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Vigilance News

Edition 26 – June 2021

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- Case report "COVID arm"
- AEFI after immunisation with COVID-19 vaccines: Herpes zoster, neuralgic amyotrophy, immune thrombocytopenia

Impressum

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

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Important information for pharmaceutical companies regarding electronic PV reporting:
From 1 July 2021 only electronic reports will be accepted.

Report of an adverse drug reaction (ADR)

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

Online reporting portal ElViS

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Editorial

Dear Reader

For this issue of Swissmedic Vigilance News, we have chosen vigilance with regard to COVID-19 vaccines as our focus topic.

As with the authorisation of medicinal products, it is necessary to verify the quality, efficacy and safety of vaccines, too. Based on the documentation available to Swissmedic, the following COVID-19 vaccines meet these requirements and have been authorised in Switzerland:

- Comirnaty® (tozinameran; marketing authorisation holder: Pfizer AG, Zurich)
- COVID-19 Vaccine Moderna (COVID-19-mRNA vaccine (nucleoside modified); marketing authorisation holder: Moderna Switzerland GmbH, Basel)
- COVID-19 Vaccine Janssen (COVID-19 vaccine (Ad26.COV2-S [recombinant]); marketing authorisation holder: Janssen-Cilag AG, Zug)

Any "adverse events following immunization" (AEFI) are recorded in the vigilance systems of the national authorities and are analysed so that appropriate risk-minimising measures can be swiftly taken.

Based on observations made during the controlled clinical trials, a number of non-serious and very frequent COVID-19 vaccine AEFI were already known at the time of authorisation. These include pain and swelling at the injection site, fatigue, shivering, fever, headache, and muscle and joint pain.

Since the vaccination campaigns were launched, a steady stream of valuable findings has been obtained regarding AEFI that were either previously unknown, occur only infrequently or are classified as severe; these are then discussed at both the national level and internationally with partner authorities.

Switzerland's Regional Pharmacovigilance Centres (RPVC) are involved in the assessment process and, based on the reports received, have produced evaluations of certain AEFI:

- Herpes zoster after immunisation with mRNA-based COVID-19 vaccines
- Neuralgic amyotrophy following administration of an mRNA vaccine against COVID-19
- COVID-19-mRNA vaccines and thrombocytopenia – focusing on immune thrombocytopenia

Swissmedic has recognised the problem of "COVID arm" and has produced a case report describing a delayed local reaction around the injection site. In addition, a Swissmedic contribution on "COVID arm" was published to supplement the regular update reports on side effects following COVID-19 vaccinations in Switzerland (see page 22).

So that healthcare professionals and patients can readily report AEFI, Swissmedic has optimised the electronic capture of these reports. You can find information about correct reporting in the article "Market surveillance of COVID-19 vaccines: reporting suspected side effects correctly".

Eva Eyal

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

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Important information

Market surveillance of COVID-19 vaccines: reporting suspected side effects correctly

Since the start of the COVID-19 vaccination campaign in Switzerland, Swissmedic has received many reports of suspected adverse drug reactions (ADR) and numerous inquiries about safety aspects of the vaccines used. Healthcare professionals and affected individuals can make a crucial contribution to the efficient market surveillance of COVID-19 vaccines by following the advice given below.

Apart from their desired effect, medicines can also produce side effects in some patients. In order to quickly identify safety signals, i.e. information about very rare or as yet unknown adverse drug reactions, correct side effect reports are essential. Only then can new drug risks be rapidly identified and safety measures promptly introduced and communicated.

As part of the worldwide vaccination campaigns against the new coronavirus, the spontaneous reporting system has, for example, enabled rare allergic reactions (anaphylaxis), delayed local skin reactions or a possible link between vector-based COVID-19 vaccines and the very rare condition of thrombocytopenia thrombosis syndrome (TTS, also known as vaccine-induced immune thrombotic thrombocytopenia (VITT)) to be identified in good time and measures to be taken to improve drug safety.

Reporting side effects: Information for healthcare professionals

Serious or as yet unknown adverse drug reactions (ADR), i.e. those not listed in the product information, should be reported. During the vaccination campaign against COVID-19, doctors should report all ADR that they feel are medically relevant.

For this purpose, please always use the electronic Swissmedic reporting portal "ElViS" (Electronic Vigilance System). Since the end of January, users with a HIN account can also use their access details to report via the Swissmedic online tool.

After authentication, a red button leads directly to a specific report form for COVID-19 vaccines. When the respective vaccine in this form is selected, some of the fields are prefilled automatically in order to further simplify the reporting process.

Reports sent using other forms or by e-mail lead to considerable delays in processing and often necessitate follow-up queries that could otherwise be avoided.

Important: Known, non-serious reactions are not subject to the reporting obligation prescribed by Art. 59 of the Therapeutic Products Act (TPA). The known, non-serious and very common reactions to COVID-19 vaccines include transitory pain and swelling at the injection site, fatigue, shivering, fever, headache and muscle and joint pain. These passing local and general reactions are normally a sign of the body dealing with the vaccine and do not need to be reported.

Anyone who reports a side effect using more than one route should mention this fact in any subsequent reports so that double-reporting can be identified if possible.

Important information for pharmaceutical companies regarding electronic pharmacovigilance reporting

From 1 July 2021 only electronic reports will be accepted.

Background

The number of reports of adverse drug reactions (ADR) has risen steadily in recent years. This trend has increasingly been observed both in Switzerland and in other countries in recent years. The increase is primarily attributable to a rise in the number of reports received from the pharmaceutical industry. To ensure that reports are processed promptly and possible risks are identified swiftly in future too, Swissmedic continually adapts its working methods and conducts them on a paperless basis as far as possible.

Consequences for marketing authorisation holders

It should be borne in mind that, as of 1 July 2021, Swissmedic will only accept electronic reports either via a Gateway connection or through the ElViS (Electronic Vigilance System) portal.

Registration processes are required for both options. The E2B Gateway is reserved for use by companies submitting more than 50 reports a year. The ElViS electronic reporting system is suitable particularly for small and medium-sized companies.

→ Gateway

→ ElViS-Portal

Thomas Schwartz, MD

Safety of Medicines division, Swissmedic

Important information for pharmaceutical companies regarding pharmacovigilance reporting of drug exposure during pregnancy to Swissmedic

Swissmedic has updated the reporting requirements as of **10 May 2021**.

Summary

The information sheet containing instructions regarding *"Drug exposure during pregnancy and parent-child reports from Switzerland"* has recently been updated on the website of Swissmedic, under the link: Instructions and information sheets (swissmedic.ch).

Consequently, the following main changes must be borne in mind with regard to reporting procedures:

- In case drug exposure during pregnancy is suspected with a substance known to be noxious, i.e. a substance which is contraindicated and should be avoided during pregnancy due to potential risk of adverse reactions for the foetus/child, **but no** complication during pregnancy occurred **and no** harmful effect on the foetus/child at the time of the report is suspected, the Individual Case Safety Report (ICSR) should be submitted as **"non-serious"** (within 60 days).
- For reporting instructions and timelines regarding safety signals, the following Swissmedic guidance document must also be consulted: MU101 20 001e WL Guidance document Drug Safety Signals HMP (PDF, 253 kB, 01.03.2021) – see Risk Management (Signalmanagement, PSURs, RMPs/RMP summaries) (swissmedic.ch).

Valeriu Toma, MD

Safety of Medicines division, Swissmedic

Drug safety and signals

Case report of a delayed local reaction at the injection site ("COVID arm")

Swissmedic is increasingly receiving reports of delayed local reactions around the injection site following a vaccination to protect against COVID-19. Most of the reports to date involve the COVID-19 vaccine from Moderna. The reports of redness and swelling predominantly occur around one week after the vaccination and have also been observed in other countries (so-called "COVID arm"). According to the latest findings, this is a temporary and harmless reaction connected with the activation of the body's immune system that disappears again after a few days. Swissmedic first reported on this issue on its website on 19 February 2021 (1).

These delayed local reactions can occur around one week after the vaccination and usually manifest themselves as a well-defined area of red, swollen skin on the injected arm, in some cases accompanied by pain and/or itching. These reactions improve without further measures after a few days.

In the authorisation study for the COVID-19 vaccine from Moderna, such reactions were observed in 0.8% of vaccinated subjects after the first dose and in 0.2% after the second dose. Accordingly, their frequency is currently classed as "uncommon" ($\geqslant$ 1/1,000 to < 1/100). In the USA these reactions have also been termed "COVID arm" in the media.

In a number of the reports to Swissmedic it appears that some people with reactions that were retrospectively considered to be probable delayed local reactions had been treated with an antibiotic, based on the presumably incorrect suspicion of a bacterial skin infection (erysipelas).

The exact mechanism underlying these reactions is not known. The interval corresponds to the first occurrence of the antibodies and immune cells induced by the vaccination. In severe cases, treatment with analgesics or antihistamines can be considered.

In some cases, there is uncertainty as to whether patients with a delayed local skin reaction should receive the second dose of the vaccine. The second dose is important for effective vaccine protection. There is no reason to skip or delay the second dose in the individuals concerned.

Some authors recommend injecting the second dose of the vaccine in the other arm.

A *letter to the editor* published in the New England Journal of Medicine on 3 March 2021 (2) described a series of 12 patients with delayed “large” local reactions after vaccination with mRNA-1273 SARS-CoV-2 vaccine. As a possible pathological mechanism, the authors suspect a delayed-type, T-cell-mediated hypersensitivity reaction. This suspicion was supported by skin biopsy specimens showing superficial perivascular and perifollicular lymphocytic infiltrates with scattered eosinophils and mast cells. All 12 patients had received the second dose of vaccine: half of them did not experience a recurrence of delayed local reactions, three patients had recurrent reactions that were similar in intensity and three had reactions that were of a lower grade.

Photos documenting the course over time of a female patient who developed COVID arm after COVID-19 vaccination with Moderna are shown below. The patient had a history of grass pollen allergy and an allergy to co-amoxicillin.

The 28-year-old woman received her first vaccination with the active substance from

Moderna. Six days later, the patient noticed stabbing pains in her armpit on moving her arm, and enlarged lymph nodes were palpable in her axilla on the same day. The patient was afebrile at all times. The local reaction developed as follows

The photos were kindly made available to Swissmedic for publication by the person concerned.

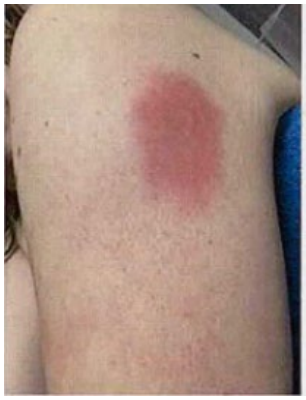

Photo 1
First reaction 7 days after vaccination: feeling of warmth, no pain

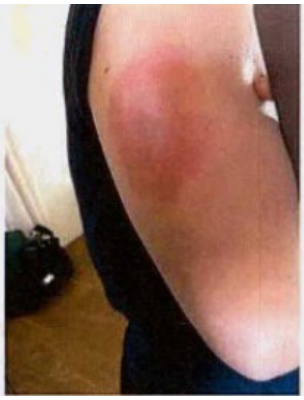

Photo 2
15 hours later: intensive feeling of warmth, pain

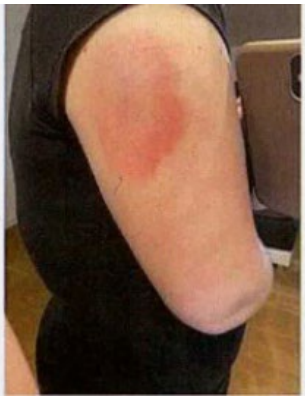

Photo 3
19 hours later: intake of antiallergic medication

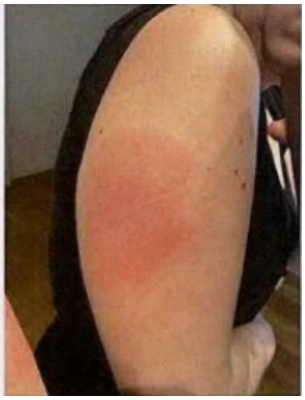

Photo 4
34 hours later: less pain, less feeling of warmth

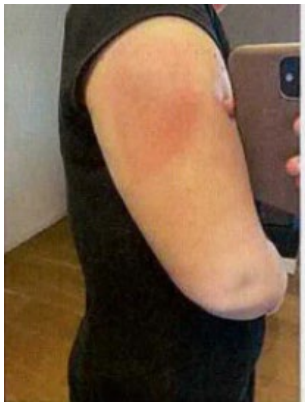

Photo 5
38 hours later: less pain, less feeling of warmth

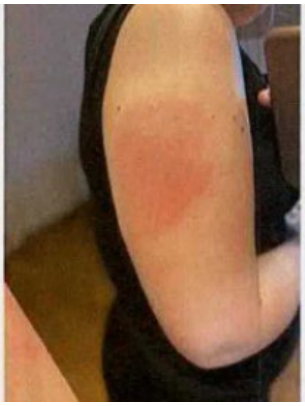

Photo 6
44 hours later: only tenderness,less feeling of warmth

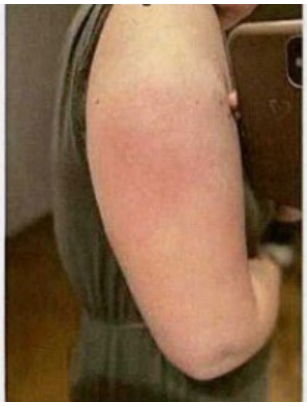

Photo 7
55 hours later: feeling of warmth and tenderness decreasing

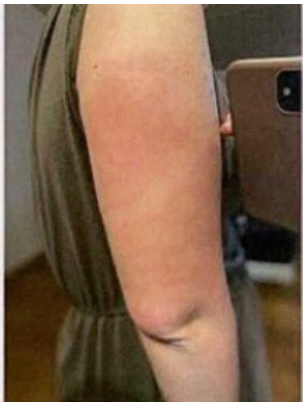

Photo 8
67 hours later: no further feeling of warmth or tenderness

The patient was given an antihistamine one hour before the second dose of vaccine, which she continued to take for several days afterwards. No symptoms occurred at the injection site, but she did experience shivering, raised temperature and malaise after the second vaccination.

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Neuralgic amyotrophy following COVID-19 mRNA vaccination

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Introduction

Neuralgic amyotrophy (NA) – also known as "Parsonage-Turner syndrome" (1) or "brachial neuritis" – is a painful peripheral neuropathy that causes a monophasic course of severe paresis, predominately in the upper extremities (2). The typical NA phenotype may be seen in a patient who awakens with new-onset unilateral pain in the shoulder, neck or upper arm that becomes unbearable (numeric rating scale score of ≥7/10) within a few hours. Several hours to 1–2 weeks later paresis develops, typically involving the long thoracic, suprascapular, and/or anterior interosseous nerves. The neuropathic pain may last up to six weeks and does not respond to conventional analgesic treatment (i.e. non-steroidal anti-inflammatory drugs and opioids). Amyotrophy usually becomes evident after a couple of weeks. The majority of NA cases are unilateral, but bilateral involvement can be seen in 30% of cases (1).

Previous estimates of the annual incidence of NA were 3/100,000/year, but more recent studies suggest a much higher incidence (1/1,000/year) (3).

The exact pathogenesis in NA is still unknown, but is most likely multifactorial. An interplay between environmental factors (i.e., infection or immune triggers), mechanical factors (repetitive or strenuous motor tasks) and genetic susceptibility (e.g. mutations in the septin 9 gene) are potentially involved in the development of NA. Preceding events such as infections, surgery and vaccination are reported in about half of NA cases (2, 4). Recently, hepatitis E emerged as a possible infectious trigger, especially in bilateral cases (5, 6). Moreover, several vaccinations have been associated with NA (4): typhoid, diphtheria, tetanus toxoid (7), smallpox, flu (9, 10), and human papilloma virus (11, 12). In these cases, NA symptoms usually start a few days/one week after vaccination (4).

Prognosis may be related to the amount of axonal damage, and later to chronic biomechanical impairment and articular degeneration of the shoulder joint, with long-term pain and fatigue (13). Most patients with NA are young, healthy and employed, and some of them cannot return to work for several months or years, depending on their type of occupation (13). Patients with phrenic nerve palsy (especially if bilateral) may need non-invasive, long-term ventilation; this can happen in up to 8% of cases (14).

Cases of COVID-19 vaccine – related NA

We describe two recent cases of suspected NA reported after vaccination with Comirnaty® and one after vaccination with COVID-19 vaccine Moderna which were evaluated for causality by the Ticino Regional Pharmacovigilance Centre, as the reference pharmacovigilance centre for COVID-19 vaccine safety:

A 40-year-old woman with no previous significant medical history or pharmacological therapy developed severe left shoulder pain 24 h after the first dose of Comirnaty® was administered in the left deltoid muscle. The pain was described as sudden onset, nocturnal, unbearable burning (neuropathic) pain

in the left shoulder and deltoid muscle region, which did not respond to paracetamol. When the pain started to decrease a couple of days later, the patient realised that the left upper limb was very weak: she was unable to abduct the arm, flex the elbow and ultimately perform hand movements. Since her upper arm was plegic, the patient was referred to a neurologist, an expert in neuromuscular diseases, who documented amyotrophy and weakness of the deltoid and biceps brachii muscles and confirmed the diagnosis of neuralgic amyotrophy. Electromyography performed one month after onset documented neurogenic recruitment in the biceps muscle with no spontaneous activity at rest. Magnetic resonance imaging of the brachial plexus and the upper arm were normal; in particular, there were no signs of muscle denervation. The patient started an intensive programme of physiotherapy and improved significantly. Based on the temporal relationship between vaccine administration and symptom development, and since other causes were excluded, the causal correlation between NA and COVID-19 vaccine administration was evaluated as possible.

A previously healthy 36-year-old man developed severe left shoulder and arm pain 18 days after the second dose of Comirnaty® was administered in the left deltoid muscle. The severe pain, which was treated by the patient with nonsteroidal anti-inflammatory drugs, was accompanied by weakness in the left arm that led to motor deficit and paresis. Three days after onset, the symptoms started to resolve. Neurological investigations confirmed a mild form of NA. Since other pathophysiological causes were excluded, the causal assessment for NA withComirnaty® administration was considered at least possible

A 67-year-old man known to have arterial hypertension treated with metoprolol, dyslipidaemia treated with pravastatin, and drug allergy to diclofenac, developed sudden severe left shoulder pain (described by the man as not dependent on movement or load and occurring in any position) 8 days after the second dose of COVID-19 vaccine Moderna was administered in the left deltoid muscle. The man denied having suffered any shoulder injury. Non-steroidal anti-inflammatory drugs did not relieve the pain. Subsequently, he was treated with cortisone and the pain gradually improved. Orthopaedic examination revealed paresis of the left shoulder and neurological investigations confirmed the diagnosis of NA. Laboratory investigation excluded inflammatory causes. Based on the plausible temporal relationship between vaccine administration and NA onset, in the absence of alternative causes, causality was assessed as possible.

VigiBase data and discussion

The official Swiss product information for Comirnaty® does not report NA among the known neurological adverse events following immunisation (AEFI), and a search in PubMed and other international databases did not yield results for the two COVID-19 mRNA vaccines authorised in Switzerland.

Up to 28 April 2021, 602,990 individual case safety reports have been reported worldwide in association with COVID-19 vaccines in VigiBase, the World Health Organization's global pharmacovigilance database of suspected adverse drug reactions. Of these, 30 individual case safety reports concerned NA. In 24 individual case safety reports NA was reported in association with Comirnaty®, in three with COVID-19 vaccine Moderna, and in three with Vaxzevria®.

The geographical distribution of COVID-19 vaccine-related safety reports of NA is heterogeneous: 10 safety reports are from the United States, 6 from the Netherlands, 5

from Germany, 4 from Spain, 3 from Switzerland, and one each from Austria, Italy and France.

21 safety reports involve women and the median age is 50 years (interquartile range, IQR, 40–57 years, range 26–89 years).

21 safety reports are categorised by the reporter as serious (for being disabling/incapacitating, n=8; for causing medically important conditions, n=9; for causing/prolonging hospitalisation, n=4). Eight safety reports were rated as non-serious while for one safety report the seriousness was not reported.

COVID-19 vaccines are the sole suspected drugs in all these safety reports.

In 24 safety reports, NA is reported in association with a single COVID-19 vaccination (unknown whether the first or the second dose), with a median time-to-onset of 5 days (IQR 1–12 days, range 0-19 days). In one safety report NA occurred 23 days after the first dose of Comirnaty® and 2 days after the second dose; in one safety report NA occurred 23 days after the first dose of Comirnaty® and 0 days after the second dose; and in one safety report NA occurred 54 days after the first dose of Comirnaty® and 18 days after the second dose. In three safety reports, it is not possible to define the NA time to onset of NA as the dates of vaccination and NA onset are only partially recorded.

Disproportionality analysis to assess whether a signal of disproportionate reporting exists for the NA/COVID-19 vaccine(s) combination shows increased reporting of NA with COVID-19 vaccines against both the proportion of NA reported in combination with any other drug recorded in VigiBase and the proportion of other adverse events reported in combination with COVID-19 vaccines. The reporting odds ratio (ROR) used as a measure of disproportionate reporting is 2.2 with the lower limit of the 95% confidence interval for the ROR measurement at 1.5. As signal detection depends on the number of safety reports gathered in VigiBase, which constantly changes, disproportionality analysis should be reassessed at regular intervals for confirmation and generation of hypotheses worthy of further investigation.

Conclusions

The three cases described above, together with the data obtained from VigiBase, raise the hypothesis that mRNA COVID-19 vaccines could be related to and potentially trigger NA. This potential safety signal deserves further investigation. Meanwhile, clinicians should be aware of this possibility in order to promptly identify and refer the patients, consider starting treatment (usually with oral corticosteroids) and report the suspected cases to Swissmedic.

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Herpes zoster after immunisation with mRNA-based COVID-19 vaccines

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Introduction

The SARS-CoV-2 vaccines Comirnaty® (tozinameran) and COVID-19 Vaccine Moderna have been authorised in Switzerland since 19 December 2020 and 12 January 2021, respectively (1). Comirnaty® is indicated for active immunisation to prevent COVID-19 caused by the SARS-CoV-2 virus in individuals 12 years of age and older. The product information recommends the administration of Comirnaty®, after dilution of the active substance, as a vaccination course of two doses at least 21 days apart (2). COVID-19 Vaccine Moderna is authorised for active immunisation to prevent COVID-19 caused by the SARS-CoV-2 virus in individuals 18 years of age and older. The product information recommends its administration, again after dilution, as a vaccination course of two doses at least 28 days apart (2). Both of these products are mRNA vaccines. mRNA vaccines are dead vaccines and do not contain any adjuvants or preservatives (3). The mRNA contains the coded information about the spikes of the SARS-CoV-2 viral envelope (glycoprotein), which is recognised by the body as foreign, thereby triggering an immune response (4).

The varicella zoster virus (VZV, human herpesvirus 3, HHV-3) is an alphaherpes virus. Eight human pathogenic herpesviruses have been described to date, including the herpes simplex viruses (HSV) HSV1 and HSV2 (5). Most people are first exposed to VZV during childhood in the form of chickenpox and usually recover without any major complications. After an initial infection, VZV remains in the sensory nerves or in satellite cells surrounding the neurons, where they can be reactivated at a later date (6). VZV reactivation occurs mainly in older individuals with a compromised immune status and manifests itself as herpes zoster (HZ, shingles). During reactivation, the VZV migrates from the sensory ganglia to the nerve endings, where it causes the visible outbreak of the infection in the area of skin innervated by the nerve endings. The skin rash is often preceded by episodes of pain. The incubation period for the primary chickenpox infection is usually 14-16 days, although incubation periods of 8-21 days have also been observed (7). The incidence of HZ increases markedly with age and the associated general weakening of the immune system: while the incidence at the age of 50 is 3 cases per 1,000, an incidence of 10 cases per 1,000 is described from the age of 80 (8). Other risk factors for herpes zoster include autoimmune diseases, organ transplants and the administration of immunosuppressive drugs, psychological stress and female gender (9).

Case reports

Between January and April 2021, 24 case reports of herpes zoster shortly after a vaccination with Comirnaty® or COVID-19 Vaccine Moderna were reported to the Regional Pharmacovigilance Centre Zurich (RPVC). The individuals affected were from 33 to 90 years of age and were distributed almost equally between the sexes. An overview of the corresponding cases is provided in **Table 1**. The median time between the immunisation with a COVID-19 vaccine and the onset of herpes zoster symptoms was 11 days.

By way of example, we describe below a number of striking case reports of patients with no known risk factors for herpes zoster:

- **Case 1:** A 33-year-old man with no history of shingles developed a herpes zoster infection in the area of dermatome L1 a few days after the first immunisation with Comirnaty®. The symptoms regressed spontaneously after two weeks. The patient was healthy and did not have any known pre-existing illnesses.
- **Case 2:** A 45-year-old woman received her first immunisation with Comirnaty® (tozinameran) 5 days before contracting a thoracic herpes zoster infection. This was her first experience of this infection, which was initially treated with valaciclovir for 7 days. The symptoms quickly regressed, and her second vaccine dose was administered on schedule. Further details on the outcome of this case were not yet available at the time of the report.
- **Case 3:** A 41-year-old woman developed a herpes zoster infection on the left side of her chest 5 days after the first vaccination with Comirnaty®. Here, too, this was the first time that the patient had experienced such symptoms. After an initial 7-day treatment with valaciclovir, the symptoms regressed. The patient did not have a history of pre-existing illnesses, including immunosuppressive disorders. The second vaccine dose was likewise administered on schedule.
- **Case 4:** A 60-year-old woman was immunised with Comirnaty®. A few days later she complained of pain in her mouth. A total of 15 days after the vaccination, the patient was diagnosed with oral shingles following a positive varicella zoster virus PCR result. She was initially treated with Brivex® (brivudine), which quickly produced a significant improvement.
- **Case 5:** A 47-year-old man received the vaccine Comirnaty® (tozinameran) as immunisation against COVID-19. 33 days after the second dose he developed herpes zoster, with classical blisters on a red background in the area of dermatomes T7 and T8. The patient did not have any pre-existing illnesses or relevant risk factors.

All patients recovered from their herpes zoster infections without any sequelae. The infections usually regressed following antiviral treatment. In one case, the herpes zoster infection resolved spontaneously.

Table 1: Patient characteristics of individual case safety reports processed by the RPVC Zurich (January–April 2021)

Summary of individual case safety reports (n=24)		n
Age		
	≥90years	2
	70-89 years	17
	50-69 years	1
	30-49 years	3
	0-29 years	1
Sex		
	Male	14
	Female	10
Herpes zoster manifestation		
	Thoracal	8
	Ophthalmic	2
	Dermatome L1	2
	Dermatome C5	1
	Enoral	1
	Cervical	3
	Facial	2
	Axillar	1
	Not defined	4
Suspected Covid-19 Vaccine		
	Comirnaty®	15
	Covid-19 Vaccine Moderna	9
Dose		
	After first dose	12
	After second dose	10
	Not defined	2

Discussion

The literature already includes a case report from Turkey involving the onset of herpes zoster after the administration of a COVID-19 vaccine. In this report, by Bostan et al., a 78-year-old male patient experienced a reactivation of thoracic herpes zoster (dermatomes T3-T4) five days after immunisation with an unspecified COVID-19 vaccine (10). He complained of an erythematous, painful and pruritic skin lesion on his chest. He was treated with oral valaciclovir for a week. He had a history of coronary heart disease, cerebrovascular accident and chronic obstructive pulmonary disease. The patient had undergone resection of a bladder tumour six years ago. At the time of immunisation, the patient was not on any immunosuppressive therapy.

A case series from Israel reported by Furer et al. describes six female patients aged 36 to 61 with pre-existing rheumatic disease who developed VZV reactivation shortly after immunisation with Comirnaty®. However, the publication also points out that patients with rheumatic disease generally are twice as likely to suffer from a VZV reactivation. As a possible explanation for the VZV reactivation associated with Comirnaty®, the authors refer to a stimulation of innate immunity through toll-like receptor-mediated (TLR) signalling pathways triggered by mRNA vaccines (11).

At the time of our searches (12 April 2021), the WHO pharmacovigilance database (Vigibase™) listed a total of 110,426 individual case safety reports for Comirnaty® received since 2020, including 274 cases of "herpes zoster" and 322 cases of "shingles". Most of these cases occurred in France (39.3%), Germany (12.7%) and Italy (11.1%). For Switzerland, the WHO database lists just 20 cases (12). For COVID-19 Vaccine Moderna, Vigibase™ documents a total of 8,077 individual case safety reports, 38 cases of "herpes zoster" and 25 cases of "shingles". Most of these cases have been observed in France (33.3%), Switzerland with 18 cases (27.3%) and the Netherlands (12.1%). For the USA, 78 cases of "herpes zoster" are listed for the product named Moderna COVID-19 Vaccine in Vigibase™ (12).

On 9 April 2021, Swissmedic published an update on the side effects of COVID-19 vaccines in Switzerland, with 44 reported cases of herpes zoster infection, 26 of which were rated as serious. The average age of the affected patients was 72, and the symptoms appeared between one and 43 days after vaccination (13).

VZV reactions have also been observed among COVID-19 sufferers in otherwise immunocompetent patients (14). Other authors suggest that this may be due to COVID-19-induced lymphopenia or functional exhaustion of CD4+ cells (15, 16).

Moreover, Walter et. al. describe various cases in which VZV reactivations also occurred after vaccinations against influenza, hepatitis A, rabies and Japanese encephalitis. The authors speculate that immunisations by vaccines may induce suppression of cell-mediated immunity and thus trigger the reactivation of VZV (17). Moodley et al. (2019) describe several cases of immunocompetent children who, shortly after a VZV vaccination, developed an HZ that appeared to be just as severe as an HZ infection with wild-type VZV (chickenpox) (18). In 2020, the Drug Commission of the German Medical Association also published several case reports of herpes zoster and zoster-like skin lesions that occurred shortly after vaccination with Shingrix®. One possible pathological mechanism discussed here is a high number of CD4-positive T lymphocytes directed against glycoprotein E and triggered by Shingrix® (19).

Conclusion

Herpes zoster of any type is not yet documented in the Swiss product information, but may be a very rare and serious adverse drug reaction to COVID-19 vaccines. As described by Walter et al., cases of VZV reactivation have already occurred after immunisation with various vaccines. The precise mechanism that causes COVID-19 vaccines to produce a VZV reactivation is still not clear. Since these vaccines have only been on the market for a short time and since only scant reports of said reactions have been described to date, further investigations are needed. However, a short-term alteration of the immune reponse by vaccination may play a role in the pathological mechanism. Although the spontaneously reported cases could involve a chance association, a close temporal relationship was observed, which means that a COVID-19 vaccination cannot be ruled out as a possible trigger of VZV reactivation. The case reports found in the WHO pharmacovigilance database indicate that herpes zoster after vaccination is not an isolated occurrence. Consequently, a more detailed analysis of the WHO database in future regarding the disproportionality between the onset of herpes zoster and COVID-19 vaccinations would be of great interest. An analysis to ascertain whether the use of vector vaccines, for example the COVID-19 vaccine from AstraZeneca, leads to an increased occurrence of herpes zoster would also be interesting.

Healthcare professionals should develop an awareness of the possibility of herpes zoster as an adverse drug reaction to COVID-19 vaccines and not hesitate to report corresponding cases.

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COVID-19 mRNA vaccines and thrombocytopenia – focusing on immune thrombocytopenia

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Introduction

Following the market authorisation in Switzerland of Comirnaty® (tozinameran) and COVID-19 Vaccine Moderna in December 2020 and January 2021, respectively, several cases of thrombocytopenia shortly after their administration have been reported to us at the Regional Pharmacovigilance Centre (RPVC) in Basel. Thrombocytopenia is not labelled as an adverse drug reaction in the prescribing information for these vaccines (1, 2). A small number of corresponding case reports can currently be found in the literature (3, 4, 5, 6), and a link between COVID-19 vaccination and immune thrombocytopenia (ITP) is currently under discussion (6). Cases of thrombocytopenia in connection with COVID-19 itself have also been described (7). In this newsletter article, we summarise the reports on thrombocytopenia associated with COVID-19 mRNA vaccination that have been submitted to RPVC Basel, focusing specifically on ITP.

Methodology

We consulted our in-house pharmacovigilance database at RPVC Basel for reports of thrombocytopenia in connection with a COVID-19 mRNA vaccination and extracted demographic and clinical data from the completed reports. We also present data on immune thrombocytopenia (ITP) obtained from VigiBase. A detailed description of the VigiBase database is provided in a publication by Lindquist (8). Using the VigiLyze system, we searched VigiBase for the vaccine names "COVID-19 mRNA Vaccine BNT162b2", "Pfizer BioNTech COVID-19 vaccine", "Comirnaty", "Vacuna COVID-19 Pfizer BioNTech", "COVID-19 vaccine Moderna", "Moderna COVID-19 vaccine" and the preferred term "Immune thrombocytopenia" according to the Medical Dictionary for Regulatory Activities (MedDRA), Version 23.1. The vaccine names were coded according to the WHO Drug Dictionary, the international reference for drug-related information.

Measured against various reporting guidelines, data from VigiBase are inhomogeneous worldwide and prone to "underreporting" and "reporting bias". Therefore the information, at least in respect of origin and the probability that the vaccine has caused the adverse drug reaction, is not homogeneous.

Results

We identified six cases (12%), from a total of 49 reports on COVID-19 mRNA vaccines, which satisfied our search criteria. All cases were serious and unexpected. Details of the cases can be found in the table below.

In four of the six cases, the thrombocytopenia was a chance finding in connection with an emergency medical consultation due to another medical event. Symptoms (case no. 5) or thrombocytopenia occurred after the first vaccination in all cases. Two patients had a history of thrombocytopenic episodes, and two had known immune thrombocytopenia (ITP or Evans syndrome).

As at 4 April 2021, 213,977 reports regarding the vaccines listed above had been entered

in VigiBase, including 115 cases related to ITP. With a statistically expected number of 58 ITP cases, the number of observed cases was therefore slightly higher than expected, fulfilling the statistical analysis criteria defined by the Uppsala Monitoring Centre for a signal in terms of an association. On the date this article was revised (20 May 2021), 381,624 reports relating to the vaccines listed above had been entered sin VigiBase, including 235 ITP cases (expected number 106).

Table: Summary of cases of thrombocytopenia after vaccination with COVID-19 mRNA vaccines, focusing on ITP cases

Case no.	Age, sex	COVID-19 vaccine	Platelet count (Ref. 150-450 G/l), Symptoms	Diagnosis	Latency	Outcome	Comments
1	77, m	Comirnaty® (tozinameran), initial dose	28 Mild epistaxis	ITP	8 days	Hospitalisation Protracted thrombocytopenia despite treatment with intravenous immunoglobulins and prednisone Responded to eltrombopag	Incidental finding during outpatient investigation of chronic anaemia Previous mild thrombocytopenic episodes (never below 100 G/l)
2	56, m	COVID-19 Vaccine Moderna, initial dose	3 Petechiae	ITP	3 days	Improved with intravenous immunoglobulins and dexamethasone	Known Evans syndrome (ITP and autoimmune haemolytic anaemia)
3	76, f	COVID-19 Vaccine Moderna, initial dose	30 None	ITP exacerbation	5 days	Discharged without symptoms after 3 days Platelet count not recovered at that point	Incidental finding after acute presentation with constipation-associated abdominal pain. Previous history of ITP
4	60, f	Comirnaty® (tozinameran), initial dose	11 Mild epistaxis	Acute thrombocytopenia	19 days	Rise in platelet count to 30 G/l after 1 platelet concentrate transfusion	Incidental finding after hospitalisation for acute cholecystitis Co-suspected medication capecitabine and oxaliplatin
5	85, m	COVID-19 Vaccine Moderna, second dose	60 Significant arterial bleeding into iliacus and psoas muscles	Acquired haemophilia A	Unclear – probably a few days	Prednisone and 4 cycles of rituximab 1x/week Clotting stabilised with recombinant clotting factor VIIa and Factor Eight Inhibitor Bypassing Activity (FEIBA)	Diverse haematomas and painful knee joint effusions after first vaccine dose Severe lower abdominal pain after second vaccine dose Thrombocytopenic episode in the past (associated with surgery)
6	70, f	COVID-19 Vaccine Moderna, initial dose	97 Rectal bleeding	Pancytopenia (haemoglobin 94 g/L [Ref. 120 – 160], neutrophils 0.67 G/L [Ref. 1.3 – 6.7])	3 days	Spontaneous recovery	Incidental finding after hospitalisation for treatment of a subcapsular femoral fracture Co-suspected medication pemetrexed and a single dose of metamizole

Discussion

The possible options considered in the differential diagnosis of a thrombocytopenia with sudden onset are numerous. They can be divided into three main groups: impaired production (haematopoietic disorder), shortened lifespan of platelets (breakdown) and redistribution. Among the cases of thrombocytopenia after a COVID-19 mRNA vaccination reported to RPVC Basel, impaired production and co-medication with bone marrow suppressants was present in two cases (case nos. 4 and 6), and a shortened platelet life span was present in four cases (case no. 5 platelet consumption with acute bleeding; case nos. 1, 2 and 3 with ITP).

The episodes of thrombocytopenia were often chance findings during a hospitalisation for other reasons. On the one hand, this may have prevented more serious outcomes. On the other hand, however, it raises the question as to whether thrombocytopenia after vaccinations might often remain unobserved. No serious bleeding occurred due to the thrombocytopenia (the serious bleeding in patient 5 was attributed to acquired haemophilia A).

A possible risk factor for the onset of thrombocytopenia after a COVID-19 mRNA vaccination could be a pre-existing predisposition to thrombocytopenia. Previous thrombocytopenic episodes were documented for four of the patients (autoimmune ITP in two cases). A recently published case report describes the onset of ITP after the first dose of tozinameran in a healthy 22-year-old man who was not on any other medication (3). Interestingly, two months before his vaccination this patient had presented with a mild thrombocytopenia in connection with an acute respiratory infection. Of the 20 cases described by Lee et al., four either had a known ITP or had experienced previous episodes of thrombocytopenia (6). Whether earlier thrombocytopenic episodes are a risk factor for ITP after a COVID-19 mRNA vaccination is currently a matter for speculation, but one that should be investigated further.

As observed by Lee at al., our cases occurred after the first dose of the vaccine (6). If the onset of ITP was purely coincidental, one would expect corresponding blood count abnormalities to be observed after a second vaccination as well. The fact that no ITP cases were reported after a second dose of the vaccine may, according to the authors, indicate a vaccine-induced reaction (6). On the other hand, this observation may be due to the much higher number of individuals having only received a first dose of a vaccine by the beginning of February 2021 compared to those who had already received two doses. It should be borne in mind that the assessment of an association with new vaccines is complicated by the scarcity of available data. The causality of an adverse event following immunisation is assessed by the WHO using a 3-point scale ("inconsistent with causal association to immunisation", "indeterminate" or "consistent with causal association to immunisation"), and all new vaccine-related events are classified as "indeterminate" (9).

The known overall incidence of ITP is approximately 3.3 per 100,000 adults/year (10). ITP often occurs in a temporal relationship with an infection in the preceding days or weeks, and has been described as a complication of COVID-19 (7). ITP in connection with vaccinations has been diagnosed in rare cases, particularly for the MMR vaccine (1-3 per 100,000 vaccinated children) and is normally associated with a mild progression (11). A vaccination can induce ITP by various mechanisms, particularly by molecular mimicry between viral and platelet proteins. Cross-reactive antiviral antibodies act as autoantibodies by binding to platelets and inducing lysis through complement activation or cellular mechanisms.

The safety signal for ITP after COVID-19 vaccinations with Comirnaty®, COVID-19 Vaccine Moderna and Vaxzevria® (formerly COVID-19 Vaccine AstraZeneca) is currently being investigated by the Pharmacovigilance Risk Assessment Committee (PRAC) of the European Medicines Agency (12).

Conclusion

Among the 49 reports linked with the administration of a COVID-19 mRNA vaccine submitted to RPVC Basel, six cases involve episodes of thrombocytopenia. An autoimmune thrombocytopenia was present in three of these cases. VigiBase, the WHO database, currently includes a higher than expected number of reports on ITP following a COVID-19 mRNA vaccination. It is important to keep a watchful eye on these serious adverse events and report them to the national drug regulatory authorities. The conclusions drawn from the post-marketing data in VigiBase originate from the authors of this publication and not from the Uppsala Monitoring Centre, the national pharmacovigilance centres or the World Health Organisation.

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Information on the Swissmedic website[1]

Side effects of COVID-19 vaccines in Switzerland

18.06.2021
Reports of suspected adverse reactions to COVID-19 vaccines in Switzerland – update
2,944 reports evaluated – the overall positive benefit-risk ratio of the vaccines remains

04.06.2021
Investigation of reports of myocarditis in connection with COVID-19 mRNA vaccines
Information for healthcare professionals

04.06.2021
Side effects of COVID-19 vaccines in Switzerland – update
2,701 reports of suspected adverse reactions to COVID-19 vaccines in Switzerland evaluated

21.05.2021
Side effects of COVID-19 vaccines in Switzerland – update
2269 reports of suspected adverse reactions to COVID-19 vaccines in Switzerland evaluated

07.05.2021
Side effects of COVID-19 vaccines in Switzerland – update
1953 reports of suspected adverse reactions to COVID-19 vaccines in Switzerland evaluated

22.04.2021
Side effects of COVID-19 vaccines in Switzerland – update
1485 reports of suspected adverse reactions to COVID-19 vaccines in Switzerland evaluated

09.04.2021
Side effects of COVID-19 vaccines in Switzerland – update
1174 reports of suspected adverse reactions to COVID-19 vaccines in Switzerland evaluated

26.03.2021
Side effects of COVID-19 vaccines in Switzerland – update
862 reports of suspected adverse reactions to COVID-19 vaccines in Switzerland evaluated

11.03.2021
Side effects of COVID-19 vaccines in Switzerland – update
597 reports of suspected adverse reactions to COVID-19 vaccines in Switzerland evaluated

26.02.2021
Side effects of COVID-19 vaccines in Switzerland – update
364 reports of suspected adverse reactions to COVID-19 vaccines in Switzerland evaluated

19.02.2021
Safety of COVID-19 vaccines: Reports of delayed local reactions
Information for healthcare professionals concerning isolated reports of redness and swelling around one week after vaccination

05.02.2021
Reports of suspected adverse reactions to the COVID-19 vaccines in Switzerland – Update
To date, 63 side effect reports in connection with COVID-19 vaccinations in Switzerland have been evaluated

29.01.2021
COVID-19 Impfstoffe und allergische Reaktionen inkl. Anaphylaxien – Hinweis für medizinische Fachpersonen
Bisherige Erkenntnisse bzgl. allergische Reaktionen

22.01.2021
Reports of suspected adverse reactions to the COVID-19 vaccines in Switzerland
Reports to date in line with the known risk profile

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

In focus

19.04.2021

Coronavirus disease (COVID-19) Pandemic

Information on the new coronavirus (SARS-CoV-2)

Healthcare Professional Communication

25.06.2021
DHPC – Xeljanz® (Tofacitinib)
Erste Ergebnisse einer klinischen Studie deuten auf ein erhöhtes Risiko für schwerwiegende unerwünschte kardiovaskuläre Ereignisse und maligne Erkrankungen (ohne NMSC) bei der Verwendung von Tofacitinib im Vergleich zu TNF-alpha-Inhibitoren hin

18.02.2021
DHPC – Fluorochinolones
Risiko Herzklappenregurgitation/-insuffizienz unter systemisch und inhalativ angewendeten Fluorchinolonen

17.02.2021
DHPC – Metamizol
Risiko eines arzneimittelbedingten Leberschadens

10.02.2021
DHPC – AmBisome® (amphotericinum B), Pulver zur Herstellung einer Infusionsdispersion
Chargenüberprüfung und Austausch der beigelegten Sartorius 5 µm Filter

29.01.2021
DHPC – Xeljanz (tofacitinib)
Streichung der 10 mg 2x täglich Dosis bei rheumatoider Arthritis und zusätzliche Angaben zum erhöhten Risiko für venöse Thromboembolien und zur Gesamtmortalität

20.01.2021
HPC – Fosfomycin-Trometamol Granulat/Pulver
Anwendungseinschränkungen sowie Streichung der 2 g Dosierung

19.01.2021
DHPC – Tecentriq® (Atezolizumab)
Identifizierung des Risikos schwerer kutaner Nebenwirkungen (Severe Cutaneous Adverse Reactions, SCARs) in Verbindung mit TECENTRIQ®

08.01.2021
HPC – Brivex (Brivudin)
Potenziell tödliche Toxizität von Fluoropyrimidinen bei der Anwendung kurz vor, gleichzeitig mit oder innerhalb von 4 Wochen nach Ende der Behandlung mit Brivudin

08.01.2021
DHPC – Ancotil®, Infusionslösung 1% (i.v.), und Protamin® Ipex (1000, Injektionslösung, und 5000, Injektionslösung)
Einstellung der Produktion / Versorgungsunterbruch von medizinisch bedeutsamen Produkten

30.12.2020
DHPC – Kadcyla, Pulver zur Herstellung eines Infusionslösungskonzentrates
Inkorrekte Rekonstitutionsangabe auf der Faltschachtel - Gefahr der Überdosierung

17.12.2020
DHPC – Xenetix (Iobitridol), Injektionslösung
Neue hautbezogene unerwünschte Arzneimittelwirkung sowie Kontraindikation nach Xenetix (Iobitridol)

Announcements

28.06.2021
COVID-19 rapid self-tests: validation and dispensing
The Federal Office of Public Health (FOPH) checks the validation of COVID-19 rapid self-tests (also known as SARS-CoV-2 self-tests)

11.06.2021
COVID-19 vaccine for young people aged 12 to 17: Moderna submits authorisation application to Swissmedic
Another indication extension under rolling review

08.06.2021
Operation PANGEA XIV: campaign against counterfeit and illegally imported medicinal products
Authorities worldwide have been checking for criminal online sales of medicines in a coordinated operation

04.06.2021
Pfizer/BioNTech COVID-19 vaccine approved for young people in Switzerland
Swissmedic approves indication extension for Comirnaty® for 12 to 15-year-olds

04.06.2021
Swissmedic Annual Report 2020
Federal Council approves Swissmedic Annual Report 2020

02.06.2021
COVID-19 vaccine from Pfizer/BioNTech can be stored in the refrigerator for up to one month
Comirnaty®: Swissmedic approves storage at 2–8 °C for up to one month

26.05.2021
New regulations applicable to medical devices as of 26 May 2021
Modification of the Medical Devices Ordinance (MedDO) in the context of pending agreements between Switzerland and the EU

26.05.2021
Revised requirements for combination products
(medicinal products with a medical device component)

15.06.2021
Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL)
updated information

18.05.2021
Adaptation of COVID-19 vaccines to new SARS-CoV-2 variants
The adapted guidance document comes into effect on 15 May 2021.

07.05.2021
Vaccine for children aged 12 to 15: Pfizer submits authorisation application to Swissmedic
The vaccine "Comirnaty®" is currently authorised for people aged 16 and over. The application asks for the authorisation to be extended to include the age group of 12-15-year-olds.

06.05.2021
Market surveillance of COVID-19 vaccines: reporting suspected side effects correctly
Reporting ADRs: important information for healthcare professionals and vaccinated individuals

20.04.2021
COVID-19 medicine from Roche Pharma (Switzerland) AG can be used in Switzerland
The active substances in "RegN-Cov 2", the COVID-19 medicinal product from Roche Pharma (Switzerland) AG, are now covered by the COVID-19 Ordinance 3 and may be placed on the market following the submission of an authorisation application to Swissmedic.

19.04.2021
CureVac Swiss AG submits application for authorisation of COVID-19 vaccine (CVnCoV) to Swissmedic
Another COVID-19 vaccine under rolling review

16.04.2021
Potential nitrosamine contamination
Update – April 2021

14.04.2021
«Visible» Nr. 3/April 2021
Independence, humanity, strength & integration: those are values we focus on in the 3rd issue of the Swissmedic magazine 'Visible'. Enjoy the read!

13.04.2021
Important information for pharmaceutical companies regarding electronic pharmacovigilance reporting
From 1 July 2021 only electronic reports will be accepted

12.04.2021
Authorisation of human medicinal products with new active substances and of additional indications 2020
New authorisations – Overview 2020

09.04.2021
COVID-19 rapid self-tests: Validation, exemptions and dispensing
The Federal Office of Public Health (FOPH) checks the validation of COVID-19 rapid self-tests (also known as SARS-CoV-2 self-tests). These may be dispensed to private individuals only by pharmacies.

30.03.2021
Swissmedic approves new storage conditions for the COVID-19 vaccine from Pfizer/BioNTech
Thanks to simpler handling, Comirnaty® can now also be used outside vaccination centres

23.03.2021
International cooperation on therapeutic products
Swissmedic authorises another medicinal product under the Access Consortium initiative

22.03.2021
COVID-19 vaccine from Johnson & Johnson: Swissmedic approves the third vaccine against COVID-19
Application for authorisation submitted by Janssen-Cilag AG approved

17.03.2021
Clinical trials of medical devices
New requirements and changes to authorisation practice as of May 2021

15.03.2021
Swissmedic grants Lonza in Visp another establishment licence for the production of COVID-19 active substances
New production site approved for Moderna's COVID-19 vaccine

10.03.2021
The Swissmedic Marketing Authorisation for Global Health Products (MAGHP) Procedure
Progress update and lessons learned

09.03.2021
COVID-19-Pandemie – Überprüfung der Konformität von medizinischen Gesichtsmasken
Landesweite Testkäufe bei Grossverteiler, Apotheken und Drogerien

04.03.2021
Illegal imports of medicinal products in 2020: medicines from the internet are still in demand
Slightly fewer medicinal products imported illegally into Switzerland

04.03.2021
Access Consortium statement on authorisations of modified Covid-19 vaccines for variants
Future vaccine modifications that respond to new variants of coronavirus to be made available quickly to recipients, without compromising on safety, quality or efficacy

02.03.2021
Modification of the form New authorisation of human medicinal products
ZL100_00_001e_FO

02.03.2021
Modification of the form Variations and extensions
ZL300_00_003e_FO

02.03.2021
Modification of the Full declaration form
ZL000_00_032e_FO

02.03.2021
Modification of the guidance document "Drug Safety Signals Human Medicinal product"
MU101_20_001e_WL

17.02.2021
Swissmedic permanently involved in Project Orbis
The participation terms and processes have been set out in a new guidance document Project Orbis HMV4

09.02.2021
Swissmedic vaccine videos – part 4
New explanatory videos on vector- and protein-based vaccines

03.02.2021
Rolling authorisation application for COVID-19 vaccines Swissmedic requests additional data
Swissmedic examines the data on the vaccine from AstraZeneca it receives on an ongoing basis

28.01.2021
Healthcare professionals with a HIN identity receive direct access to the Electronic Vigilance Reporting Portal (ElViS)
Healthcare professionals can use their HIN access to use ElViS, Swissmedic's online reporting tool

25.01.2021
Meetings of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) and of the International Pharmaceutical Regulators Programme (IPRP)
Continued Advancement of ICH's Global Public Health Mission 30 Years On

25.01.2021
The International Coalition of Medicines Regulatory Authorities (ICMRA) encourages the stakeholders to apply the concept of "regulatory reliance", i.e. to support each other in their activities
Statement from Global Medicines Regulators on the Value of Regulatory Reliance

12.01.2021
Swissmedic grants authorisation for the COVID-19 vaccine from Moderna
Second COVID-19 vaccine authorised in Switzerland

11.01.2021
Swissmedic warns of the danger of buying vaccines or other medicines online
If you purchase medicines or vaccines from an unregulated source you are putting your health at risk

04.01.2021
COVID-19 vaccine Comirnaty from Pfizer/BioNTech: Information for healthcare professionals concerning the sixth vaccine dose
Corona vaccine Comirnaty® (BNT162b2) from Pfizer/BioNTech: up to 6 doses per vial possible

01.01.2021
Information about electronic pharmacovigilance reports
The required tools have been available for years

30.12.2020
Media reports about a fatality following a COVID-19 vaccination in Switzerland: no apparent correlation with the vaccination
To date, no unknown side effects of vaccinations against the novel coronavirus have emerged

28.12.2020
Monitoring the safety of COVID-19 vaccines
To report side effects, healthcare professionals should register now for the online reporting tool ElViS

19.12.2020
Swissmedic grants authorisation for the first COVID-19 vaccine in Switzerland
Vaccine from Pfizer/BioNTech authorised in the rolling review procedure after close scrutiny of the risks and benefits

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