bijwerkingen centrumlareb

Overview of reports of adverse drug reactions following monkeypox vaccination

Introduction

IMVANEX (Modified Vaccinia Ankara – Bavarian Nordic live virus), manufactured by Bavarian Nordic, has been registered in Europe as vaccine for active immunisation against smallpox in adults since 2013. In the Netherlands, the vaccine was used off-label since May 2022 as *post-exposure prophylaxis against monkeypox following high and moderate risk exposure to individuals infected with monkeypox*. On July 22th 2022, the European Medicines Agency (EMA) officially registered IMVANEX for use against monkeypox due to the increasing number of monkeypox infections. Shortly thereafter, at the end of July 2022, a national pre-exposure vaccination campaign commenced in the Netherlands primarily targeted at individuals at high risk of exposure to monkeypox, mainly including men who have sex with men (MSM). Individuals in the MSM group who are prescribed PrEP (emtricitabine/tenofovirdisoproxil; HIV inhibitors) or who are on a waiting list for a PrEP prescription, as well as individuals who are known to the Centre of Sexual Health (CSG) for high risk behaviour towards potential infection with sexually transmitted diseases are invited to be vaccinated. In addition, laboratory personnel working with monkeypox virus strains and healthcare professionals at risk of occupational exposure to infected individuals are to receive monkeypox vaccination. The estimated 32.000 individuals in these selected groups receive a personal invitation from their local public health centre (GGD), general practitioner or attending physician [1]. Approximately 13.000 individuals have been vaccinated until September 29th 2022, of which 5.000 received a second vaccination as well [2].

IMVANEX contains the living modified vaccinia virus. Immunisation is carried out via subcutaneous injection in the upper arm. Primary vaccination for individuals whom have not been vaccinated against smallpox, monkeypox or vaccinia viruses before and immunocompromised patients are to receive two doses of 0.5 ml, where the second dose should be administered at least 28 days after the first dose. Individuals whom received a previous vaccination against smallpox (in the Netherlands this was part of the National Immunisation Programme (Rijksvaccinatieprogramma) until 1974), monkeypox or vaccinia virus, a single booster dose of 0.5 ml suffices [3].

This overview summarizes the adverse drug reaction reports following monkeypox vaccination received at the Netherlands Pharmacovigilance Centre Lareb until September 29th 2022.

Reports

Until September 29th 2022, 118 unique individual case reports on monkeypox vaccination were received at the Netherlands Pharmacovigilance Centre Lareb. All reporters were requested to answer follow-up questions regarding the outcome and duration of the reported adverse reactions, whether they had a previous smallpox or monkeypox vaccination or infection, concomitant use and coexisting medical conditions including skin conditions. No deaths or reactions with a serious outcome (according to CIOMS seriousness criteria) were reported.

The top 20 reported reactions mainly included injection site reactions and general systemic reactions commonly observed after vaccination (Figure 1). In case an injection site swelling and/or injection site erythema was reported, the reporting form included a question whether the reaction was to such extent that it spread over the adjacent joint or was visible on both the inside and outside of the arm, in which case the reaction was additionally coded as extensive swelling of vaccinated limb (ELS). This reaction was reported 10 times. All other top 20 reactions are mentioned in the SmPC [3]. A detailed list of all reported reactions is provided in Appendix A.

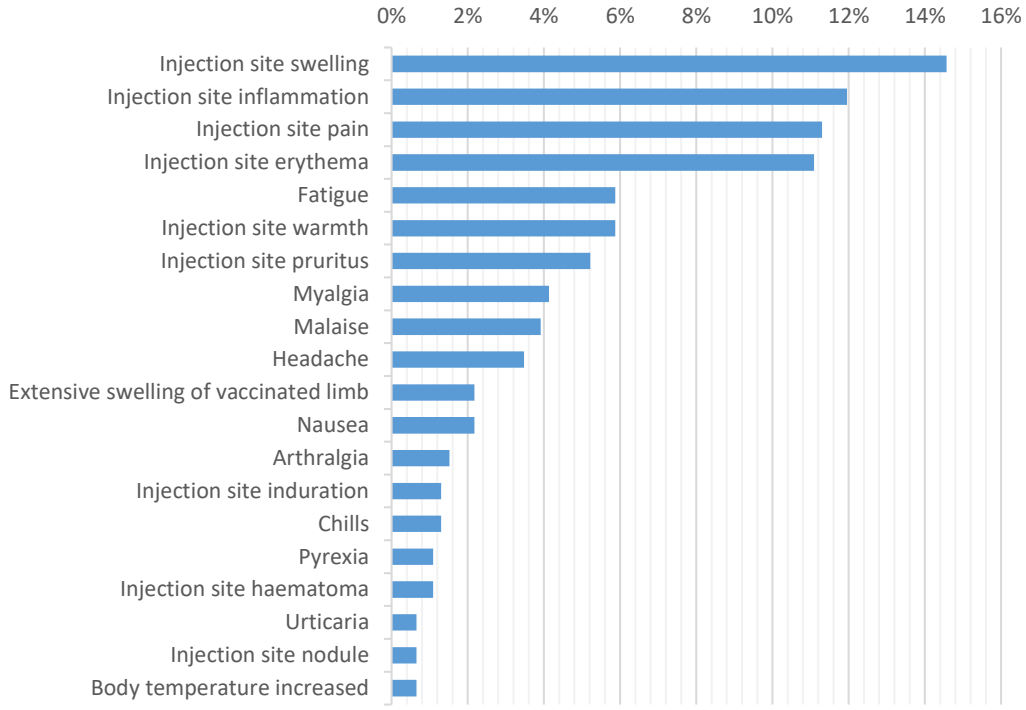

Figure 1 Top 20 most commonly reported reactions (% of total) following monkeypox vaccination in The Netherlands.

The mean latency of the reported reactions was 1.7 (0-21) days. At the time of most recent contact with the reporter, 50.0% of the reactions had not recovered, 20.9% was recovering, 0.2% recovered with sequelae, 28.7% recovered and 0.2% of the reaction outcomes was unknown. The mean duration of the recovered reactions, as far as known, was 8.1 (0-21) days.

Most reports (97.6%) originated from consumers or non-healthcare professionals, the remainder (2.4%) was reported by physicians or other healthcare professionals. 96% of the vaccinated individuals was of male gender, 4% was female. 27% of the vaccinated individuals indicated to use HIV inhibitors as concomitant medication. None of the vaccinated individuals had been infected with monkeypox.
Of the 118 individual case reports, 9 individuals indicated to have been vaccinated against smallpox as a child. 12 reports concerned a second vaccination, of which 1 individual reported to have had the same adverse reactions to the first administration as well (diarrhea and stomach discomfort).

Other sources of information

Global data on reported adverse reactions

Data retrieved from the global database (VigiLyze®) on the top 20 most commonly reported adverse reactions following monkeypox vaccination (registered as drugs with active ingredient smallpox vaccine) shows mainly general systemic reactions and injection site reactions (Figure 2) [4]. Furthermore, several other reactions mentioned in the SmPC are frequently reported, including dizziness and skin reactions [3, 4]. Of the total 934 received reports, 54 reports (5.8%) concerned a CIOMS serious reaction, mainly comprising other medically important conditions including vaccination complications and monkeypox infections [4].
The reports from The Netherlands have currently not all been included in the global database yet due to a delay in coding and processing of the reports, however it is expected that they will be added shortly.

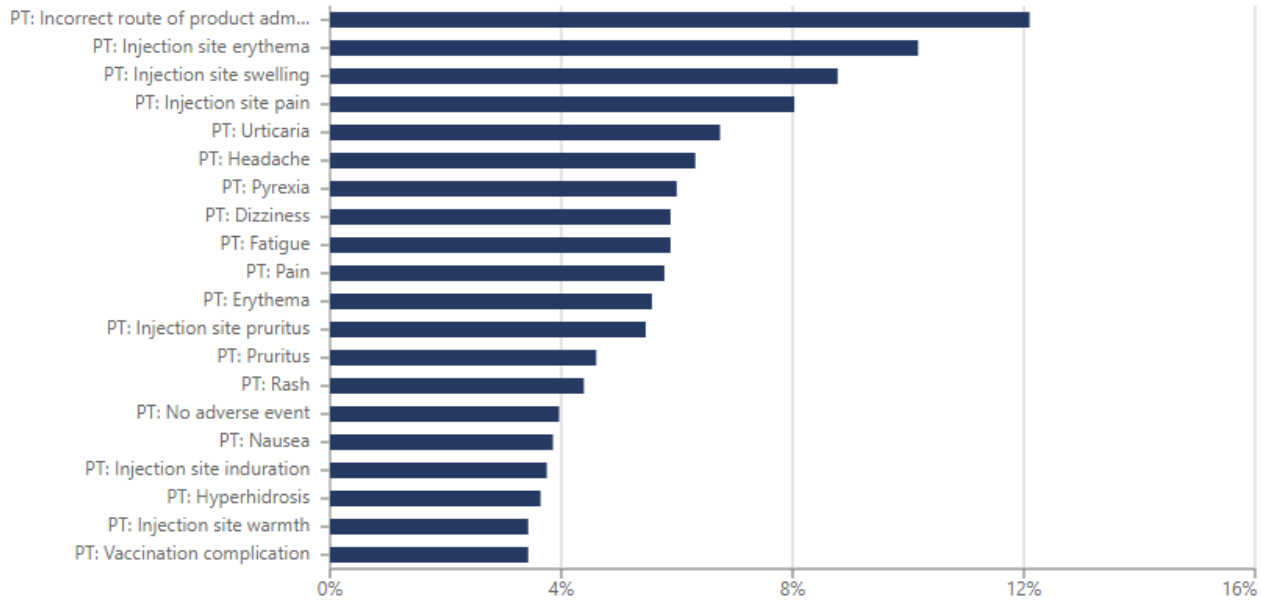

Figure 2 Top 20 most commonly reported adverse reactions (% of total) worldwide following smallpox vaccination (active ingredient) in 2022 (WHO VigiLyze) [4].

Literature

To date, no post-marketing case reports or studies regarding adverse events following monkeypox immunisation with IMVANEX have been published. Clinical trials showed that the most common adverse reactions were injection site reactions and systemic reactions typical for vaccines, with mild to moderate intensity. The adverse reactions resolved within seven days following vaccination without intervention. The rates of adverse reactions reported after either vaccination dose (first, second or booster) were similar during these clinical trials [3].

Discussion and conclusion

This overview provides insight into the safety profile of IMVANEX in daily practice. No serious adverse reactions, nor deviant patterns have been detected in the reported adverse drug reactions following monkeypox vaccination in The Netherlands thus far. However, as for several other vaccines, the occurrence of extensive swelling of the vaccinated limb (ELS) following vaccination with IMVANEX is plausible. The Netherlands Pharmacovigilance Centre Lareb will remain vigilant as the monkeypox vaccination campaign continues.

References

1. RIVM. LCI RIVM Richtlijn monkeypoxvaccinatie 2022 [updated 20-09-2022. Available from: https://lci.rivm.nl/richtlijnen/monkeypoxvaccinatie]. (Access date:26-09-2022)
2. RIVM. Vaccinatie monkeypox (apenpokken) 2022 [Available from: https://www.rivm.nl/monkeypox-apenpokken/vaccinatie]. (Access date:29-09-2022)
3. EMA. SmPC IMVANEX [Available from: https://www.ema.europa.eu/en/documents/product-information/imvanex-epar-product-information_en.pdf]. (Access date:26-09-2022)
4. WHO-UMC. VigiLyze. 2022.

This signal has been raised on November 15, 2022. It is possible that in the meantime other information became available. For the latest information, including the official SmPC's, please refer to website of the MEB www.cbg-meb.nl

Supplements

Appendix A: Detailed listing of reported reaction PT's following monkeypox vaccination in The Netherlands

Reaction PT's	Times reported (N)	Percentage of total
Injection site swelling	67	14.6%
Injection site inflammation	55	12.0%
Injection site pain	52	11.3%
Injection site erythema	51	11.1%
Injection site warmth	27	5.9%
Fatigue	27	5.9%
Injection site pruritus	24	5.2%
Myalgia	19	4.1%
Malaise	18	3.9%
Headache	16	3.5%
Nausea	10	2.2%
Extensive swelling of vaccinated limb	10	2.2%
Arthralgia	7	1.5%
Chills	6	1.3%
Injection site induration	6	1.3%
Injection site haematoma	5	1.1%
Pyrexia	5	1.1%
Body temperature increased	3	0.7%
Injection site nodule	3	0.7%
Urticaria	3	0.7%
Back pain	2	0.4%
Dizziness	2	0.4%
Hyperhidrosis	2	0.4%
Influenza like illness	2	0.4%
Pain in extremity	1	0.2%
Pharyngitis	1	0.2%
Photophobia	1	0.2%
Semen viscosity decreased	1	0.2%
Disturbance in attention	1	0.2%
Lymphadenopathy	1	0.2%
Acne	1	0.2%
Irritability	1	0.2%
Feeling cold	1	0.2%
Vomiting	1	0.2%
Drug interaction	1	0.2%
Vision blurred	1	0.2%
Daydreaming	1	0.2%
Yawning	1	0.2%
Rash	1	0.2%
Vaccination site lymphadenopathy	1	0.2%
Abdominal discomfort	1	0.2%
Pustule	1	0.2%
Folliculitis	1	0.2%

Injection site irritation	1	0.2%
Throat irritation	1	0.2%
Somnolence	1	0.2%
Erythema	1	0.2%
Pruritus	1	0.2%
Secretion discharge	1	0.2%
Presyncope	1	0.2%
Diarrhoea	1	0.2%
Injection site exfoliation	1	0.2%
Palpitations	1	0.2%
Trigeminal neuralgia	1	0.2%
Blood pressure decreased	1	0.2%
Injection site discomfort	1	0.2%
Pain	1	0.2%
Nightmare	1	0.2%
Abnormal loss of weight	1	0.2%
Increased upper airway secretion	1	0.2%
Musculoskeletal stiffness	1	0.2%
Night sweats	1	0.2%
Total	***460***	***100.0%***