swissmedic

Vigilance News

Edition 24 – May 2020

In this edition

- Guest article: valproate during pregnancy
- Asthma triggered by Aspirin?
- Nitro-resistant, triptan-induced acute coronary syndrome
- ICH E2D Guideline revision

Sign up for e-mails

Subscribe to Swissmedic's Vigilance News and register for the **newsletter on drug safety**!

You will be constantly kept up to date by e-mail with information from the fields of pharmacovigilance (Health Professional Communication) and market monitoring (batch recalls, out-of-stock announcements): www.swissmedic.ch/newsletter-en

Impressum

Editorial team
Martina Schäublin, Eva Eyal, Helena Bill

Authors
Patrick Beeler, Eva Eyal, Cedric Müntener, Thomas Schwartz, Valeriu Toma, Esther Wullimann

Guest authors
Sarah Banholzer, pharmacist and
Prof. Manuel Haschke, MD (RPVC Bern)

We would like to thank all colleagues for their contribution to producing this edition of Swissmedic Vigilance News.

Contact
Please send any suggestions or feedback on this issue of Swissmedic Vigilance News to news.vigilance@swissmedic.ch.

Report of an adverse drug reaction (ADR)

Swissmedic recommends using the reporting portal (direct-entry or XML file upload).

Online reporting portal ElViS

Contents

Editorial 3

Drug safety and signals 4

An interesting case: nitro-resistant, triptan-induced acute coronary syndrome 4

Asthma triggered by Aspirin? 5

Guest article / Case report on valproate during pregnancy – congenital malformations and developmental disabilities 7

Regulatory 11

ICH E2D Guideline revision launched by recently established new Expert Working Group 11

Swissmedic Medicines Expert Committees (SMEC) 13

Statistical Review 15

Vigilance for veterinary medicinal products 2018 15

Information on the Swissmedic website 16

Healthcare Professional Communication 16

In focus 17

Announcements 17

Editorial

Dear Reader

Back when we were planning this edition of Swissmedic Vigilance News, we had no idea that just a few weeks later the entire world would be turned upside down due to COVID-19. Despite, or precisely because of this, we decided to keep the same topics and publication date for this edition.

The current situation highlights the importance of interactions between patients, healthcare professionals and the authorities. The information obtained from spontaneous reports of adverse drug reactions (ADR) can be crucial for the assessment of a medicinal product. This may even be a single clinical *case report*, as illustrated by "nitro-resistant, triptan-induced acute coronary syndrome".

As serious ADR can sometimes only become apparent years after a drug has been authorised, the continuous reporting of ADR by both healthcare professionals and the pharmaceutical industry is extremely important. This is highlighted in the article "Case report on valproate during pregnancy – congenital malformations and developmental disabilities", which elucidates the current discussion regarding Depakine® from the point of view of a regional pharmacovigilance centre.

Some illnesses are only recognised after they have been triggered by ADR, such as the disease *aspirin-exacerbated respiratory disease (AERD).*

Legal regulations are needed in order to evaluate the large volume of safety data from various sources. We report on the work of the *ICH E2D(R1) Expert Working Group (EWG)* of the ICH *(International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use)* at an international level, as well as on the significance of the national *Swissmedic Medicines Expert Committees (SMEC).*

We hope our readers enjoy this edition and stay healthy.

Eva Eyal

Pharmacist / editor of Swissmedic Vigilance News
Safety of Medicines division, Swissmedic

Please send any suggestions or feedback on this issue of Swissmedic Vigilance News to:
news.vigilance@swissmedic.ch.

Drug safety and signals

An interesting case: nitro-resistant, triptan-induced acute coronary syndrome

A working group at Bern University Hospital had reported on a female 47-year-old patient who was hospitalised due to chest pain radiating out to the left shoulder. Examination revealed negative T-waves in leads V2-V4 and elevated troponin T. Pre-existing risk factors were hyperlipidaemia and smoking. Before onset of the chest pain, the patient had received 20 mg rizatriptan for the first time as treatment for a migraine attack.

When coronary angiography was performed, a lesion was identified in the left anterior descending artery after intracoronary administration of nitroglycerin. This persisted after renewed administration of nitroglycerin, thus leading to the suspected diagnosis of a ruptured plaque. However, an arteriosclerotic event was ruled out when optical coherence tomography (OCT) was subsequently performed. This revealed a non-obstructive fibrous plaque with coronary spasm. The treating physicians proceeded on the assumption of triptan-induced vasospastic angina non-responsive to nitroglycerin.

As the symptoms eased following administration of a calcium antagonist, the patient was discharged after 24 hours. Treatment was continued with acetylsalicylic acid, a statin and a calcium antagonist. The patient was also advised to stop smoking. She remained symptom-free on ceasing to use triptans and a stress test performed 6 months after the event was normal.

Conclusion

This case shows that triptans can trigger an acute coronary syndrome by way of coronary vasospasm in which the coronary spasm may be nitro-resistant. OCT can reveal the underlying pathophysiology of the acute coronary syndrome and avoid unnecessary stenting.

This literature report was submitted to us by a company that distributes rizatriptan in Switzerland. The information for healthcare professionals on rizatriptan-containing products states the following: "Rare: angina pectoris. One suspected case of coronary ischaemia was reported". However, the *Information for healthcare professionals* on other triptans, such as sumatriptan or zolmitriptan, explicitly mentions coronary vasospasm as well as myocardial infarction.

Like spontaneous reports, Swissmedic continuously assesses literature reports and reviews them in particular for their signal impact.

Literature

Otsuka T, Räber L, Acute coronary syndrome triggered by nitro-resistant triptan-induced coronary spasm, European Heart Journal 2019; 40(24): 1919

Thomas Schwartz, MD

Safety of Medicines division, Swissmedic

Asthma triggered by Aspirin?

Introduction

Samter's triad is characterised by nasal polyps, asthma, and sensitivity to aspirin and similar analgesics. Aspirin belongs to a class of drugs called cyclooxygenase 1 inhibitors (COX-1 inhibitors). In patients suffering from Samter's triad, also known as "aspirin-exacerbated respiratory disease" (AERD), COX-1 inhibitors typically trigger asthma-like symptoms including shortness of breath, wheezing, coughing, difficulty breathing, and chest tightness.

A review article on AERD recently published in the *New England Journal of Medicine (NEJM)* (1) lists highly selective COX-1 inhibitors that initiate such respiratory reactions in AERD patients: acetylsalicylic acid (i.e. Aspirin®), antipyrine-benzocaine, benoxaprofen, diclofenac, etodolac, fenoprofen, flurbiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, meclofenamate, metamizole (also known as dipyrone), mefenamic acid, naproxen, oxaprozin, piroxicam, and tolmetin.

Cahill et al. (2) developed a computer program that searched a high number of health records for the features nasal polyposis, asthma and COX-1 inhibitor sensitivity. If all three features were present in a patient, the authors suspected AERD. Upon detailed review of those patient charts, it was determined that the computer correctly identified AERD patients in about 80% of the cases. That percentage rose to nearly 90% if COX-1 inhibitor sensitivity involved respiratory reactions. Surprisingly, about 10% of the patients with AERD had no mention of that diagnosis in their charts and were unaware of their disease. Some of them had refrained from taking aspirin and other COX-1 inhibitors for years. Further, patients unaware of their disease received care from allergy or immunology specialists in less than 40%, as opposed to those with an AERD diagnosis, who had been seen by specialists in over 90% of the cases.

Methods and Results

"Aspirin-exacerbated respiratory disease" is a *preferred term* (PT) in the *Medical Dictionary for Regulatory Activities* (MedDRA). On February 28, 2020, we searched VigiBase, the WHO pharmacovigilance database, for reports featuring that PT and found 391 cases – the first was reported in 2007. The *lowest level terms* (LLT) related to those AERD cases were: "Aspirin asthma", "Analgesic asthma syndrome", "Samter's syndrome", "Aspirin-sensitive asthma", "Widal syndrome", "Asthma aspirin-sensitive". Besides AERD, concomitant reactions reported were "Asthma", "Eye disorder", "Nasal disorder", "Tympanic membrane perforation", "Drug hypersensitivity", "Middle ear effusion", "Dyspnoea", "Nasal congestion", "Rhinorrhoea", and "Wheezing". The most frequent drugs triggering asthma-like symptoms were acetylsalicylic acid, ibuprofen, naproxen, diclofenac, loxoprofen (which is not mentioned in the NEJM publication by White and Stevenson (1)), and metamizole. The age and sex distributions from the AERD reports are illustrated in Figs. 1 and 2, respectively. While AERD in children is very rare, a literature case report from Switzerland about a 9-year old patient (3) was entered into our own Swiss pharmacovigilance database and subsequently added to the records in VigiBase, the international pharmacovigilance database.

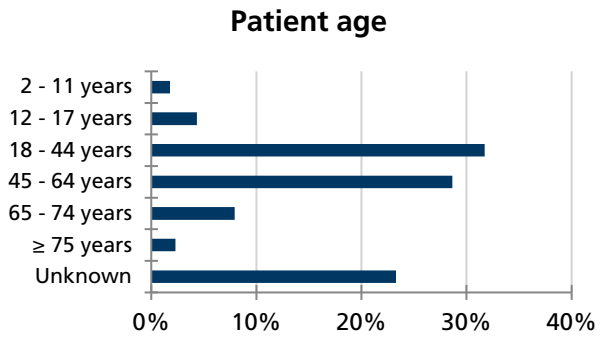

Figure 1. Age distribution of AERD reports in VigiBase.

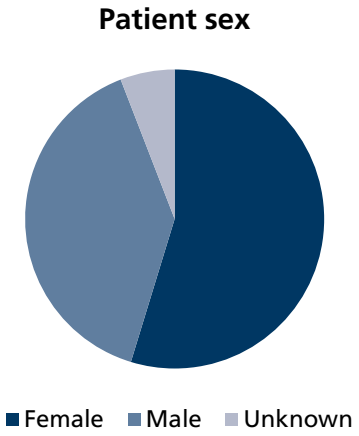

Figure 2. Sex distribution of AERD reports in VigiBase.

Discussion and Conclusion

In conclusion, some patients may not know that they have AERD when they are suffering from Samter's triad including nasal polyps, asthma and sensitivity to COX-1 inhibitors. COX-1 inhibitors frequently triggering asthma-like symptoms in AERD patients are acetylsalicylic acid, ibuprofen, naproxen, diclofenac, loxoprofen, and metamizole. In terms of pharmacovigilance, AERD is most likely underreported, particularly for COX-1 inhibitors other than aspirin, since the respective PT and several LLTs explicitly name "aspirin" as trigger. Fortunately, however, when AERD is recognised, patients may benefit from effective disease-specific therapy.

Literature

(1) White AA, Stevenson DD. Aspirin-Exacerbated Respiratory Disease. N Engl J Med. 2018 Sep 13; 379(11):1060-1070. doi: 10.1056/NEJMra1712125.

(2) Cahill KN, Johns CB, Cui J, Wickner P, Bates DW, Laidlaw TM, Beeler PE. Automated identification of an aspirin-exacerbated respiratory disease cohort. J Allergy Clin Immunol. 2017 Mar;139(3): 819-825.e6. doi: 10.1016/j.jaci.2016.05.048. Epub 2016 Jul 25.

(3) Geidel C, Stirner KH, Jung A, Lauener R. Analgesic Intolerance in a 9-Year-Old Patient. Respiration. 2011.

Patrick E. Beeler, MD

Safety of Medicines division, Swissmedic

Guest article

Case report on valproate during pregnancy – congenital malformations and developmental disabilities

Sarah Banholzer, pharmacist;
Prof. Manuel Haschke, MD

Regional Pharmacovigilance Centre Bern,
Clinical Pharmacology and Toxicology,
University Department of General Internal Medicine,
Inselspital Bern

Introduction

The report issued by the Federal Council in December 2019 (1) in response to the postulate "Depakine scandal – Analysis of the situation in Switzerland" written by Councillor of States Liliane Maury Pasquier triggered considerable interest among Swiss media at the start of 2020. This led to some additional reports from consumers and other non-health professionals about adverse drug reactions (ADR) in the form of congenital malformations and developmental disabilities resulting from the maternal administration of valproate during pregnancy. We use a case report to highlight the pharmacovigilance findings related to valproate in Switzerland.

Case Narrative

A young woman was treated for epilepsy with valproate (Depakine®) at the start of the 1990s and became pregnant for the first time after approximately three years. The treatment with valproate was continued throughout the pregnancy, and available records indicate retrospectively that the woman suffered three epileptic seizures during her pregnancy. Based on an ultrasound scan during the pregnancy, the unborn child was diagnosed with laparoschisis (gastroschisis). In view of an abnormal CTG and suspected volvulus, the child was delivered by caesarean section in the 37th week of pregnancy. The laparoschisis was treated surgically after birth. Shortly after birth, the neonate had a parenchymal intracranial haemorrhage on the left and subsequently experienced a tonic-clonic seizure. The neonate also suffered from repeated episodes of hypoxaemia, managed with oxygen administration. Examinations by the cardiologist, however, did not reveal any pathology. On reaching preschool age, the child was found to have impaired psychomotor and cognitive development and was therefore referred to a school for children with special educational needs.

After the birth of the first child, the mother started treatment with lamotrigine (Lamictal®) in addition to the valproate (Depakine®). At the end of the 1990s, she became pregnant again and remained seizure-free throughout the pregnancy while she was on valproate and lamotrigine. All ultrasound scans during the pregnancy were normal, and the second child was delivered by caesarean section in the 39th week of pregnancy. Due to the absence of spontaneous breathing, the neonate had to be ventilated with a mask for 60 minutes. A hypoglycaemia of 1 mmol/L was corrected with intravenous 10% glucose. Foetal valproate syndrome was suspected shortly after birth because the neonate showed several signs of dysmorphia (hypertelorism, broad nasal base, low-set ears, narrow lips, small mouth, long hands and feet, some overlapping toes). Since chromosomal analysis did not provide any evidence of a numerical or structural anomaly, a familial or genetic disorder seemed unlikely. Delayed psychomotor development was already observed in early childhood. A secundum atrial septal defect without pulmonary hypertension was diagnosed, and a connection with the valproate treatment during pregnancy was considered to be probable. In the further course, the child was found to have impaired cognitive development, impaired speech development, and an intermittent divergent squint

in the right eye. The second child also attended a school for children with special educational needs in order to support its individual development. Subsequent interventions were performed to close the atrial septal defect and correct dorsal scoliosis and hyperkyphosis of the thoracic spine and hyperlordosis of the lumbar spine. Mandibular prognathism was surgically corrected with a sagittal split osteotomy and a mandibular setback.

Although both children subsequently showed a largely stable status, they have suffered permanent harm/disabilities since birth.

Discussion

Depakine®, with the active ingredient valproate, has been authorised as a medicinal product in Switzerland in 1972 (2). Since the end of the 1970s, the Information for healthcare professionals for valproate-containing medicinal products has included a statement to the effect that the benefit of treatment in pregnant women and women of childbearing age should be carefully weighed against the risks to the child (1). SANZ, the Swiss Drug Monitoring Centre, was formed as a foundation in Switzerland in 1979, and began to collect and assess reports of suspected adverse drug reactions (ADR) (3). At the start of the 1980s, since evidence from animal studies increasingly indicated a risk of malformation (teratogenicity), a corresponding warning was included in the Information for healthcare professionals (1). Since the increased risk of malformations in humans was recognised at around the same time, the risk of neural tube defects (severe malformations of the brain and spine) was added to the Information for healthcare professionals in 1982, and in 1989 a reference to other possible malformations (1). In 1990, the Pharmacovigilance Centre of the Intercantonal Office for the Control of Medicines (IOCM) started work, and in 1991, Switzerland became a member of the "WHO Programme for International Drug Monitoring" (3). Since the Therapeutic Products Act entered into force in January 2002, the reporting of certain suspected ADR has been mandatory in Switzerland (1, 4). Evidence of developmental disabilities related to valproate slowly began to accumulate from 2000 (1). In 2006, corresponding warnings were added to the Information for healthcare professionals in Switzerland and internationally (1). It is now known that approximately 10% of children exposed to valproate in utero are born with malformations, while severe developmental disabilities occur in 30 to 40% of cases (1, 5). These rates are higher than in the general population, where malformations occur in approx. 2–4% of live births, while developmental disabilities or developmental delays are estimated to occur in 17% of children (6, 7). Between 6 and 15% of children aged 3–17 present developmental delays (mental disorders, autism spectrum disorder, etc.), depending on the specific disorders investigated (8–10).

Various measures were subsequently introduced to inform healthcare professionals and thereby increase patient safety (1).

At the time of the two pregnancies in the 1990s described in this report, the risk of malformations, but not the risk of developmental disabilities, related to valproate was known and mentioned in the Swiss Information for healthcare professionals for Depakine®. Data from the WHO pharmacovigilance database are presented in Table 1 (11). For the disorders listed in this table, more cases were reported than would be expected in the population (positive IC_{025} values).

During the second pregnancy, the mother had also taken lamotrigine in addition to the valproate. The Swiss Information for healthcare professionals for lamotrigine (Lamictal®) mentions that the available data do

not suggest a substantial increase in the risk of congenital malformations (5). It also mentions, however, that the combined administration (lamotrigine concomitant with other antiepileptic drugs) involves an increased risk of congenital malformations, but that the available data are insufficient to determine whether a malformation risk associated with other drugs is influenced by the concurrent administration of lamotrigine (5). In the prospective cohort study of the EURAP registry, the rate of congenital malformations reported for lamotrigine was 2.9%, i.e. no higher than in children whose mothers had not taken antiepileptic drugs (12).

Table 1: Data from the WHO pharmacovigilance database concerning valproic acid, de-duplicated dataset from 19.04.2020 (11)

Valproic acid	De-duplicated dataset 19.04.2020		until 31.12.2019	until 31.12.2009	until 31.12.1999	until 31.12.1989
Reaction (PT)	$N_{observed}$	IC_{025}	$N_{observed}$	$N_{observed}$	$N_{observed}$	$N_{observed}$
Exposure during pregnancy	827	1.8	810	146	0	0
Foetal exposure during pregnancy	1501	4.2	1413	3	0	0
Foetal anticonvulsant syndrome	619	7.7	600	117	20	0
Atrial septal defect	173	3.2	168	37	9	2
Prognathism	21	4.4	14	0	0	0
Gastroschisis	7	1.3	6	1	0	0
Psychomotor skills impaired	193	4.5	169	25	10	1
Cognitive disorder	583	2.6	548	66	0	0
Mental impairment	269	1.9	266	43	0	0
Total Individual Case Safety Reports (ICSR) related to valproic acid*	**75520**		**74022**	**28229**	**13055**	**3678**

$N_{observed}$: the total number of case reports for the active ingredient and reaction in question

IC_{025}: the lower endpoint of a 95% credibility interval for the Information Component (statistical disproportionality measure based on the observed and expected numbers of case reports). A positive value for IC_{025} is the traditional statistical basis for signal detection at Uppsala Monitoring Center.

***** Total number of individual case safety reports (ICSR) in the WHO pharmacovigilance database related to valproic acid (also concerning other reactions not mentioned here), at different points in time

Conclusion

This case report highlights the importance of pharmacovigilance in identifying ADR, particularly late complications of ADR. Especially the reporting of suspected cases with no confirmed causal link is critical to identify possible connections that were formerly unknown. At the time of both pregnancies in the presented case report, the obligation to report ADR was not yet enshrined in Swiss law. The mandatory reporting by healthcare professionals and the optional reporting by consumers and other non-health professionals are designed to increase drug safety by identifying new suspected ADR, implement signal investigations and any required measures. While the recognition of drug safety issues is imperative, the communication of such new findings is another important challenge not to be underestimated.

Reporting adverse reactions

For reporting adverse drug reactions (ADR), Swissmedic recommends the use of its own reporting portal specifically developed for this purpose (Electronic Vigilance System, ElViS). All necessary details can be found at www.swissmedic.ch.

Literature

(1) Bundesrat Schweizerische Eidgenossenschaft. Depakine-Skandal. Untersuchung der Situation in der Schweiz, Bericht des Bundesrates in Erfüllung des Postulates 18.3092, Ständerätin Maury Pasquier Liliane, 7. März 2018; 06.12.2019; Available from: https://www.newsd.admin.ch/newsd/message/attachments/59458.pdf.

(2) Swissmedic. List of authorised medicines. Available from: https://www.swissmedic.ch/swissmedic/en/home/services/listen_neu.html#319575900

(3) M, G., Die SANZ verabschiedet sich definitiv per Ende Mai 2001: Eine unglaubliche Geschichte. Schweizerische Ärztezeitung, 2001. **82**(22): p. 1135-1136.

(4) Egger, S.S., R.G. Schlienger, S. Krähenbühl. Vorgehen bei unerwünschten Arzneimittelwirkungen. in Swiss Medical Forum. 2005. EMH Media.

(5) Arzneimittelinformation-Publikationssystem (AIPS), (electronic version). Swissmedic, Bern, Switzerland. Available at: https://www.swissmedicinfo.ch.

(6) UpToDate® (electronic version). UpToDate Inc., Waltham, MA, USA. Available at: http://www.uptodate.com.

(7) National Center on Birth Defects and Developmental Disabilities (NCBDDD) Fiscal Year 2018 Annual Report. 2018; Available from: https://www.cdc.gov/ncbddd/aboutus/report/documents/ncbddd-fiscal-year-2018-annual-report.pdf.

(8) Boyle, C.A., et al., Trends in the prevalence of developmental disabilities in US children, 1997-2008. Pediatrics, 2011. **127**(6): p. 1034-42.

(9) Zablotsky, B., et al., Estimated Prevalence of Autism and Other Developmental Disabilities Following Questionnaire Changes in the 2014 National Health Interview Survey. Natl Health Stat Report, 2015(87): p. 1-20.

(10) Zablotsky, B., L.I. Black, and S.J. Blumberg, Estimated Prevalence of Children With Diagnosed Developmental Disabilities in the United States, 2014-2016. NCHS Data Brief, 2017(291): p. 1-8.

(11) VigiLyze. Uppsala Monitoring Center - WHO individual case safety report (ICSR) database system. Available from: https://vigilyze.who-umc.org/.

(12) Tomson, T., et al., Comparative risk of major congenital malformations with eight different antiepileptic drugs: a prospective cohort study of the EURAP registry. Lancet Neurol, 2018. **17**(6): p. 530-538.

Regulatory

ICH E2D Guideline revision launched by recently established new Expert Working Group

Introduction

The *International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH)* is bringing together the regulatory authorities and pharmaceutical industry to discuss scientific and technical aspects of drug registration. Since its foundation in 1990, ICH has gradually evolved to respond to the increasingly global face of drug development. ICH's overall mission is to achieve greater harmonisation worldwide and to ensure that safe, effective, and high quality medicines are developed and registered in the most resource-efficient manner.

Since its announcement of organisational changes in October 2015, ICH has grown as an organisation and now includes 16 Members and 32 Observers. As a *Standing Regulatory Member Swissmedic*, the Swiss Agency for Therapeutic Products, is constantly participating in the activity of most of the *ICH Expert Working Groups (EWG)*.

The ICH E2D Guideline

"E2D Post-Approval Safety Data Management: Definitions and Standards for Expedited Reporting" is a fundamental guideline for the handling of drug safety information. The ICH Harmonised Guideline was finalised under Step 4 in November 2003. This document provides a standardised procedure for post-approval safety data management and the guidance for gathering and reporting information, with consideration as to how the terms and definitions can be applied in the post-approval phase of the product life cycle.

Since the finalisation of the ICH E2D Guideline in 2003, new sources of post-approval safety information have emerged or are more frequently utilised (e.g. social media, market research programs, patient support and assistance programs) which vary in characteristics and contribution to the quality of post-approval safety information. The definitions and regulatory guidance in ICH E2D are no longer sufficient to provide guidance on the current practices and needs. Therefore, the definitions and standards for the management of post-approval safety information need to be revised in order to support appropriate safety surveillance and actions. Furthermore, in the current situation significant resources are being spent on handling increasing volumes of ICSRs *(Individual Case Safety Reports)* that are of variable value to post market safety surveillance. There is a need to establish principles on how to manage these more effectively to support patient safety.

The ICH E2D(R1) Expert Working Group

The E2D(R1) EWG is currently working on the revision of the E2D Guideline *"Post-Approval Safety Data Management: Definitions and Standards for Expedited Reporting"* with a view to clarifying the management of post-approval safety information from new or increasingly used data sources, including the need to adapt definitions and standards. The ICH Assembly endorsed this new topic in June 2019 and soon after that, in September 2019, the formation of an informal working group has been approved. Later on, during the ICH Meeting in Singapore in November 2019, the ICH Management Committee endorsed the Concept paper, the Business Plan and the new formal Expert Working Group (EWG) for Revision 1 of ICH E2D has been es-

tablished. The EWG is composed of 22 experts in total, 11 of which are representing regulatory agencies and 11 are representatives of the pharmaceutical industry.

The main deliverable of the EWG is the final revised ICH E2D(R1) Guideline. To achieve this goal, monthly meetings by teleconference and face-to-face meeting twice a year have already been scheduled. It is anticipated that it will take two years to reach step 2 of the revision process, including the ICH consensus and endorsement of the revised guideline. After 6 months' consultation it will take a further one year to complete step 4 with final adoption of the ICH Harmonised Guideline.

The overall beneficial impact of this revision is to provide pragmatic solutions that can be adopted globally to ensure consistent collection, review, analysis and reporting of safety information from various data sources to ensure global data can be leveraged to optimise patient safety. The revision project is intended to harmonise the way of reporting information from new or more frequently utilised sources of post-approval safety information, believing that harmonisation and implementation of this procedure are feasible. The aim is to implement ICH E2D(R1) under the current respective legislative framework with adaptations in local regulatory guidance where applicable.

Valeriu Toma, MD

Safety of Medicines division, Swissmedic

Swissmedic Medicines Expert Committees (SMEC)

Election for the 2021–2024 term of office

As part of the authorisation, market surveillance and approval of human and veterinary medicinal products, the Swissmedic Medicines Expert Committees (SMEC) perform an independent second review of the scientific documentation in authorisation applications – a valuable contribution to ensuring that effective, safe and high-quality medicinal products are available to Swiss doctors for their day-to-day activities.

Like all internationally leading drug regulatory authorities, the Swiss Agency for Therapeutic Products Swissmedic seeks the advice of external expert committees on scientific issues: the Human Medicines Expert Committee (HMEC) for human medicinal products and the Veterinary Medicines Expert Committee (VMEC) for veterinary medicinal products. Cooperation with external experts is an important element in ensuring the quality of the decisions that are taken. The European EMA draws on various Scientific Advisory Groups for this purpose, and the American drug regulatory authority FDA works closely with its Advisory Committees.

The Swissmedic Medicines Expert Committees (SMEC) are made up of ordinary, extraordinary and advisory members and are elected by the Swissmedic Agency Council for a four-year term of office. Their experts have documented professional qualifications and expertise in medicine, pharmacy or science and wide-ranging experience in the clinical environment.

Looking for experts from research and the practical setting

The 4-year term of office of the SMEC expires at the end of 2020 and the elections for the 2012–2024 period are due. Swissmedic would like to take this opportunity to further reinforce the expertise of the committees. In human medicine Swissmedic is particularly looking for experts in the following areas: oncology, pneumonology, gastroenterology, ophthalmology, gynaecology, urology, paediatrics, allergology, immunology/vaccinology, infectiology/virology, endocrinology and clinical pharmacology.

If you are interested in joining the committee, please do not hesitate to contact Ms Esther Wullimann, Responsible for the External Experts Committee.

A summary of the main points

- External expert committees support Swissmedic with academic and practical knowledge and in this way make an important contribution to providing Swiss doctors with effective, safe and high-quality medicinal products for their day-to-day activities.
- Between 2017 and 2019, the experts issued a total of 233 recommendations on the first authorisation of, and indication extensions for, medicinal products in Switzerland. In the area of human medicinal products there was a major emphasis on cytostatic agents.
- Swissmedic is looking for candidates as the date for the elections to the expert committees at the end of 2020 approaches. Interested individuals are invited to get in touch with Swissmedic.

Esther Wullimann, PhD

Responsible for the External Experts Committee, Regulatory Operations and Development Department, Swissmedic

General information about experts affiliated with Swissmedic

Swissmedic SMEC
Regulatory Operations and Development Department
Hallerstrasse 7
3012 Bern

Esther Wullimann

Scientific Staff and Responsible for
the External Experts Committee

✉ Esther Wullimann

Statistical Review

Vigilance for veterinary medicinal products: adverse reactions reported in 2018

Further increase in reports submitted

A total of 329 reports of adverse reactions to veterinary medicinal products were received during 2018, representing an increase of 7.5% compared to the previous year. The majority of these reports related to reactions concerning companion animals (205 dogs and 77 cats). The number of reports relating to cattle and to horses was 27 and 9 respectively.

As in previous years, most of the reported reactions were linked to the use of antiparasitics (174 reports), hormone products (32 reports) and anti-inflammatory products (22 reports).

33 reports were generated from consultations with Tox Info Suisse in Zurich. These mainly involved the excessive intake of flavoured tablets and, in some cases, the use of products under the cascade regulation (applied to a species other than that authorised). Seven signals were identified from the reports, resulting in revisions of the product information in the sections addressing contraindications or adverse reactions.

Owing to the spontaneous nature of the reporting system, the reasons for the increase cannot be established. A spontaneous reporting system is subject to numerous factors – new authorisations, for example, or raising of awareness due to reports in social or other media. Therefore, the number of reports can be expected to vary in line within the usual fluctuation band. Pharmacovigilance for veterinary therapeutic products remains an important tool for improving safety in use. Every report submitted can prove decisive for this.

Cedric R. Müntener, D.V.M.

Veterinary Medicines department, Swissmedic

Complete report 2018 (available in German):
Reports of adverse reactions to veterinary medicinal products 2018

Information on the Swissmedic website[1]

Healthcare Professional Communication

02.04.2020
DHPC – Esmya® (Ulipristalacetat)
Risiko für Leberschädigung

18.03.2020
DHPC – Esbriet® (Pirfenidon)
Medikamenteninduzierte Leberschädigung (Drug-induced liver injury, DILI)

28.02.2020
DHPC – Picato® (Ingenolmebutat)
Sistierung der Zulassung - Risiko von Hautkrebs bei Patienten mit aktinischer Keratose

21.01.2020
DHPC – Actemra® (Tocilizumab)
Beschränkung der Verwendung des Actemra® (Tocilizumab) Fertigpens auf Patienten mit sJIA/pJIA ab 12 Jahren aufgrund des möglichen Risikos einer intramuskulären Injektion bei Patienten unter 12 Jahren

16.01.2020
DHPC – Ecalta® (Anidulafungin), Pulver zur Herstellung einer Infusionslösung
Anpassung des Lagerungshinweises der Infusionslösung notwendig

05.12.2019
DHPC – Umfassende Überarbeitung der ganzen Fachinformation von Haldol®
Korrigendum / Klarstellung

[1] Most of the links are available in German/French only

In focus

01.05.2020
Coronavirus disease (COVID-19) Pandemic
Information on the new coronavirus (SARS-CoV-2)

Announcements

14.05.2020
Out-of-Stock – COVID-19 – Authorisations for the temporary import and distribution of human medicines – Update
Licences in accordance with art. 4m para. 3 of the COVID 19 Ordinance 2

13.05.2020
Swissmedic authorises a medicinal product under the Marketing Authorisation for Global Health Products (MAGHP) procedure for the first time
This approval in Switzerland paves the way for the approval and introduction in low- and middle-income countries

11.05.2020
Fettgewebe und Stromal Vascular Fraction zur autologen Transplantation
Rechtliche Klassifizierung

07.05.2020
Update on inspections in Switzerland during the COVID-19 pandemic
Swissmedic is adapting its therapeutic products sector inspections practice

07.05.2020
Swissmedic Journal
Latest edition
Swissmedic Journal April 2020

06.05.2020
Changes to the guidance document Authorisation of human medicinal products under Art. 13 TPA HMV4
ZL000_00_019e_WL

06.05.2020
Changes to the guidance document Authorisation of veterinary medicinal products under Art. 13 TPA HMV4
ZL000_00_018e_WL

05.05.2020
Australia, Canada, Singapore, Switzerland Consortium regulators pledge support to tackle COVID-19
The ACSS Consortium is building on its proven ability to benefit from work-sharing

04.05.2020
Guidance document Authorisation according to Art. 14 para. 1 abis-quater TPA HMV4 updated
ZL000_00_022e_WL

01.05.2020
New coronavirus: Swissmedic issues warning about non-conforming face masks
Potentially inferior-quality products are increasingly being offered in Switzerland too

01.05.2020
Gesetzliche Rahmenbedingungen zur COVID-19 Testung in der Schweiz
Bedingungen zur Durchführung von COVID-19 Tests in der Schweiz

01.05.2020
New coronavirus: Swissmedic issues warning about illegal medicinal products from the Internet and false claims of curative properties
Officially licensed and controlled distribution channels are the only guarantee of safe, flawless-quality medicines

01.05.2020
Placing on the market of important non-conforming medical devices for combating the COVID-19 pandemic
Exemptions for non-conforming medical devices

30.04.2020
MU500_00_014e_MB Coronavirus Covid 2019
Information regarding the responsibilities of placing protective masks, gloves, hand sanitisers and coronavirus tests on the market

29.04.2020
Swissmedic informs of the risk of serious adverse drug reactions from hydroxychloroquine and chloroquine
Both active substances are currently being used to treat COVID-19 patients in clinical trials.

23.04.2020
Pharmacovigilance: change in procedure for requesting follow-up information for individual case safety reports
This change applies to all authorisation holders and is initially for a limited period up to 30 June 2020.

22.04.2020
Empfehlung bezüglich COVID-19 für die autologe Blutstammzellspende
Beschluss Vorschriften SBSC – Blutstammzellspende

21.04.2020
Evaluation of potential nitrosamines in connection with new authorisations
The new requirements enter into force immediately

21.04.2020
Umfrage zu Monographien der Pharmacopoea Helvetica
Welche Monographien werden noch angewendet

20.04.2020
International medicinal product regulatory authorities hold online workshops to improve treatment options for coronavirus disease 2019 (COVID-19)
Experts discuss findings from data in workshop organised by the International Coalition of Medicines Regulatory Authorities (ICMRA)

15.04.2020
Swissmedic approves first COVID-19 therapy study with convalescent plasma
This form of therapy is also known as passive immunisation

14.04.2020
Antiparasitics for external use in dogs and cats as a possible risk to tits and other wild birds
Substances harmful to birds in brushed-out dog or cat hair

14.04.2020
Public Summary SwissPAR – Beovu® (brolucizumab)

09.04.2020
ICH Guideline Q12: Implementation in Switzerland
Swissmedic is adopting the temporary restrictions issued by the EMA as of 1.04.2020

08.04.2020
Implementation of the new medical devices regulations – update
COVID-19 pandemic: European Commission postponing introduction of the MDR by one year

06.04.2020
COVID-19: early market release by Responsible Persons (RPs)
Criteria for early market release by RPs

06.04.2020
COVID-19: Exceptions from import provisions for medicinal products
Notification requirement for importing medicinal products that are not authorised in Switzerland for the treatment of COVID-19 patients

03.04.2020
Federal Council introduces measures to counter shortages of essential medical supplies for combating the COVID-19 pandemic
Range of measures to improve the availability of essential medical supplies for preventing and combating the coronavirus disease (COVID-19)

03.04.2020
Potential nitrosamine contamination: request to perform a risk evaluation
COVID-19: Deadline extension

03.04.2020
Information about off-label use
Use of medicinal products for indications other than those authorised

01.04.2020
Update of eCTD specification documents
The published documents are valid as of 1 April 2020.

01.04.2020
Anpassung der Liste der Länder mit vergleichbarer Tierarzneimittelkontrolle
ZL000_00_012d_VZ

01.04.2020
Nachtrag 10.1 der Europäischen Pharmakopöe in Kraft
Der Institutsrat hat den Nachtrag 10.1 der Europäischen Pharmakopöe auf den 1. April 2020 in Kraft gesetzt.

01.04.2020
Changes to the guidance document Temporary authorisation of human medicinal products HMV4
ZL109_00_001e_WL

01.04.2020
Nonsteroidal anti-inflammatory medicines and coronavirus disease COVID-19
No reliable findings on the effect of ibuprofen, acetylsalicylic acid and other drugs – influence is being investigated

26.03.2020
Election of the Swissmedic Medicines Expert Committees (SMEC) for the 2021-2024 term of office
Independent experts as an additional quality-assurance element in the authorisation process

26.03.2020
Pandemic by SARS-CoV-2
The spread of the new coronavirus (SARS-CoV-2) also poses a major challenge for clinical trials of medicinal products in Switzerland.

25.03.2020
Empfehlungen bezüglich COVID-19 für die autologe und gerichtete Spende (Familienmitglied) von Blut-Stammzellen aus dem Nabelschnurblut
Beschluss Vorschriften SBSC – Cord Blood

24.03.2020
HPC – Swissmedic warnt vor dem gefälschten Tierarzneimittel Micotil 300mg/ml
In Schottland sind Fälschungen des Tierarzneimittels Micotil 300mg/ml Solution for Injection entdeckt worden.

19.03.2020
International Operation PANGEA week: Authorities confiscate 48,564 shipments of illegal pharmaceuticals worldwide
The number of medicinal products ordered online and illegally imported into Switzerland is declining.

19.03.2020
Public Summary SwissPAR – Ultomiris® (Ravulizumab)

14.03.2020
Swissmedic participates in FDA Project Orbis
Pilot project for parallel reviews for the authorisation of innovative cancer drugs

06.03.2020
Swissmedic and the Bill & Melinda Gates Foundation (BMGF) to continue their cooperation
Finance agreement signed for a further three years

05.03.2020
Illegal imports of medicinal products 2019: simplified procedure proves its worth
Number of confiscated shipments more than doubled

03.03.2020
Update – Warning about the slimmers' teas Esillaa and Alpiflor
Swissmedic is issuing an urgent warning regarding the slimming products Esillaa and Alpiflor Tea

25.02.2020
International cooperation on therapeutic products
Swissmedic authorises a new active substance (NAS) under the ACSS Consortium initiative for the first time

19.02.2020
Public Summary SwissPAR – Cablivi® (caplacizumab)

19.02.2020
Public Summary SwissPAR – Onpattro® (patisiran)

11.02.2020
Modification of various documents relating to authorisation - Veterinary medicines
ZL000_00_028e_WL / ZL000_00_043d_VL / ZL000_00_044d_VL

07.02.2020
Completion of the Public Review for eCTD M1 Specification v1.5

01.02.2020
Guidance document Authorisation according to Art. 14 para. 1 abis-quater TPA HMV4 updated
The new version of the guidance document enters into force on 1 February 2020.

24.01.2020
Warning regarding HAVYCO-Vy&Tea slimmers' tea
Swissmedic is issuing a warning regarding the slimming product

20.01.2020
Notes on using Swissmedic templates for Information for healthcare professionals and Patient information
There are two versions of Swissmedic's templates for Information for healthcare professionals and Patient information for human medicinal products

20.01.2020
Update of the form «PSUR/ PBRER for human medicines HMV4»
The «PSUR/ PBRER for human medicines HMV4» form has been updated.

15.01.2020
Change in the authorisation practice with regard to innovative human medicinal products for the prevention of communicable diseases
Application of Art. 13 TPA – streamlining of the review procedure for specific medicinal product categories on request

15.01.2020
Updating of guidance document on authorisation of human medicinal products under Art. 13 TPA HMV4
Changed procedure for "Justified cases" pursuant to Art. 18 para. 2 TPO

08.01.2020
Vigilance for veterinary medicinal products: adverse reactions reported in 2018
Further increase in reports submitted

01.01.2020
Neue Ausgabe der Europäischen Pharmakopöe in Kraft
Der Institutsrat hat die Ausgabe 10.0 der Europäischen Pharmakopöe auf den 1. Januar 2020 in Kraft gesetzt.

01.01.2020
New guidance document on Medicinal Product Names HMV4
ZL000_00_043e_WL

23.12.2019
Public Review of the new eCTD M1 Specification v1.5

19.12.2019
Adaptation of the strategic document SMEC Code
ZL003_00_001de_SD

18.12.2019
Swissmedic and the Korean regulatory authority extend their cooperation in the area of therapeutic products
Swissmedic and the Korean Ministry of Food and Drug Safety (MFDS) sign an agreement on Good Manufacturing Practice

17.12.2019
ICH Assembly in Singapore, November 2019
Expert meeting adopts new Guidelines on quality and medicinal product safety

06.12.2019
Trace amounts of a nitrosamine impurity found in individual diabetes medicines
Isolated traces of the nitrosamine NDMA have been detected in individual diabetes preparations with the active substance metformin – investigations are ongoing worldwide.

03.12.2019
13 new psychoactive substances added to Narcotics List
FDHA has prompted to add substances to the Narcotics List to combat drug trafficking

02.12.2019
Kontrolle von Nitrosamin-Verunreinigungen in Sartanen – Revision von fünf Monographien der Europäischen Pharmakopöe
Die Sartan-Monographien der Europäischen Pharmakopöe (Ph. Eur.) wurden revidiert. Neu gelten strenge vorübergehende Limiten für Nitrosamin-Verunreinigungen. Die revidierten Monographien treten am 1. Januar 2020 in Kraft.

01.12.2019
Modification of various documents relating to authorisation
ZL000_00_024e_WL / ZL101_00_007e_WL / ZL300_00_001e_WL

29.11.2019
Aufsichtsabgabe 2019 – Selbstdeklaration
Eingabefrist: 24. Januar 2020

29.11.2019
Laboratories (OMCL)
Swissmedic laboratory publishes another extended test method for nitrosamines in sartans

27.11.2019
Cancelled: Information event on the revised medical devices legislation for healthcare professionals and hospitals
Monday, 4 May 2020, Kursaal Bern

25.11.2019
Update to the safety notice: Securidrap from the company Mulliez-Flory
Warning against use

12.11.2019
Information from the european environment
The EU commission informed about the status of the implementation of Eudamed

06.11.2019
End of transition period for changeover to eCTD DTD v1.4

05.11.2019
Revised requirements regarding combination products

The complete list is available at the following web address www.swissmedic.ch/updates-en