when taking products containing gestodene, desogestrel or drospirenone.
- The increase to the risk is, however, small in absolute numbers: according to data currently available and the European evaluation, the annual occurrence of a VTE is, on average:
  - 2 out of 10,000 women taking no combined hormonal contraceptives.
  - 5–7 out of 10,000 women taking combined contraceptives containing levonorgestrel.
  - 9–12 out of 10,000 women taking combined contraceptives containing desogestrel, gestodene or drospirenone.
  - 6–12 out of 10,000 women taking non-oral combined hormonal contraceptives (vaginal ring containing etonogestrel or patches containing norelgestromin).
  - The risk of a VTE when taking products that contain other gestagens (chlormadinone, dienogest, or nomegestrol) – some of which also contain other oestrogens – has not yet been conclusively proved. It is, however, at least as high as that when taking products containing levonorgestrel.
- The occurrence of a VTE is even higher during pregnancy (10–30 out of 10,000 pregnancies) and postnatal (50–100 out of 10,000 periods of 12 weeks).
- Moreover, the risk of an arterial thromboembolism (myocardial infarction, stroke, arterial occlusion) is higher, independently of the gestagen contained, for all combined products, although the increase is extremely small.

Risk minimisation measures: Since 2009, Swissmedic has regularly provided information to healthcare professionals and the general public in the form of articles and communications on its website, and has adapted the product information in 2010 and 2012.

In November 2010, Swissmedic also published an article in the Swiss Medical Journal (*Schweizerische Ärztezeitung*) to raise awareness among physicians regarding the symptoms of an embolism of the lung – often extremely difficult to identify. The aim was to promote more rapid intervention should such embolisms occur.

In July 2013, and in consultation with Swissmedic, the SGGG published information material to provide support regarding medical advice. It promotes in-depth medical advice and regular follow-up checks every time that a hormonal contraceptive is prescribed.

Recommendations

In summary, combined hormonal contraceptives are – provided that they are indicated and that the product information is respected – a safe, effective method of preventing unwanted pregnancies. The following aspects should be taken into consideration regarding their use:

- In-depth advice is necessary prior to every prescription. Contraindications and individual risk factors (overweight, personal or family history of a thrombosis, tobacco use, general state of health), and the user's background and needs should be noted and discussed, in order to decide on the most appropriate form of contraception. The user's participation in the medical decision – i.e. shared decision making – is an important component of the advice provided and requires each woman wishing to take hormonal contraception to be provided with comprehensive information.
- If a combined hormonal contraceptive is chosen, precedence should be given to products containing levonorgestrel because of the lower risk of VTE. For women using a product containing drospirenone, gestodene, desogestrel or other gestagens and who tolerate it well, there is no reason to change the prescription. If they have any questions or wish to discontinue use of their product, they should consult their physician.
- Users should be informed of alarm signals indicating an arterial or venous thrombosis. In the case of severe pain and swelling in one leg, sudden unexplained breathlessness, rapid breathing or cough, chest pain, and weakness or numbness of the face, arm or leg, a physician should be consulted immediately. Further information can be found in the information sheet for users of combined hormonal contraceptives, see link to the SGGG website, Information sheet for users of combined hormonal contraceptives (status June 2013). Available in German and French.

All documents on hormonal contraceptives published by Swissmedic since 2009 can be found on the Swissmedic website (Market surveillance > Human medicines > Specific topics (column to the left): http://www.swissmedic.ch/marktueberwachung/00091/01962/index.html?lang=en

In addition to the communications and materials by the Swiss Association for Gynaecology and Obstetrics (SGGG), these references comprise an overview of all hormonal contraceptives approved in Switzerland and data on spontaneous reports of ADRs (In der Schweiz zugelassene hormonale Verhütungsmittel – eine Übersicht in German and French only). Both are updated regularly.

1. *In the EU, products containing the gestagens chlormadinone, desogestrel, dienogest, drospirenone, etonogestrel, gestodene, nomegestrol, norelgestromin and norgestimate were examined. These are also contained in the combined hormonal contraceptives authorised in Switzerland.*

Chlorhexidine: anaphylactic reactions

Chlorhexidine, an antiseptic active ingredient in widespread use, can cause acute and immediate hypersensitivity reactions (anaphylaxis). Following recent reports, Swissmedic is issuing a reminder about this very rare but potentially serious risk, and is drawing attention to the guidelines for treating reactions of this kind.

Chlorhexidine is a disinfectant and antiseptic agent that has been widely used for decades. Due to its strong antimicrobial effect, it is an ingredient found in many mouthwash solutions, skin creams, wound sprays, lubricants, powders and cosmetics, and it is also used in medical devices, e.g. to impregnate catheters and dressing materials.

It should be assumed that anaphylactic reactions to chlorhexidine are very rare. The precise frequency is unknown, but an increasing incidence and an "underreporting" are very probable (1).

In the past eight years, 18 reports of serious anaphylactic reactions to drugs containing chlorhexidine have been submitted to Swissmedic; of these, nine were life-threatening and one patient died.

In addition, over the past twelve years, there have been six reports to Swissmedic of incidents involving anaphylactic reactions – some of them life-threatening – following the use of medical devices cleaned beforehand with disinfectant agents containing chlorhexidine.

Anaphylaxis is a medical emergency and early medical treatment is therefore of critical importance. A number of studies have revealed that, in many cases, national and international guidelines for the acute treatment of severe allergic reactions are not followed properly. In particular, adrenaline, the most important drug for treating severe allergic reactions, is administered too rarely and too late. Further forms of treatment are volume substitution, the administration of antihistamines and glucocorticoids, placing the patient in the shock position and securing the airways, checking the vital signs, supplying oxygen via a mask or nasal cannula and, if necessary, resuscitation and defibrillation (2, 3).

If there is a known chlorhexidine allergy, it is essential that products containing this ingredient are avoided. Even application to intact skin can trigger a hypersensitivity reaction.

In the case of an unexplained allergic reaction, it should also be checked whether products containing chlorhexidine have been used.

References

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Salmon-Calcitonin: the impact of the new trials

For decades, salmon calcitonin (sCT), produced using biotechnology, was used to treat post-menopausal osteoporosis (PMO) under the brand name Miacalcic® in the form of ampoules and, primarily, a nasal spray. Although it was also used in the treatment of Paget's disease, cancer-related hypercalcaemia and algodystrophy (Sudeck's atrophy), these indications were less significant in terms of sales.

In around 2003, development of an oral form of sCT (with absorption enhancers) was launched, and this was initially tested in two major randomised, placebo-controlled trials conducted over the course of two years on patients with osteoarthritis of the knee. In an early interim analysis, a number of cases of prostate cancer were observed in the sCT group that were not observed in the placebo group, but the final results, which included PSA values, did not reveal any increased risk of prostate cancer. Nevertheless, this suspicion of carcinoma trig-

gered a review procedure by both the EMA and Swissmedic. Another placebo-controlled trial that was started at a later date and conducted over the course of three years on approximately 4,600 women with PMO revealed a complete lack of effectiveness, which clearly impacted negatively on the risk/benefit analysis for the treatment of osteoporosis (further information is available in the Summary of Product Characteristics of Miacalcic®).

At the instigation of the EMA, the authorisation holder was required to carry out a meta-analysis on the basis of 20 randomised controlled clinical trials (including the data relating to the oral formulation) with regard to malignant diseases. This meta-analysis revealed a small but statistically significant increase in the incidence of malignant diseases when calcitonin was used on a long-term basis. An increase in the absolute rate of tumours compared to the placebo group was identified. This rate varied; depending on the formulation, it was between 0.7% and 2.36% (nasal spray) and while the first numerical discrepancies between the sCT and the placebo groups occurred after six months, they became more pronounced after several years of treatment. No pattern of specific tumour types was observed.

Since in the EU (unlike in Switzerland), the nasal spray was only authorised for treating PMO, authorisation for the nasal spray was withdrawn and the treatment duration applicable to the solution for injection was restricted. In Switzerland, as a result of more recent data, a restricted duration of use (two months for the solution for injection / three months for the nasal spray) has been authorised for the prevention of osteoporosis in cases of acute bone atrophy due to sudden immobilisation (e.g. osteoporosis fractures). An upper limit of treatment duration for the other indications has now also been applied (cf. Health Professional Communication of April 2013, in German and French only): http://www.swissmedic.ch/marktueberwachung/00091/00092/02367/index.html?lang=en.

Note: Well-designed trials involving a new galenic form can cause a treatment that has been well-established for many years (PMO) to falter and even come to a complete stop!

The risks of intravenous treatment of iron deficiency

Summary

The prescription of iron replacement medicines for parenteral administration has increased significantly in recent years. This development runs parallel to the increasing number of patients who have been diagnosed with an iron deficiency.

However, even recent products of the so-called third generation (such as ferumoxytol or ferric carboxymaltose) carry the risk of a severe and sometimes fatal hypersensitivity reaction. The predisposition criteria for such reactions are unknown.

Therefore it is necessary to consider carefully the therapeutic indication for each patient and to weigh the benefit-risk profile for each method of administration (oral or intravenous).

Current situation

For several years, the number of publications on the subject of treating patients with an iron deficiency (as a result of increased blood loss, an inadequate iron intake or an increased iron need), with or without anaemia, is increasing. This issue, neglected for many years, is now increasingly in the spotlight.

The main symptoms of iron deficiency are chronic fatigue in young women, impaired cognitive functions in children and even cardiac problems (1; 2). These symptoms affect an extremely wide population, to the extent that iron deficiency is now considered a public health problem (3).

In the past, patients were given medicines in oral form which all too often were ineffective or poorly tolerated. The first medicines given intravenously were based on dextrans and associated with a serious risk of anaphylactic reactions. Injections of test doses had been required prior to the actual drug infusion. As a result, the number of prescriptions was limited for a long time. The new products (ferumoxytol and ferric carboxymaltose) have a better safety profile.

The administration of a test dose is no longer required and much higher doses of iron can be administered in a single injection or an infusion (4; 5). However, the risk of a severe hypersensitivity reaction still exists (6). In light of this risk, the French medicines agency *ANSM (Agence nationale de sécurité du médicament et des produits de santé)* asked the EMA to re-assess the risk-benefit balance of all iron-containing medicines available on the market. The response by the EMA was published in June 2013. It concluded that the benefits of these medicines are greater than their risks, provided that adequate measures are taken to minimise the risk of allergic reactions. The marketing authorisation holders in question were required to update the corresponding Summary of Product Characteristics (involving that staff trained to evaluate and manage anaphylactic and anaphylactoid reactions are immediately available as well as resuscitation facilities). These updates will also be the subject of a Health Professional Communication in Switzerland.

Treatment risks – reported adverse events

In this context, we are publishing here the updated statistics, as per 1 October 2013, relating to adverse events associated with intravenous iron-containing medicines reported in Switzerland since 1 January 2010. These are the follow-up statistics to those published in Vigilance-News in June 2010.

- **Ferinject®** (ferric carboxymaltose): 340 ADRs (Adverse Drug Reactions), 239 of which were serious, equally spread over four years (79 in 2010, 56 in 2011, 50 in 2012 and 54 in 2013). Of three fatal cases, there was one anaphylactic shock in a patient with a severe underlying disease. In the two other fatal cases with Ferinject causality was assessed as unlikely (one report of cerebral haemorrhage 3 weeks after the last administration and one of foetal death)*. Furthermore, 185 anaphylactic reactions, including 21 of anaphylactic shock, were reported. These ADRs primarily affect young or middle-aged women following or during an intravenous iron injection, regardless of the dose administered.
- **Venofer®** (iron-hydroxide sucrose complex): 30 ADRs, 27 of which were serious, with the number decreasing each year (17 in 2010, 7 in 2011, 4 in 2012 and 2 in 2013); 16 anaphylactic reactions, including 2 anaphylactic shocks, but no deaths. Once again, these ADRs primarily affect young or middle-aged women following or during an intravenous iron injection, regardless of the dose administered.
- **Rienso®** (ferumoxytol): 4 ADRs in 2013, of which 3 were serious (and one death). These ADRs affect both men and women following or during an intravenous iron injection, regardless of the dose administered.

Discussion and conclusion

These statistics confirm that a certain percentage of patients who receive third generation medicines still suffer serious hypersensitivity reactions, a number of which have proved fatal. The predisposition criteria for reactions of this kind are still unknown.

Consequently, it is necessary to consider the indication for each patient and assess to weigh the benefit-risk profile for each method of administration (oral or intravenous).

Moreover, the recent (2nd quarter of 2013) and unexplainable rise in the number of hypersensitivity reactions in Switzerland following the administration of Rienso® has triggered a recall of the product and a requirement for the manufacturer to carry out the necessary tests.

Update 20.12.2013

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CONFERENCE

SWISSMEDIC INFORMATION EVENT
GOOD PHARMACOVIGILANCE PRACTICE:
THE NEW EU PHARMACOVIGILANCE MODULES AND SWITZERLAND
HIGHLIGHTS

On 9th September 2013, an information event entitled "*Good Pharmacovigilance Practice: the New EU Modules and Switzerland*" was held at the Kursaal Bern. The full-day event organised by Swissmedic was aimed at pharmacovigilance professionals working for industry or authorities and attracted more than 170 people. National and international speakers gave presentations, divided into four key topic areas, on the ongoing reform of the EU pharmacovigilance modules and the implementation of these in Switzerland.

Dr Karoline Mathys Badertscher, Director of the Market Surveillance division at Swissmedic, opened the event by providing an overview of the new challenges and emphasising the general objective, namely that of establishing a good foundation for cooperation between industry and Swissmedic within the field of pharmacovigilance.

- **Professor Ragnar Löfstedt**, Director, King's Centre for Risk Management, King's College London: **"Risk Communication and Transparency in the Pharma Sector: What Does the Evidence Show?"**

  Professor Löfstedt presented evidence of the existing pronounced and increasingly political pressure placed on regulatory authorities in

the EU to be proactive about making their safety data accessible to the public. He described this trend of ensuring that all information is fully visible as "fishbowl transparency". However, to date there has been no scientific evaluation of these transparency initiatives from a risk communication perspective. Professor Löfstedt raised the question of what the consequences of this "tsunami" might be. A recently published study from the USA involving 433 physicians and 1000 adults revealed that some 25% of patients would stop taking their medication if it had an associated safety warning. Professor Löfstedt presented the results of a study conducted by his working group (previously unpublished data) involving a survey of a representative random sample of 5,648 people in the EU, along similar lines to the US study.

If there were indications of a safety problem, 52% of people would stop taking their medication, while 36% would seek further information. The speaker called these two groups of people "stoppers" and "seekers". One interesting factor is the clear differences between the various nations. The Netherlands, for example, have a much higher percentage of "seekers" (67% seekers, 18% stoppers), while Spain has a higher percentage of "stoppers" (61% stoppers, 33% seekers). In Europe, just 3% of patients would continue to take their medication as before. 55% want information – and this is before a scientific evaluation has taken place.

Professor Löfstedt concluded that, with this continuing "fishbowl transparency", the negative impact on compliance in Europe is greater than it is in the USA. GPs are being inundated with queries – to a greater extent than regulatory authorities or industry – and it is possible that drugs will be stigmatised. Professor Löfstedt also stated that the EMA is not prepared for the cultural differences.

- **Rudolf Stoller**, Head of the Safety of Medicines department at Swissmedic: **"Introduction to the Next Topics of the Day"**

  Following the keynote address, Rudolf Stoller introduced the fundamental reason behind the event – the new modules of the EU Good Pharmacovigilance Practice and their implementation in Switzerland – and explained how this topic would be addressed in the next presentations of the day.

- **Dr Martina Schäublin**, Head of the Vigilance unit at Swissmedic: **"Reporting Individual Case Report, Compliance with Swiss Guidelines"**

  Dr Schäublin started by discussing the intent and purpose of spontaneous reports and examined the associated expectations, as well as why, when and by whom such reports must be made. She then went on to explain the system of spontaneous reports, the regional pharmacovigilance centres and the legal background.

  Martina Schäublin provided information about the current situation regarding the electronic data exchange of individual case reports via the E2B gateway. Swissmedic is currently in the pilot phase with five pharmaceutical companies and is exchanging prolific quantities of data. In August 2013, a meeting was held with other companies who are interested in becoming involved in the electronic data exchange at a later stage. Before additional companies are given access to the E2B gateway, Swissmedic is going to convert the database system to MedDRA, recode the existing cases in the database and make further improvements to the system. Starting in 2014, Swissmedic is going to encode Individual Case Safety Reports (ICSR) in MedDRA and transmit these to companies. Swissmedic accepts ICSR in the national languages of Switzerland and in English, but the regional pharmacovigilance centres use the national languages of Switzerland for the case documentation. Reports about adverse drug reactions occurring within the context of clinical trials of drugs which are not authorised in Switzerland (SUSARs) cannot be accepted via the gateway. By law, SUSARs must be reported to the Clinical Trials department in the conventional way.

  The main focus was on practical instructions and information about the procedure for re-

porting suspected adverse drug reactions (ADR). Dr Schäublin provided further definitions of terms relating to the seriousness of ADRs and interactions and illustrated these by means of examples. She also focussed on reports relating to drugs and pregnancy.

- **Dr Oliver Hellstern**, Head of the Risk Management unit at Swissmedic: **"Signals"**

  Dr Hellstern started his presentation by giving a meticulous definition of the term "signal". He attached particular importance to the fact that a signal can originate from various sources, that it was previously unknown and that the information has hitherto not been defined as a signal, or that a new aspect relating to the frequency and severity of a known adverse drug reaction has come to light. A signal exists when it has effects on public health necessitating further action.

  The various ways of detecting signals were another key focus of his presentation. Dr Hellstern gave a detailed description of the various qualitative and quantitative ways and methods of detecting signals, and stressed the responsibilities of both the headquarters and the affiliates.

  Dr Hellstern also talked about the duty to report signals and described the information expected by Swissmedic in these circumstances. He illustrated the Swissmedic expectations with a wide range of examples.

- **Prof. Dr Axel Thiele**, Federal Institute for Drugs and Medical Devices (BfArM), Germany: **"Good Pharmacovigilance Practice – the New EU Regulations"**

  Dr Thiele introduced the objectives of the new EU pharmacovigilance legislation: to prevent counterfeit products and illegal trade, to provide better protection for patients and to ensure that citizens have better access to information. He stressed that implementation of the new legislation is mandatory in all member states. In addition, a Good Pharmacovigilance Practice (GVP) guide has been issued which is set within the legal framework of a regulation and a directive. He pointed out that, although not all of the modules had yet been completed, it was expected that they would be completed by the end of 2013. Complex transitional arrangements are in place.

  Key reforms are being made in the following areas:

  Each company must show evidence of a pharmacovigilance system. Each company must create a Pharmacovigilance System Master File (PSMF) that explains the system, but must only produce this if requested to do so; otherwise it is only a very brief summary of the pharmacovigilance system that must be submitted as a mandatory requirement within the context of marketing authorisation applications.

  ADRs have been redefined and, in future, will also include off label use, overdose, drug errors etc.; the previous "when used as intended" provision will no longer apply. All serious ADRs must be reported and non-serious ADRs must also be reported in future, although this latter requirement applies only to ADRs from within the EU. In Germany, the reporting of non-serious ADRs, with the exception of a few product groups, will not be required until EudraVigilance is fully functional – this will not be before 2014/2015. Each year, the BfArM receives approximately 35,000 reports including follow-ups about ADRs, which have occurred in Germany alone, resulting in around 25,000 cases each year.

  A Risk Management Plan is required as part of the product-specific Risk Management System for each new authorisation including generic drugs.

  For PSURs, there will be no fixed submission dates in future; instead there will be individually set submission dates for individual active ingredients in the published EU Reference Dates List (EURD).

  In future, the newly created PRAC (Pharmacovigilance Risk Assessment Committee) will play a key role. In Europe, the pharmacovigilance referrals will be made via the PRAC in future. The PRAC recommendation will be

submitted to the CHMP in the case of centrally authorised drugs, or to the CMDh (Co-ordination group for Mutual recognition and Decentralised procedures-human), when no central authorisations are affected, and ultimately to the EU Commission for the final binding decision.

In future, communication will be on a very wide scale. Ultimately, everything that is known to pharmacovigilance will have to be published on both the EMA website and the websites of the national authorities.

- **Dr Thomas Munz**, Clinical Reviewer, Risk Management unit at Swissmedic: **"The New PBRER – Recommendations from Swissmedic"**

The Periodic Benefit-Risk Evaluation Report (PBRER) as described by ICH Guideline E2C (R2) created a need within the Swiss pharmaceutical companies for questions to be answered and uncertainty dispelled. Following an investigation by "scienceindustries" in Switzerland by the "Pharmacovigilance" and "Regulatory Affairs" working groups, as well as an international survey conducted by the "Implementation Working Group" a number of key questions had come to light before the conference:

- In which aspects does Swissmedic differ from the EMA (EU)?
- Can the PBRER periodicity specified by Swissmedic be adapted to the EU periodicity?
- How detailed should the presentation of the benefit be?

Dr Munz clearly stated that Swissmedic is fundamentally adopting the ICH Guideline E2C (R2) because this is mandatory on an international basis. He went on to say that it is therefore not a change that is being made without assessment or a case of blindly following the EU. The unchanged legal basis in Switzerland was presented in support of this.

If a company makes an application to change the reporting period to that of the EU, Swissmedic will generally agree to this following a review of the application, but this cannot be seen as setting any precedent for other medical products or companies.

Dr Munz made it clear that optimal compliance with the guideline involves information about the benefit on a wide scale. However, this should be restricted to "re-evaluated" and the description should be short and concise. He provided a number of examples of this.

The previous PSUR form has also been modified into a PBRER form and this is due to be published on the Swissmedic homepage shortly. Two eminently important points remain:

- Data about exposure in Switzerland and international exposure in the reporting period
- Relevant differences between EU-SmPC and the summary of product characteristics in Switzerland.

The question and answer session from the floor left no question unanswered.

- **Dr Hans-Georg Lippmann**, Senior Clinical Reviewer, Risk Management unit at Swissmedic: **"Pharmacovigilance Planning ICH E2E / Risk Management Plans (RMP)"**

Similarly to the presentation by Dr Munz on the periodic benefit-risk evaluation reports, there was also a need for information on this topic as a result of the EU reforms and this had taken the form of a survey of the specified industry associations. The sole focus in this case was on the impact of the new EU modules on practical procedure in Switzerland, because unlike the PSUR/PBRER topic, the underlying ICH Guideline in this case is unchanged.

Following an introduction to terminology and abbreviations that are often misunderstood even by experts, Dr Lippmann explained the legal basis for this topic in Switzerland.

The main focus of the presentation was on a selection of the most important reforms in the EU GVP Module V on RMP, always with a comparison to the practice in Switzerland.

The majority of the EU reforms have little or no impact on the established submission

practice. This applies in particular to applications which must always include an RMP in the documentation submitted. This requirement is closely related to ICH and not to the GVP that extends beyond this. The structure and format of the RMP in line with the EU will continue to be accepted and requested.

The key messages related to transparency and measures to minimise risk:

- Swissmedic considers the implementation of measures to minimise risk along the same lines as the EU (Risk Minimisation section in the EU RMP), with no major time delay or mitigation of the content, to be a fundamental and important Risk Management goal.
- The new legal requirement in the EU to publish an RMP summary is being taken as an opportunity to require this publication in Switzerland too. As far as possible, the content and form can and should correspond to the EU Public Summary RMP. This document should contain not only the known and possible risks and gaps in knowledge, but should also present the benefit briefly and precisely. However, practical implementation experience is also required in the EU.
- New and clearer instructions for industry will replace the current instructions on the Swissmedic website shortly.

This was then followed by a round table discussion which almost exclusively involved questions and answers relating to the understanding of the topic.

STATISTICAL REVIEW 2012

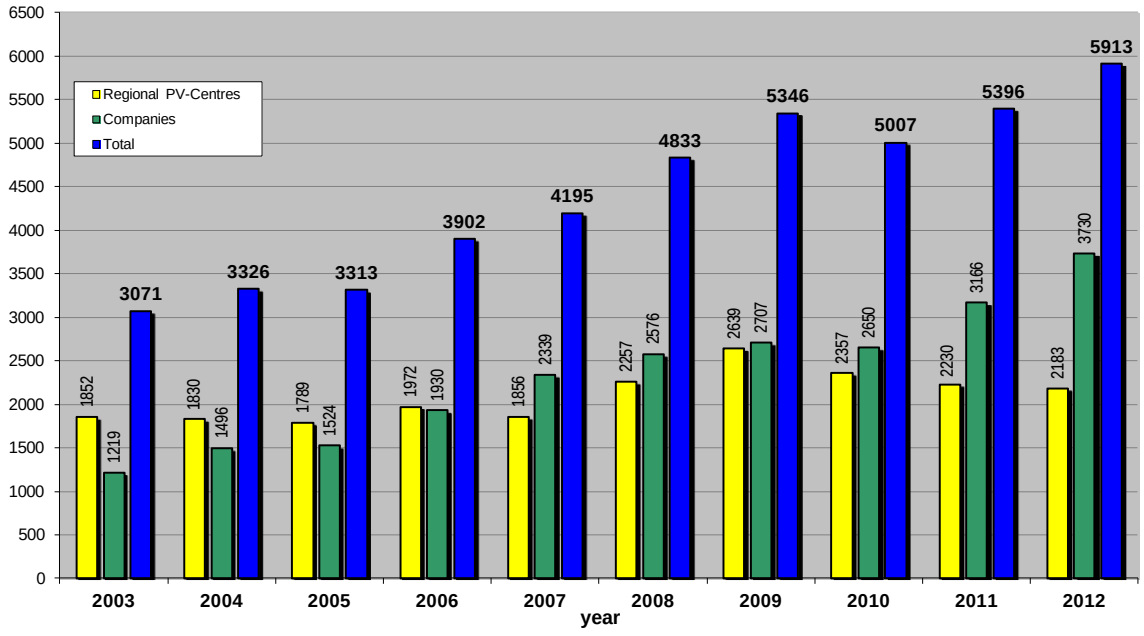
VIGILANCE OF HUMAN MEDICINES:

Within the framework of the pharmacovigilance network, reports on adverse drug reactions are evaluated and recorded in the national database, by six regional pharmacovigilance centres (RPVCs) on behalf of Swissmedic. The reporting health professionals receive appropriate feedback. Further reports on adverse drug reactions from within Switzerland are sent to Swissmedic by the pharmaceutical.

Activities

- In 2012, Swissmedic received and evaluated 5,913 reports of adverse drug reactions from the six RPVCs and from industry. Compared with the previous year, the reporting frequency increased by 10%, which is the result of a further increase in the number of reports sent by the pharmaceutical companies.
- Given the high reporting rate in Switzerland in international comparison, and its constant growth since the system has existed, emphasis was placed on the further improvement of the quality of the reports. The topic "What is a good report?" was the subject of a workshop at the specialised conference organised for the companies, was addressed at a meeting with the RPVCs, and an article on the topic for professionals was published in the Vigilance-News.
- The project for the electronic exchange of ADR reports between companies and Swissmedic (gateway) was successfully completed. Currently, five companies are using this reporting possibility. After encoding conversion from WHO-ART to MedDRA in the first quarter of 2014, further interested companies will be given access to the gateway.

Swissmedic Pharmacovigilance-Centre: Reporting Frequency



VACCINOVIGILANCE:

SUMMARY OF ADVERSE EVENTS FOLLOWING IMMUNISATION REPORTED IN SWITZERLAND

In 2012, 183 reports of adverse events following immunisation (AEFIs) were received by Swissmedic, representing an increase of 43 AEFIs (28%) as compared with previous year 2011. Despite this moderately increased number of reports, the rate of spontaneous AEFIs reporting remains very low, considering the high number (millions) of immunisations performed during the year.

Of these reports, 49 (26.8%) were assessed as non-serious, 93 (50.8%) were medically important events and 41 (22.4%) of the AEFIs included events with serious consequences like e.g. hospitalisation. The relative frequencies (percentages) of serious and medically important reports were very similar to those recorded during previous year 2011.

A single AEFI case with fatal outcome was received, namely a literature report as published in 2012[1]. This case occurring during 2009 concerns a 40-year-old male patient with acute myelocytic leukaemia, who developed multiple viral infections following allogeneic hematopoietic stem cell transplantation. He had been vaccinated with seasonal/pandemic influenza vaccine. However, the severe pre-existing (background) immunosuppression of the patient and the emergence of therapy-resistant viral strains during hospitalisation provide more probable alternative explanations for the reported adverse events and fatal outcome of this case.

As previously, Swissmedic continues to actively encourage good quality in spontaneous reporting of AEFIs. Since 2010, important topics with regard to AEFIs are evaluated in Swissmedic with the participation of the Human Medicines Expert Committee.

Please find the complete report on the Swissmedic website:
http://www.swissmedic.ch/marktueberwachung/00091/01962/02431/index.html?lang=en

Reference

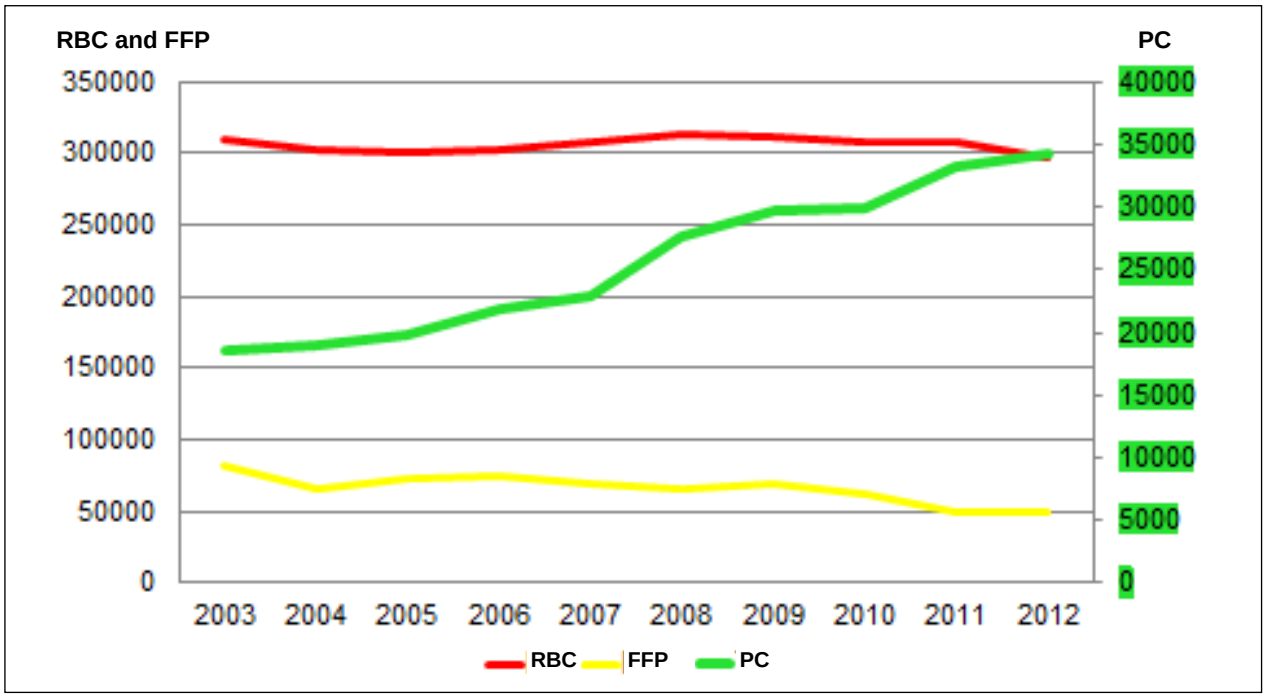
1. *Mohty B, Thomas Y, Vukicevic M, Nagy M, Levrat E, Bernimoulin M, Kaiser L, Roosnek E, Passweg J, Chalandon Y, Clinical features and outcome of 2009-influenza A (H1N1) after allogeneic hematopoietic SCT, Bone Marrow Transplant. 2012 Feb;47(2):236-42*

HAEMOVIGILANCE: TRANSFUSION SAFETY IN SWITZERLAND

In Switzerland, the annual demand for red blood cell concentrates (RBC) and plasma for transfusion (FFP) has decreased slightly over the last 5 years. In 2012, approximately 300,000 units of RBC and 50,000 units of plasma were transfused.

The number of platelet concentrates (PC) transfused per year has increased by around 10% per year on average.

Fig. 1: Use of blood products in Switzerland



All haemovigilance reports recorded within the framework of the mandatory spontaneous reporting system concerning suspected adverse transfusion events are systematically evaluated by Swissmedic. The data produced from them demonstrates the current status of transfusion safety and the type and magnitude of the risks.

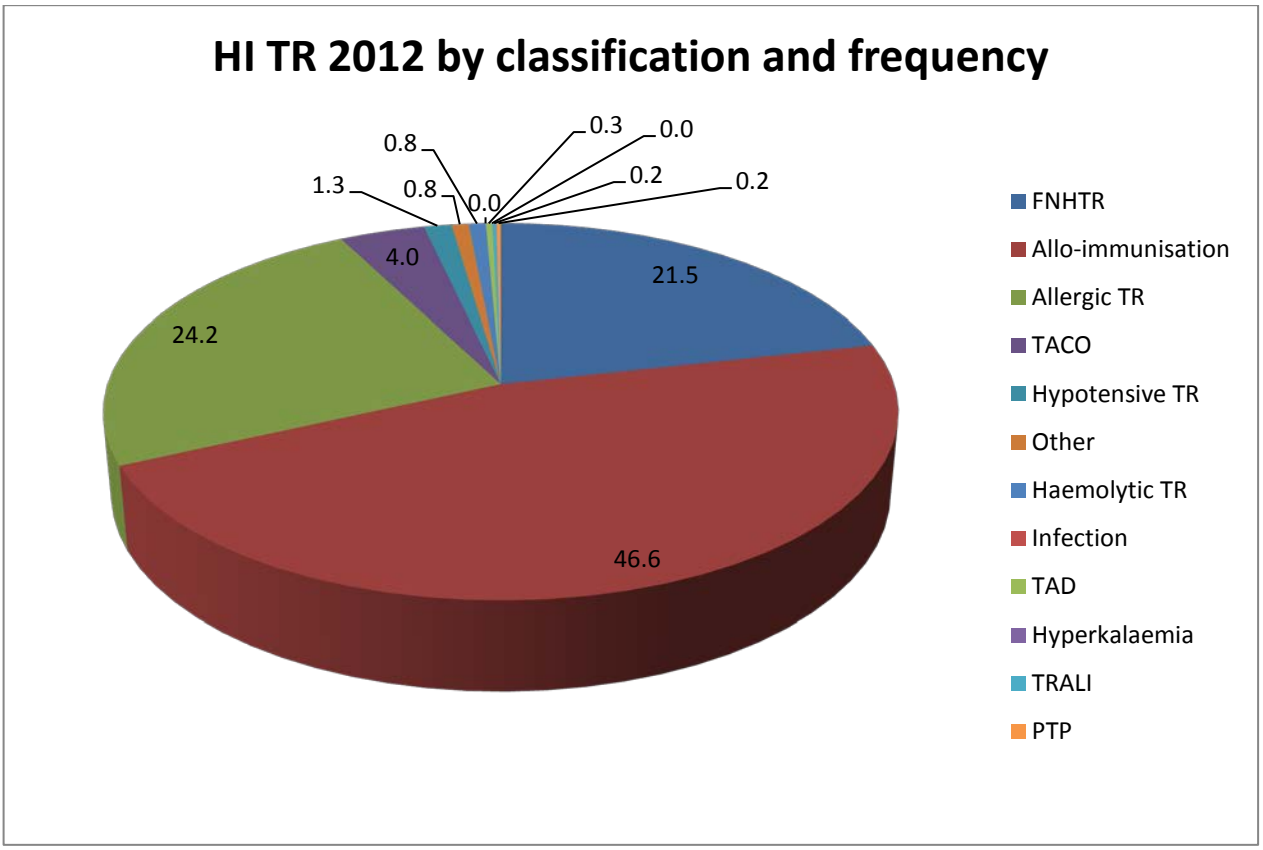
The reporting rate (number of haemovigilance reports per 1,000 units of blood components delivered) has increased continuously. At present, at a level of 4.4, this is in the upper range when compared internationally (in 2011, the levels were 3.9 for Switzerland, 2.8 for France and 3.9 for the Netherlands). The rate indicates a high level of willingness to report, and that relevant events are reliably identified within daily clinical work.

The number of near miss events and transfusion errors reported has increased in comparison with the previous year, while the number of re-

ports on suspected transfusion reactions (TRs) received has remained virtually stable.

Only those TRs with high imputability (i.e. cases in which the transfusion was certainly or probably the cause of the clinical incident observed) are taken into account in order to quantify the transfusion risks. This concerned approx. 60% of the reports in 2012. Among these TRs, those occurring most frequently were – as in the past – febrile non-haemolytic transfusion reactions (FNHTR), allo-immunisations and allergic transfusion reactions. Together, these account for approx. 90% of the TRs reported. In fourth and fifth place regarding frequency are reports on transfusion-associated circulatory overload (TACO) and hypotensive transfusion reactions (see Fig. 2).

Fig. 2

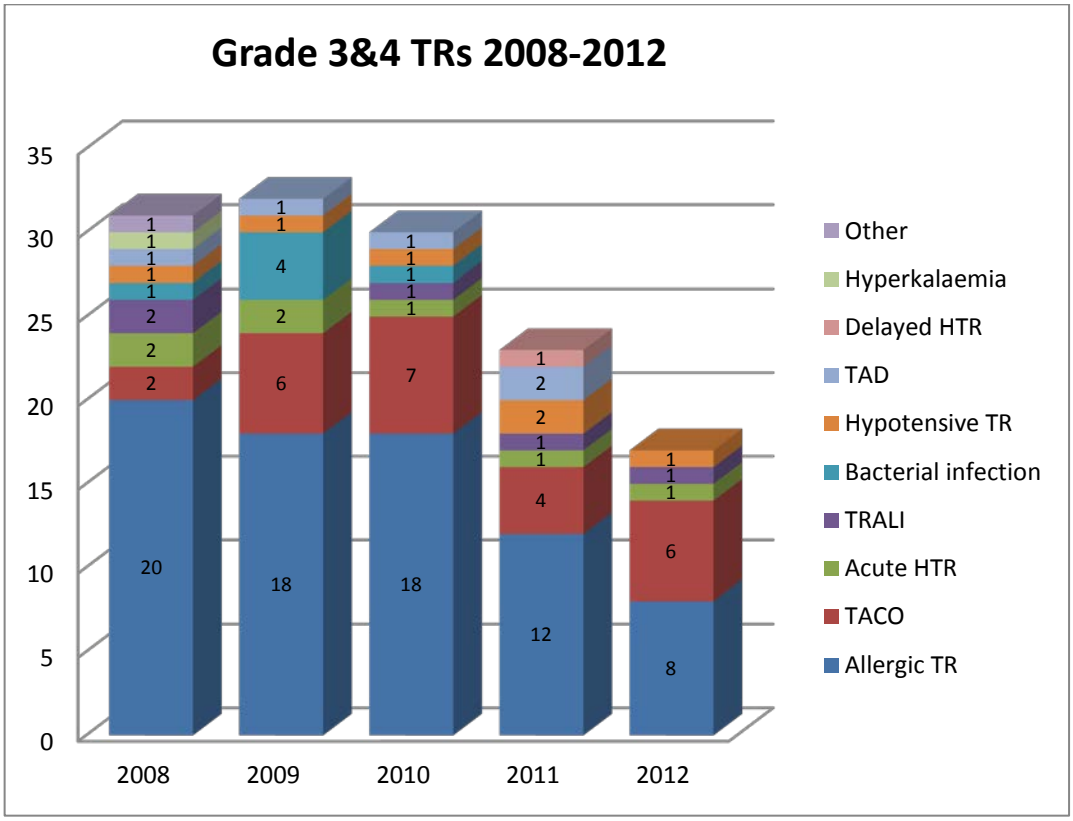


The analysis of the degree of severity shows that in 2012, 47% of the TRs were non-severe (i.e. Grade 1), and a further 50% were severe or have caused permanent damage (Grade 2). Most of them were allo-immunisations, which restrict the choice of compatible blood components for future transfusions. Life-threatening (Grade 3) or fatal (Grade 4) transfusion reactions represented around 3% of the cases. Here, the development over recent years has been a reduction in the number of cases. Most of them concerned allergic transfusion reactions and transfusion-associated circulatory overload.

Since the introduction of the Intercept procedure for pathogen inactivation of all platelet concentrates in 2011, as expected, no more cases of transfusion reactions from bacterially contaminated platelet concentrates were observed. The number of severe allergic transfusion reactions has also decreased: probably as a result of the process-related use of an additive solution for suspending the platelets instead of plasma, which was widely used in the past. For that reason, the exposure to plasma proteins, which are often assumed to trigger allergic reactions, was lower.

For transfusion-associated circulatory overload (TACO), the absolute figures change but it is still the second most frequent category reported among Grade 3 or 4 TRs (see **Fig. 3**).

Fig. 3



Not all transfusion reactions can be avoided with the medical and technical possibilities available today (e.g. FNHTR, allergic TRs).

The quantification of transfusion risks, taking into account the medical and techical possibilities available today, is particularly important because it reveals those measures that can be used to achieve the greatest increase in transfusion safety.

The risks for product-specific events are today relatively low thanks to various measures for obtaining and manufacturing blood components. These include more sensitive tests for viral infection that are carried out on every donation, the introduction of pathogen inactivation of all platelet concentrates to reduce transfusion transmitted bacterial and viral infections, and manufacturing plasma for transfusions from donations only with a considerably reduced risk of containing HLA-specific antibodies (in order to avoid cases of transfusion-associated acute lung injury (TRALI) as a result of the antibodies contained in this product). The mentionned product-related risks are one or several orders of magnitude lower than the administration-related risks for TACO and of incorrect blood component transfused (IBCT) or transfusion errors (see **Table 1**).

Table 1: Risk of transfusion errors that are in principle avoidable

TACO	**1:16,000 transfusions**[1)]
IBCT **Transfusion errors as such**	**1:7,000 transfusions**[1)] **1:27,000 transfusions**[1)]
Haemolytic TRs	**1:95,000 transfusions**[1)]
TRALI	**1:140,000 (2002-2007)**[2)] **1:330,000 (2008-2012)**[3)]
Bacterial infection	**1:800,000**[4)]
HBV	**1:600,000 donations**[5)]
HIV	**1:4,000,000 donations**[5)]
HCV	**1:10,000,000 donations**[5)]
TaGvHD	**~ 1:4,000,000** (1 case 2002 – 2012)

1) Swiss haemovigilance data for 2012
2) Swiss haemovigilance data for 2002 – 2007
3) Swiss haemovigilance data for 2008 – 2012
4) Swiss haemovigilance data for 2011 – 2012
5) Blood transfusion service Bern, advanced training course 29.11.2011

Further publications and presentations on haemovigilance in Switzerland are available at: http://www.swissmedic.ch/marktueberwachung/00159/00160/00435/index.html?lang=en

VIGILANCE OF VETERINARY MEDICINES

OVERVIEW

Note: This contribution is a shortened version of the annual report that is published on the Swissmedic website (in German only). (Market surveillance > Veterinary medicines > Reporting undesirable side-effects (TAM vigilance) > Publications).

In comparison to 2011 (167 reports), the number of adverse reactions in 2012 increased to 197, i.e. by 18%. Similarly to previous years, approximately half of all the reports were submitted by distributors or manufacturers (52.8%, 104 reports). In many cases, practising veterinarians report the reactions observed to the relevant distributors, who then forward the report to Swissmedic because of the legal obligation to do so. Nevertheless, 35 reports were submitted directly (17.8%). In addition, 45 reports (22.8%) came from consultations with the Swiss Toxicological Information Centre (STIZ) in Zurich. The remaining reports were contributed either by animal owners (7 reports, 3.5%) or other administrative entities (6 reports, 3%).

Breakdown by animal species and categories of medicines

Table 1 shows the reports submitted, broken down according to type of animal. The largest number concerned reactions following the administration of veterinary medicines to dogs (94, or 47.7%) and cats (53 or 26.9%). For livestock, and with 29 reports, bulls, cows and calves constitute the largest group. For all other types of animal, with the exception of horses (8) and sheep (6 reports), fewer than five reports were submitted for the entire year.

The breakdown by categories of medicines, sorted by ATCvet Code, is shown in **Table 2**. This also shows that over the years, the distribution is stable with the largest number of reports concerning antiparasitics (74, 37.6%), followed by antiinfectives (31, 15.7%) and non-steroidal anti-inflammatory drugs (ATC vet Code QM, 23, 11.7%). These three classes also belong to the most widely used veterinary medicines, both for domestic animals and livestock. In 2012, this was followed by reconverted medicines (i.e. used for a different indication or on a different species of animal), with 18 reports, 9.1%. For the latter medicines, some reports concerned the use on cats of products intended for dogs.

Causality assessment

In 23.9% of the reports, it was possible to confirm a causal link between the application and the reaction ("probable"), and for 21.8%, at least one alternative cause existed ("possible"). For most of the reports (91), too little information was available (46.2%) and for the remaining 16 reports (8.1%), a link could be conclusively excluded.

Paradox reaction under acepromazine

This case was reported to us by a Cantonal Veterinary Office. A 9-months-old male Rottweiler weighing 36 kg, was given an intramuscular injection of butorphanol and 0.08 mg/kg of acepromazine at 8 a.m. as premedication prior to castration. The surgery followed under full anaesthesia with isofluran, after induction with ketamine and diazepam. At 9.15 a.m. the dog awoke slowly, and left the practice at 1.30 p.m. able to walk but still sedated. At 6 p.m., the owner enquired, by phone, whether it was normal that the dog still seemed "sedated" and was told that the effects of acepromazine could last until the following morning, and that the dog should be monitored. One hour later, when a child attempted to remove an apple from its mouth, the dog bared its teeth and then bit the child in the foot several times, exposing the Achilles tendon. The question of causal relation to the products used was therefore raised. Acepromazine is the strongest neuroleptic from the phenothiazines group[1], and in addition to premedication before surgery it is also used for se-

[1] *Löscher W.: Pharmaka mit Wirkung auf das Zentralnervensystem. In: Pharmakotherapie bei Haus- und Nutztieren. Hrsg. W. Löscher, F. R. Ungemach und R. Kroker, Enke Verlag, Stuttgart, 2010, 64-133*

dation prior to examinations or to calm unruly animals[2]. Among the adverse reactions to the active pharmaceutical ingredient are the inhibition of pressoric circulatory regulation, and parasympatholytic effects, as well as photosensitisation and hypothermia. For excited dogs, the danger of paradox reactions also exists[1]. Such cases are described in literature: in one case, a German shepherd under the influence of acepromazine attacked another dog that it grew up with and with which it had lived together peacefully for years[3]. Another case described a 3-year-old terrier that attacked the veterinarian around 15 minutes after the injection of 1.1 mg/kg acepromazine, causing serious injury to the hands[4]. The same veterinarian had already experienced aggression from a Chihuahua around 15 minutes after an intramuscular injection. Neither of the two dogs had ever demonstrated that type of behaviour in the past. Meyer also mentions two additional cases that were reported to the FDA in 1993. A Shar-pei became aggressive 30 minutes after an intramuscular injection of 0.1 mg/kg and a Chow-chow, weighing 36 kg, bit a babysitter 8 hours after the last oral administration of 50 mg acepromazine[3]. In the presently described case, several active pharmaceutical ingredients affecting the central nervous system were administered. The dose of butrophanol was in the lower range, and only nervousness but not aggression are mentioned as adverse reactions in the scientific literature[5]. Because of its short serum half-life of 2.5 to 3.2 hours in dogs, diazepam cannot reasonably be taken into consideration[6]. For that reason, only ketamine would be considered as a theoretical alternative to acepromazine. Although the half-life after intravenous administration also appears to be too short (94+/-36 minutes under isofluran anaesthesia, with considerable individual variations[7]), cases of behavioural changes are mentioned. On the forum of the American College of Veterinary Anesthesists[8], a veterinarian from Missouri State University mentions that the US army no longer uses ketamine for total intravenous anaesthesia of military dogs, because it apparently causes behavioural changes potentially lasting several weeks. Such changes were also apparently identified in hunting dogs. Such adverse reactions are not mentioned in reference works. The safety profile of ketamine does, however, indicate mainly cardiovascular effects, hypersalivation and symptoms of agitation or even convulsions. Based on the existing reports in the literature, plus the plausible kinetics (the duration of the effect of acepromazine following an intramuscular injection of 0.15 mg/kg is around 24 hours[9]), the causality between the use of acepromazine and the aggression was assessed as possible. The safety measures - such as keeping the sedated dog away from children - were nevertheless insufficient, and the fact that the male Rottweiler did not seem fully socialised no doubt played an additional role.

Stevens-Johnson syndrome after the administration of a selective COX-2-inhibitor

A 14-year old female crossbreed (border collie x golden retriever) weighing 13 kg was given two 30 mg doses, at a two-week interval in line with the product information, of the specific COX-2 inhibitor Macavoxib in order to treat an elbow dysplasia[2]. One week after the final dose, the dog was brought to the practice with gingivitis and enlarged mandibular lymph nodes, and was treated with amoxicillin / clavanulic acid and prednisone. Five days later, after a short-lived

[2] *Tierarzneimittelkompendium der Schweiz, Hrsg. D. Demuth und C. R. Müntener, Institut für Veterinärpharmakologie der Universität Zürich, 2013*

[3] *Meyer, E.K.: Rare, idiosyncratic reaction to acepromazine in dogs. J. Am. Vet. Med. Assoc., 210: 1114-1115, 1997*

[4] *Waechter RA. Unusual reaction to acepromazine maleate in the dog. J. Am. Vet. Med. Assoc. 180: 73–74, 1982*

[5] *Plumb D.C.: Butorphanol tartrate. In: Plumb's Veterinary Drug Handbook, Sixth Edition. Hrsg. D. C. Plumb, Blackwell Publishing, Iowa, USA, 2008, 156 – 160*

[6] *Plumb D.C.: Diazepam. In: Plumb's Veterinary Drug Handbook, Sixth Edition. Hrsg. D. C. Plumb, Blackwell Publishing, Iowa, USA, 2008, 368 – 372*

[7] *Pypendop BH & Ilkiw JE: Pharmacokinetics of ketamine and its metabolite, norketamine, after intravenous administration of a bolus of ketamine to isoflurane-anesthetized dogs. Am J Vet Res 66: 2034-2038, 2005*

[8] *Last access to www.acva.org, on 29 August 2012*

[9] *Ungemach, F.R.: Magen-Darm-wirksame Pharmaka. In: Pharmakotherapie bei Haus- und Nutztieren. Hrsg. W. Löscher, F. R. Ungemach and R. Kroker, Enke Verlag, Stuttgart, 2010, 217-243*

improvement, the dog developed the following symptoms: ulcerated lesions on all mucocutaneous junctions (lips, ears, vulva, anus) and the cuticle on all paws became completely detached two days later. The dog was treated with antibiotics, immunoglobulins, corticosteroids and analgesics, and by the time the report was received, the lesions were healing. A biopsy was carried out on the lesions, and Stevens-Johnson syndrome (SJS) was diagnosed based on the results. This syndrome has already been reported in recent years: it was confirmed in one cat [10] and suspected in two other cats[11]. In the first case, the suspected cause was amoxicillin, and in the other, the cause could not be identified conclusively because of a lack of references in literature. Mavacoxib is closely related to celecoxib[12], but thanks to structural modifications, it has a considerably lower clearance and a correspondingly extremely long elimination half-life, of 39 days on average[2]. It is a specific COX-2 inhibitor: measured on the IC80 dose, the active pharmaceutical ingredient is around 38 times more specific for COX-2 than for COX-1[13]. It is used to treat pain and inflammation in connection with degenerative diseases in dogs[2]. The adverse reactions described are primarily related to the gastrointestinal tract (vomiting, diarrhoea, ulcers) and more rarely to the kidneys. To date, SJS has not been described as an adverse reaction of mavacoxib. The syndrome has, however, been linked to other selective COX-2 inhibitors for human use on several occasions[14] and in 2005, medical products containing valdecoxib were withdrawn from the market because of severe skin reactions, including SJS[15]. On the basis of the plausible time correlation, the histological examination and the published reports for related active pharmaceutical ingredients, the causality was classified as "possible". It was not possible to exclude the possibility of another active pharmaceutical ingredient (e.g. amoxicillin) causing the reaction.

Adverse reactions to veterinary vaccines

In addition to the reports regarding veterinary medicines authorised by Swissmedic, the Swiss Institute for Virology and Immunoprophylaxis (IVI) in Mittelhäusern – as supervisory authority for veterinary vaccines – submitted 96 reports.

[10] Müntener CR, Bruckner L, Gassner B, Stürer A, Demuth DC, Althaus FR, Zwahlen R.: Gemeldete unerwünschte Wirkungen von Tierarzneimitteln im Jahr 2006. Schweiz. Arch. Tierheilk., 149: 439–448, 2007

[11] Müntener CR, Bruckner L, Stürer A, Althaus FR, Caduff-Janosa P.: Vigilance der Tierarzneimittel: Gemeldete unerwünschte Wirkungen im Jahr 2008. Schweiz. Arch. Tierheilk. 151: 583–590, 2009

[12] Cox SR et al.: The pharmacokinetics of mavacoxib, a long-acting COX-2 inhibitor, in young adult laboratory dogs. J Vet Pharmacol Ther 33: 461-470, 2010

[13] Lees P et al: Pharmacokinetics and pharmacodynamics of mavacoxib in the dog. J Vet Pharmacol Ther 32 Suppl 1: 105-106, 2009

[14] Layton D et al.: Serious skin reactions and selective COX-2 inhibitors: a case series from prescription-event monitoring in England. Drug saf. 29: 687–696, 2006

[15] See, for example, FDA: Information for healthcare professionals: Valdecoxib (marketed as Bextra), 7 April 2005. See www.fda.gov

Table 1: Reports received in 2012, by animal species

Animal species	Number	% Total
Dog	94	47.7 %
Cat	53	26.9 %
Horse / donkey	8	4.1 %
Cow / calf	29	14.7 %
Pig	2	1 %
Sheep / goat	8	4.1 %
Pets / zoo animals	2	1 %
Human	1	0.5 %
Total	**197**	**100 %**

Table 2: Reports received in 2012, sorted by ATCvet Code

The QZ code is fictitious but allows the specific grouping of reports to reconverted products (i.e. not used for the authorised animal species and / or indication).

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Category of medicines according to ATCvet code	Number of reports (% of total)	
QA: Alimentary tract	6	(3 %)
QB: Blood and blood forming organs	1	(0.5 %)
QD: Dermatologicals	2	(1.2 %)
QG: Genito-urinary system and sex. hormones	5	(2.5 %)
QH: Hormonal preparations (except hormones and insulin derivatives)	15	(7.6 %)
QJ: Anti-infectives	31	(15.7 %)
QL: Antineoplastic and immunomodulating agents	1	(0.5 %)
QM: Musculo-skeletal system	23	(11.7 %)
QN: Nervous system	16	(8.1 %)
QP: Antiparasitics	74	(37.6 %)
QR: Respiratory system	1	(0.5 %)
QS: Sensory organs	1	(0.5 %)
QZ: Reconverted products	18	(9.1 %)
ALP: Registered products, animal care products, etc.	3	(1.5 %)
Total	**197**	**(100 %)**

INFORMATION ON THE SAFETY OF MEDICINES – PUBLISHED ON THE SWISSMEDIC WEBSITE

Weiterer Schritt im Kampf gegen Designerdrogen
10.12.2013 *

Batch recall: FRAGMIN Inj Lös 5000 E /0.2 ml
06.12.2013 *

Batch recalls: Sintrom, Tabletten
06.12.2013 *

DHPC – Wichtige Information bezüglich möglicher Fehler bei der Zubereitung von Jevtana ® (cabazitaxel)
06.12.2013 *

DHPC – Efient® (Prasugrel): Erhöhtes Risiko für Blutungen in NSTEMI Patienten, die eine perkutane Koronarintervention (PCI) erhalten, wenn EFIENT vor der diagnostischen Koronarangiographie verabreicht wird
04.12.2013 *

DHPC – Arzerra® (Ofatumumab): Aktualisierung des Warnhinweises zur Hepatitis-B-Virus-Reaktivierung - Voruntersuchung auf Hepatitis B bei allen Patienten vor der Behandlung
29.11.2013 *

DHPC – Zofran® (Ondansetron): neue Dosierungsempfehlungen für die wiederholte Verabreichung und die Anwendung bei älteren Patienten - Serotoninsyndrom und toxisch epidermale Nekrolyse
19.11.2013 *

Chargenrückruf / Wichtige Informationen: Jext 150/300 Mikrogramm, Injektionslösung in einem Fertigpen
14.11.2013 *

DHPC - Neupogen® (Filgrastim) und Neulasta® (Pegfilgrastim) sind mit dem Risiko von Kapillarlecksyndrom (Capillary leak syndrome, CLS) bei Krebspatienten und gesunden Spendern assoziiert
13.11.2013 *

DHPC – MabThera® (Rituximab): Voruntersuchung auf Hepatitis B bei allen Patienten vor der Behandlung
12.11.2013 *

Preliminary project on the revision of the Swiss Medical Devices Ordinance (MepV)
30.10.2013

Botulinumtoxin vom Typ A: Zugelassene Arzneimittel und Indikationen, korrekte Anwendung, Risiken und Vorsichtsmassnahmen
30.10.2013 *

DHPC – Erivedge® (Vismodegib): Verlängerung der empfohlenen Dauer der Kontrazeption von 7 Monaten auf 24 Monate nach Ende der Behandlung mit Erivedge bei gebärfähigen Frauen
28.10.2013 *

Chargenrückruf von NovoMix® 30 in 13 Europäischen Ländern (inhomogene Abfüllung / Gefahr einer Über- oder Unterdosierung) Schweiz vom Chargenrückruf nicht betroffen
25.10.2013 *

Press Release - Counterfeit drugs with no active ingredients
18.10.2013

DHPC – Numeta Ped G16%E, Infusionslösung zur totalen parenteralen Ernährung - Mögliches Risiko für das Auftreten einer Hypermagnesiämie
15.10.2013 *

Abolition of the authorisation status "Generics" – information regarding changes to current practice
01.10.2013

Antibiotics in veterinary medicine: increasing resistance despite declining sales
26.09.2013

Dangerous erectile stimulants obtained via the Internet
06.09.2013

Supplement 11.1 zur Pharmacopoea Helvetica 11 in Kraft
04.09.2013 *

Thromboembolierisiko unter hormonalen Verhütungsmitteln – Neue Unterlagen der Schweizerischen Gesellschaft für Gynäkologie und Geburtshilfe (SGGG) zur Unterstützung der medizinischen Beratung und Verschreibung
(23.08.2013) *

Drug regulators from the Heads of Agencies Consortium meet in Canberra May 20-22, 2013 to advance worksharing efforts in the review of generic drugs
(18.07.2013)

International Conference on Harmonisation (ICH) Meeting in La Hulpe, Belgium
(02.07.2013)

Illegally imported medicinal products: effects seen as a result of Swissmedic's measures
(16.05.2013)

Handhabung von Firmenmeldungen von nicht schwerwiegenden unerwünschten Arzneimittelmeldungen (UAW)
(01.03.2013) *

MEDIENMITTEILUNG: Swissmedic zur aktuellen Diskussion über hormonale Verhütungsmittel
(01.02.2013) *

Please find the complete list at the following web address:
http://www.swissmedic.ch/aktuell/00003/index.html?lang=en

* ***in German and/or French only***