25 June 2026
EMADOC-1700519818-3368880
Committee for Medicinal Products for Human Use (CHMP)

Assessment report

Imvanex

Common name: Smallpox and monkeypox vaccine (live modified vaccinia virus Ankara)

Procedure No. EMA/VR/0000337204

Note

Variation assessment report as adopted by the CHMP with all information of a commercially confidential nature deleted.

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List of abbreviations

Abbreviation	Explanation
AE	adverse event
AESI	adverse event of special interest
BMI	body mass index
CI	confidence interval
CSR	clinical study report
DRC	Democratic Republic of the Congo
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GMT	geometric mean titre
GMTR	geometric mean titre ratio
IEP	immunogenicity evaluable population
Inf.U	infectious units
LCL	lower confidence limit
LLOQ	lower limit of quantitation
MAAE	medically attended adverse event
mITT	modified intent-to-treat
Max	Maximum
Min	Minimum
nAb	neutralizing antibody
N	Number of participants with available data
NE	not evaluable
MVA	Modified Vaccinia Ankara
MVA-BN	Modified Vaccinia Ankara Virus - Bavarian Nordic
PRNT	plaque reduction neutralization test
SAE	serious adverse event
SD	standard deviation
TEAE	treatment-emergent adverse event
UCL	upper confidence limit
Yoa	Years of age
Yrs	Years

1. Background information on the procedure

1.1. Type II variation

Pursuant to Article 16 of Commission Regulation (EC) No 1234/2008, Bavarian Nordic A/S submitted to the European Medicines Agency on 11 March 2026 an application for a variation.

The following variation was requested:

Variation requested		**Type**
C.6.a	C.6.a) Addition of a new therapeutic indication or modification of an approved one	Variation type II

Extension of indication to include the active immunisation against smallpox, monkeypox and disease caused by vaccinia virus in individuals 2 years of age and older for IMVANEX, based on interim results from study POX-MVA-045; this is an open-label, multicenter immunogenicity and safety trial of the modified vaccinia Ankara-Bavaria Nordic (MVA-BN) vaccine in children from 2 years to less than 12 years of age compared to adults for the prevention of smallpox, mpox, and related orthopoxvirus infections. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Annex II and Package Leaflet are updated in accordance. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI.

The variation requested amendments to the Summary of Product Characteristics and Package Leaflet.

Information on paediatric requirements

Pursuant to Article 8 of Regulation (EC) No 1901/2006, the application included an EMA Decision EMA/PE/0000223819 on the agreement of a paediatric investigation plan (PIP) for the prevention of smallpox, mpox and disease caused by vaccinia virus.

At the time of submission of the application, the PIP EMA/PE/0000223819 had not yet been completed as some measures had been deferred.

The PDCO issued on 09 March 2026 a positive partial compliance check for PIP EMA/PE/0000223819, in relation to study 1, study 2, study 3 and study 5. For study 6 only date of initiation was assessed and compliance was confirmed.

Information relating to orphan market exclusivity

Similarity

Pursuant to Article 8 of Regulation (EC) No. 141/2000 and Article 3 of Commission Regulation (EC) No 847/2000, the MAH did not submit a critical report addressing the possible similarity with authorised orphan medicinal products because there is no authorised orphan medicinal product for a condition related to the proposed indication.

Scientific advice

The MAH did not seek Scientific Advice at the CHMP.

1.2. Steps taken for the assessment of the product

The Rapporteur and Co-Rapporteur appointed by the CHMP were:

Rapporteur: Jan Mueller-Berghaus Co-Rapporteur: Not applicable

Timetable	Actual dates
Submission date	11 March 2026
Start of procedure	28 March 2026
CHMP Rapporteur's assessment report	26 May 2026
ETF meeting	29 May 2026
CHMP member comments	15 June 2026
Updated CHMP Rapporteur's assessment report	18 June 2026
CHMP opinion	25 June 2026

2. Scientific discussion

2.1. Introduction

2.1.1. Problem statement

Disease or condition

Smallpox

Smallpox, caused by variola virus infection, is a member of the family Poxviridae belonging to the subfamily *Chordopoxviridae* and genus *Orthopoxvirus*. This disease was eradicated (last known case in 1977) because of the WHO global campaign.

Monkeypox (Mpox)

Mpox, another virus of the genus *Orthopoxvirus* genus, is a viral zoonosis caused by the mpox virus (MPXV) infection, has symptoms very similar to smallpox, although milder and with a substantially lower-case fatality rate. This virus was first isolated in 1958 and the first cases in humans were observed in the Democratic Republic of Congo (DRC) in the 1970s.

Mpox virus has two primary genetic clades: central African (Congo Basin) clade I that originated in the DRC and is endemic to the Central African countries, particularly in the Congo Basin region, and west African clade 2, endemic in West African countries. Clade I is generally associated with more severe disease and mortality rates as high as 11% versus 1-3% for clade II.

The animal reservoir of the virus has yet to be fully identified, but primates and rodents are implicated. Mpox occurs when a person comes into close contact with an animal, human, or materials contaminated with the virus. People who live with or have close contact (including sexual contact) with someone who has mpox, or who has regular contact with animals who could be infected, are most at risk of infection.

Since 1970s, mpox in humans has been reported repeatedly throughout Sub-Saharan Africa, including West Africa and Central Africa, with rising frequency in recent years. In May 2022, a clade

II global outbreak, resulted in nearly 100,000 cases in 117 countries. WHO declared mpox a PHEIC for the first time in July 2022 that lasted until May 2023. In August 2024, Sweden became the first country outside the African continent to confirm mpox clade I in an individual with travel history to central Africa. The confirmation of the case came just one day after WHO declared mpox a PHEIC for the second time, until September 2025.

Even if cases in children <12 years of age were uncommon during the global outbreak, they are occurring in substantial numbers in an ongoing outbreak in the DRC. In areas of the country where the disease is endemic, most suspected cases involve children under 15 years of age.

Other orthopoxviruses

In laboratories working with replicating orthopoxviruses such as vaccinia, accidental exposure of laboratory personnel is an occupational health risk. Cases of needle-stick injuries or similar accidents leading to local infections with replicating vaccinia have repeatedly been reported. In addition, there are rare case reports of other orthopoxvirus transmissions, such as human cowpox infections.

State the claimed the therapeutic indication

Cases and case fatality rates are trending upward, from 2,993 suspected cases country-wide and a 2.7% case fatality rate in 2021 to 2,609 cases in the first 8 weeks of 2024 alone and a case fatality rate of 8.4%. Therefore, there is interest and public health urgency in establishing the immunogenicity and safety of MVA-BN in the paediatric population and specifically the non-inferiority of the immune response compared to that of adults, for whom there is evidence of effectiveness against mpox from the 2022 outbreak.

Interim immunogenicity and safety data in children from 2-11 years of age from clinical study POX-MVA-045 have become available and support the administration of MVA-BN in this age group. At the time of this submission, the study is still ongoing.

2.1.2. About the product

Imvanex is a live, highly attenuated, non-replicating viral vaccine for protection against smallpox, mpox and disease caused by vaccinia virus in adults. The vaccine is a suspension for injection. One dose (0.5 mL) contains MVA-BN live virus no less than 5×10^7 infectious units.

Imvanex is manufactured based on the manufacturer's proprietary strain of the orthopoxvirus MVA-BN that is grown in chicken embryo fibroblast cells, harvested, concentrated, and purified.

Imvanex was approved under exceptional circumstances in the EU on 31 July 2013 for active immunisation against smallpox in adults. On 22 July 2022, an extension of indication to include active immunisation against mpox and disease caused by vaccinia virus in adults was approved. On 19 September 2024, an extension of indication to include active immunisation in individuals from 12 to 17 years of age was approved.

The primary vaccination schedule consists of two doses of the vaccine administered subcutaneously at interval of no less than 28 days, whereas a single dose of 0.5 mL is considered for booster vaccination whenever necessary in individuals previously vaccinated against smallpox. For immunocompromised patients, two booster doses separated by 28 days or longer should be given.

2.2. Non-clinical aspects

No new non-clinical data have been submitted in this application, which was considered acceptable by the CHMP.

2.3. Clinical aspects

2.3.1. Introduction

GCP

The clinical trials were performed in accordance with GCP as claimed by the MAH.

The MAH has provided a statement to the effect that clinical trials conducted outside the community were carried out in accordance with the ethical standards of Directive 2001/20/EC.

2.4. Clinical efficacy

2.4.1. Main study

POX-MVA-045: Open-label, multicenter, immunogenicity and safety trial of MVA-BN vaccine in children from 2 years to less than 12 years of age compared to adults for the prevention of smallpox, mpox, and related orthopoxvirus infections.

Methods

Study participants

The trial population for this trial are both paediatric (2 to <12 years of age) and adult (18 to 50 years of age) healthy volunteers in DRC and Uganda.

Eligibility criteria exclude individuals with a history of prior mpox infection or prior vaccination against smallpox. Also excluded are individuals with various conditions that could compromise participant safety or the scientific validity of the assessment of immune response. The former represents a group for whom safety of vaccination may need to be assessed in later stages of research or for whom vaccination may remain contraindicated and who may best be protected by herd immunity.

To ensure that younger children are appropriately represented in the trial, children in the lower age range of 2 to <6 years of age are targeted to comprise at least 20% of the vaccinated paediatric population. That is, enrolment in the older age subgroup will be capped to implement the minimum enrolment of 23 children in the younger age subgroup.

Treatments

The trial intervention is the standard regimen of liquid frozen MVA-BN vaccine. The investigational product was produced as Jynneos and distributed in single-dose vials. Each 0.5 mL dose is formulated to contain 0.5×10^8 to 3.95×10^8 Inf.U of MVA-BN live virus. The vaccine was administered to both the paediatric and adult cohorts at the standard dose and schedule (i.e. two vaccinations given 4 weeks apart) by subcutaneous injection into the deltoid region of the upper arm.

Objectives

Primary:

- To assess the immunogenicity of the MVA-BN standard regimen in eliciting neutralizing antibodies against the vaccinia virus in children compared to adults;
- To assess the safety and reactogenicity of the MVA-BN standard regimen in children and adults.

Secondary:

- To assess neutralizing antibody response to the MVA-BN standard regimen;
- To assess durability of neutralizing antibody response to the MVA-BN standard regimen.

Exploratory:

- To assess immunogenicity of the MVA-BN standard regimen in terms of total antibodies against monkeypox virus.

Outcomes/endpoints

Primary Endpoints:

- Titer of serum neutralizing antibodies against vaccinia virus as measured by PRNTs 2 weeks after the second MVA-BN vaccination;
- Occurrence of any:
    - SAE at any time during the trial period;
    - AESI at any time during the trial period;
    - MAAE at any time during the trial period;
    - Grade 3 or higher related AE on the day of or within 28 days after either vaccination;
    - Solicited local AE on the day of or within 7 days after either vaccination;
    - Solicited systemic AE on the day of or within 7 days after either vaccination;
    - Unsolicited AE on the day of or within 28 days after either vaccination.

Secondary Endpoints:

- Seroconversion in neutralizing antibodies as determined by vaccinia-specific PRNT at all serum sampling time points after vaccination (i.e., defined as either the appearance of antibody titer at or above the LLOQ for participants with baseline values below the LLOQ or doubling or more of the antibody titer compared to baseline for participants with a baseline antibody titer at or above the LLOQ);
- Serum neutralizing antibody titer as determined by vaccinia-specific PRNT at 6 months and 1 year after second MVA-BN vaccination.
- Titer and seroconversion in total antibodies against vaccinia virus at all serum sampling time points after vaccination, as determined by ELISA.

Sample size

Target enrolment for each age cohort (children and adults) is 230 participants. Each participant receives 2 vaccinations 4 weeks apart, with 1 year of follow-up after the second vaccination. Enrollment is projected to take 4 months, and the total trial duration from the start of enrolment until the end of participant follow-up is expected to be 19 months (i.e. 1 month for the initial screening period, 4 months to enrol the trial population, and then, for the last participant enrolled, 1 month between vaccinations, 1 year of follow-up after the second vaccination, and another month for the allowed window beyond the targeted date for the 1-year visit).

Randomisation

All participants will receive the same trial intervention (i.e., the MVA-BN standard regimen). Therefore, there is no method of assignment to trial intervention.

Blinding (masking)

Study POX-MVA-045 is open-label which is considered appropriate for the purpose of comparing GMTs in different age populations.

Statistical methods

The first primary objective, regarding neutralizing antibodies against the vaccinia virus, is the objective that will be formally tested for non-inferiority in children compared to adults. Safety is included as a second primary objective, as establishing the safety in children is essential to the trial rationale and to the generation of data that may support future emergency use in children. However, the safety endpoints will not be subjected to formal testing.

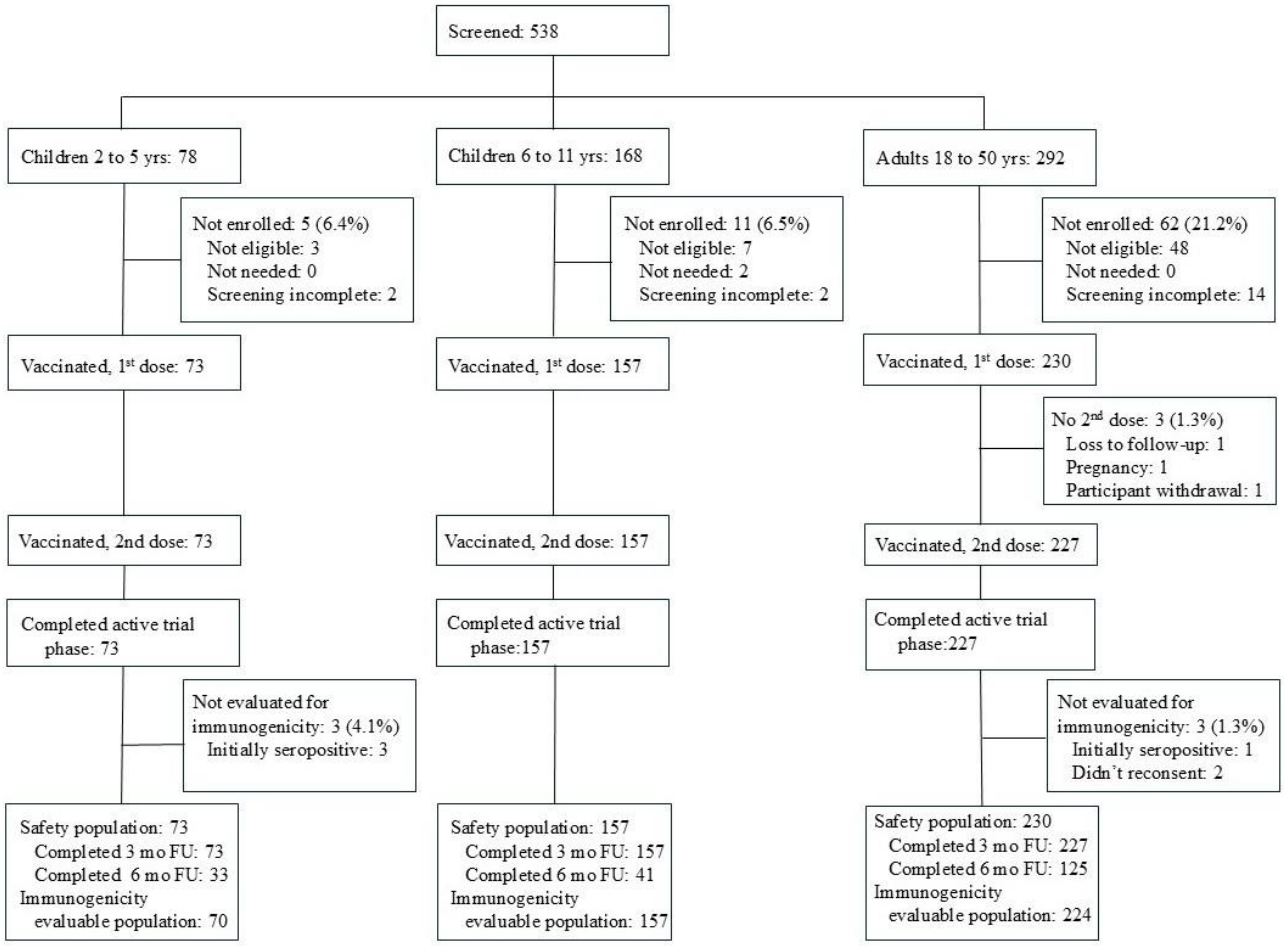
The primary estimand corresponding to the primary objective to be formally tested is defined as the GMT ratio (children / adults) in vaccinia-specific neutralizing antibody titers as measured by PRNT 2 weeks after the second dose of MVA-BN vaccine in children 2 to <12 years of age and adults who are seronegative (below the limit of quantitation) for vaccinia-specific neutralizing antibodies, irrespective of intercurrent events.

Results

Participant flow

The disposition of participants is captured in Figure 1. Most screened children (93%) were enrolled and vaccinated. For the adults, 79% were enrolled and vaccinated, as more adults either failed to meet eligibility criteria or did not complete screening. Of the 230 children enrolled, 73 (32%) were in the younger age group (2 to 5 years of age).

Figure 1: Consort Chart



Recruitment

Demographic and baseline characteristics for all 460 participants who were enrolled and received at least 1 trial vaccine (the safety population) are presented in Table 1. Among the 230 children enrolled, 155 (67%) were enrolled at 2 sites in Uganda and 75 (33%) at 1 site in the DRC. Among the 230 adult participants, 100 (43%) were from Uganda and 130 (57%) from the DRC.

Children in the younger age group had a median age of 4 years, and for those in the older group, a median age of 8 years. The adults had a median age of 30 years.

Among the children, 54% were female, while among the adult participants, 59% were male. All participants were Black. The adult participants had a median body mass index (BMI) of 22.7 kg/m2.

Table 1: Demographics and Baseline Characteristics (Safety Population)

	MVA-BN (Children)			MVA-BN (Adults)
	2-5 yrs (N=73)	6-11 yrs (N=157)	Overall (N=230)	Overall (N=230)
Age (Years)				
n	73	157	230	230
Mean (SD)	3.9 (0.99)	8.2 (1.54)	6.9 (2.46)	30.8 (8.14)
Median	4.0	8.0	7.0	30.0
Min, Max	2, 5	6, 11	2, 11	18, 49
Sex, n (%)				
Male	33 (45.2)	74 (47.1)	107 (46.5)	135 (58.7)
Female	40 (54.8)	83 (52.9)	123 (53.5)	95 (41.3)
Race/Ethnicity, n (%)				
Black/African	73 (100.0)	157 (100.0)	230 (100.0)	230 (100.0)
Other	0	0	0	0
Not Reported	0	0	0	0
Height (cm)				
n	73	157	230	230
Mean (SD)	100.3 (10.08)	126.9 (10.46)	118.4 (16.15)	166.4 (8.72)
Median	101.0	128.0	121.0	167.0
Min, Max	80, 122	99, 161	80, 161	143, 184
Body Weight (kg)				
n	73	157	230	230
Mean (SD)	15.65 (3.282)	25.64 (5.771)	22.47 (6.913)	65.13 (10.579)
Median	16.00	25.40	22.00	63.00
Min, Max	9.1, 25	14, 56	9.1, 56	43, 97.5
BMI (kg/m^2)				
n	73	157	230	230
Mean (SD)	15.44 (1.437)	15.73 (1.563)	15.64 (1.527)	23.62 (4.024)
Median	15.57	15.62	15.59	22.72
Min, Max	11.4, 18.7	12.2, 21.8	11.4, 21.8	18.5, 34.8

	MVA-BN (Children)			MVA-BN (Adults)
	2-5 yrs (N=73)	6-11 yrs (N=157)	Overall (N=230)	Overall (N=230)
Arm Length (cm)				
n	73	157	230	230
Mean (SD)	34.6 (4.66)	44.9 (5.23)	41.6 (6.94)	60.2 (4.26)
Median	34.0	45.0	42.0	60.0
Min, Max	25, 50	33, 60	25, 60	49, 73
Country, n (%)				
DRC	33 (45.2)	42 (26.8)	75 (32.6)	130 (56.5)
Uganda	40 (54.8)	115 (73.2)	155 (67.4)	100 (43.5)

Numbers analysed

The primary analysis was based on the IEP. This population is defined as all participants who had a seronegative neutralizing antibody titer result (less than the lower limit of quantitation [LLOQ]) at baseline who also: (1) received both vaccinations; (2) had evaluable serum sample results for the primary immunogenicity endpoint within an appropriate window 2 weeks after the second vaccination; and (3) had no important protocol deviation deemed exclusionary or other reason to be excluded (e.g., mpox infection) as defined prior to database lock for the interim analysis and the transfer of week 6 immunogenicity results.

The IEP also was used to analyse the secondary endpoint of seroconversion, defined for topline analyses as a seropositive (≥LLOQ) neutralizing antibody titer at week 6 in initially seronegative participants.

Supportive primary and secondary analyses were based on the modified intent-to-treat population, which more broadly included participants who were seronegative at baseline and who received at least 1 dose of trial vaccine.

Outcomes and estimation

Analysis of Immunogenicity

Primary Analysis and Supportive Analysis

The primary analysis of the IEP (see Table 2) showed that the GMT ratio (children / adults) of vaccinia-specific neutralizing antibody titers by PRNT at 2 weeks after the second MVA-BN vaccination was 2.552 (2-sided CI: 2.173, 2.998). The immune response in enrolled children was non-inferior to those of the adult participants, as the lower bound of the CI around the GMT ratio exceeded the predefined non-inferiority margin of 0.667. In fact, the GMTs for both groups of children were higher than the GMT for the adults, and the GMT ratio for the younger and older groups of children compared to the adults were 3.002 and 2.374, respectively. Both CIs for the GMT ratio excluded 1.

Table 2: Vaccinia-specific Neutralizing Antibody Titer by PRNT at 2 Weeks After Second Vaccination (Immunogenicity Evaluable Population)

	MVA-BN (Children)			MVA-BN (Adults)
	2-5 yrs (N=70)	6-11 yrs (N=157)	Overall (N=227)	Overall (N=224)
NAb Titers at Baseline				
n	70	157	227	224
GMT[a]	10.0	10.0	10.0	10.0
95% CI [LCL, UCL]	[NE, NE]	[NE, NE]	[NE, NE]	[NE, NE]
NAb Titers 2 Weeks after Second Vaccination				
n	70	157	227	224
GMT[GMTa]	618.1	488.7	525.4	205.9
95% CI [LCL, UCL]	[511.5, 746.8]	[440.8, 541.8]	[479.0, 576.3]	[180.4, 235.0]
GMT Ratio (Children / Adults)[b]	3.002	2.374	2.552	
95% CI [LCL, UCL]	[2.386, 3.777]	[2.008, 2.806]	[2.173, 2.998]	
Noninferiority Met[c]			Yes	

a Assay results below the LLOQ are included in the calculation with a value of ½ × LLOQ (ie, 10). Baseline results for all participants in this population are below LLOQ by definition.

b Comparison of GMT is performed between each children' s group (ages 2 to 5 yrs, 6 to 11yrs, and overall) and adult cohort. The mean difference is assessed on logarithmic scale using a Student's t-test, with Satterthwaite's adjustment, applied to the log10-transformed neutralizing antibody titer results. This mean difference is subsequently back transformed to the original scale by exponentiation, yielding the ratio for hypothesis testing conclusion.

c Non-inferiority testing is based on the hypothesis that H0: GMT ratio (children / adults) ≤0.667 versus H1: GMT ratio (children / adults) > 0.667, comparing the overall paediatric cohort to the adult cohort.

The supportive analysis of the mITT population included 3 additional adults at baseline but yielded the same results at 6 weeks as the primary analysis of the IEP.

Secondary Analysis and Supportive Analysis

In secondary analysis of the IEP for seroconversion in vaccinia-specific neutralizing antibodies by PRNT (see Table 3), 100% of each of the 2 groups of children had seroconverted to seropositivity by 2 weeks after the second MVA-BN vaccination. For the adult participants, 97.3% had seroconverted. Therefore, the difference between children and adults was 2.7% for each of the 2 groups of children compared to the adults. For the older group, which contained more than twice as many children as the younger group and therefore had a narrower CI, this interval excluded 0. This was the case for children overall as well.

Table 3: Seroconversion in Vaccinia-specific Neutralizing Antibody Titer by PRNT at 2 Weeks After Second Vaccination (Immunogenicity Evaluable Population)

	MVA-BN (Children)			MVA-BN (Adults)
	2-5 yrs (N=70)	6-11 yrs (N=157)	Overall (N=227)	Overall (N=224)
Participants with Available NAb Result	70	157	227	224
Seroconversion, n (%)	70 (100.0)	157 (100.0)	227 (100.0)	218 (97.3)
95% CI [LCL, UCL][a]	[94.9, 100.0]	[97.7, 100.0]	[98.4, 100.0]	[94.3, 99.0]
Difference in Seroconversion Rate (%)	2.7	2.7	2.7	
95% CI [LCL, UCL][b]	[-2.6, 5.7]	[0.3, 5.7]	[1.0, 5.7]	

a The interval estimate of seroconversion rate is based on the Clopper-Pearson Method.

b The interval estimate of the difference between seroconversion rates (children minus adults) is based on the Miettinen and Nurminen method.

The supportive analysis of seroconversion in the mITT population yielded the same results as the secondary analysis of seroconversion in the IEP.

Summary of main study

The following tables summarise the efficacy results from the main studies supporting the present application. These summaries should be read in conjunction with the discussion on clinical efficacy as well as the benefit risk assessment (see later sections).

Table 4: Summary of Efficacy for trial POX-MV-045

Title: Open-label, multicenter, immunogenicity and safety trial of MVA-BN vaccine in children from 2 years to less than 12 years of age compared to adults for the prevention of smallpox, mpox, and related orthopoxvirus infections		
Study identifier	POX-MV-045 (NCT06549530)	
Design	Open-label study to compare immunogenicity and safety in the age group 2-11 years of age to results from adults 18-50 years of age.	
	Duration of main phase:	28 Day Treatment + 14 Day FU

	Duration of Run-in phase: Duration of Extension phase:		not applicable 1 year after 2nd vaccination
Hypothesis	Non-inferiority		
Treatments groups	2-11 yoa		MVA-BN vaccination, 230 subjects enrolled
	18-50 yoa		MVA-BN vaccination, 230 subjects enrolled
Endpoints and definitions	Co-Primary endpoint	NI for GMTs	Titer of serum neutralizing antibodies against vaccinia virus as measured by PRNTs 2 weeks after the second MVA-BN vaccination.
	Co-Primary endpoint	Safety	Occurrence of any SAE, AESI, MAAE, any grade 3 or higher AE assessed as related, solicited local AE, solicited systemic AE, or unsolicited AE.
	Secondary endpoints	Immunogenicity	• Seroconversion in nAbs • nAb at 6 months and 1 year • total antibodies against vaccinia virus and seroconversion by ELISA
Database lock	Interim Analysis for results 2 weeks after 2nd vaccination.		

Results and Analysis

Analysis description	**Primary Analysis**		
Analysis population and time point description	IEP 2 weeks after 2nd vaccination (Day 42)		
Descriptive statistics and estimate variability	Treatment group	2-11 yoa (Children)	18-50 yoa (Adults)
	Number of subjects	227	224
	GMT	525.4	205.9
	95% CI	[479.0, 576.3]	[180.4, 235.0]
Effect estimate per comparison	Co-Primary endpoint: Non-Inferiority	2-11 yoa vs. 18-50 yoa	Children / Adults
		GMT Ratio	2.552
		95% CI	[2.173, 2.998]
	Secondary endpoint: Difference in Seroconversion	2-11 yoa vs. 18-50 yoa	Children / Adults
		Difference in Seroconversion rate (%)	2.7

	rate (%)	95% CI	[1.0, 5.7]
Notes	Age sub-group analyses demonstrated similar results with a trend of higher GMTs in 2-5 yoa as compared to 6-11 yoa. GMT ratios Children / Adults were 3.002 [2.386, 3.777] and 2.374 [2.008, 2.806], respectively.		
Analysis description	**Interim analysis**		

2.4.2. Discussion on clinical efficacy

In accordance with the protocol, an interim analysis was performed on the immunogenicity and safety data through 4 weeks after the second vaccination. At the time of the submission, the study was still ongoing. The top-line report was compiled using data from the locked database and included the following results:

- Primary analysis of vaccinia-specific neutralizing antibody titers by PRNT at 2 weeks after second vaccination;
- Secondary analysis of seroconversion in vaccinia-specific neutralizing antibody titers by PRNT at 2 weeks after second vaccination;
- Counts, frequencies, and grading of solicited (local and systemic) AEs from the day of each vaccination to 7 days thereafter;
- Counts, frequencies, grading, and relatedness of unsolicited AEs from the day of each vaccination to 28 days thereafter;
- Counts and frequencies of SAEs, MAAEs and AESIs serious through the time of database lock.

The trial population for this trial was both paediatric (2 to <12 years of age) and adult (18 to 50 years of age) healthy volunteers from three sites in DRC and Uganda. While the trial population does not reflect the general population in the EU, it is not expected that immunogenicity and safety results vary substantially by ethnicity and race. The study was conducted in DRC and Uganda because people in this region are at risk of acquiring mpox disease and would therefore potentially benefit from the vaccinations with MVA-BN. Therefore, study conduct in DRC and Uganda is acknowledged. Demographics and baseline data are well weighted and balanced.

The trial intervention was the standard regimen: 2 vaccinations given 28 days apart on study days 1 and 29, by subcutaneous injection).

Target enrolment for each age cohort (children and adults) was 230 participants. The size is acceptable for the non-inferiority immunogenicity comparison. Of the 230 children enrolled, 73 (32%) were in the younger age group (2 to 5 years of age) which is considered acceptable.

The first primary objective, regarding neutralizing antibodies against the vaccinia virus, is the objective that was formally tested for non-inferiority in children compared to adults which is acknowledged.

Use of the established PRNT assay against vaccinia virus for determination and comparison of GMT values is acceptable.

2.4.3. Conclusions on the clinical efficacy

The interim analysis showed that the GMTR in children versus adults of vaccinia-specific neutralizing antibody titers by PRNT at 2 weeks after the second MVA-BN vaccination was 2.552. Therefore, it was demonstrated that the immune response in enrolled children was non-inferior to those of the adult participants. The GMT ratio for the younger and older groups of children compared to the adults were 3.002 and 2.374, respectively, indicating a tendency of higher immunogenicity in the 2-5 years of age group.

2.5. Clinical safety

Introduction

Clinical safety has been presented in the clinical overview and in the interim report, comparing the safety profile of children and adults. Safety is included as a second primary objective, as establishing the safety in children is essential to support future use in children.

No specific risk beyond the known safety-profile of similar vaccines has been identified based on the available safety data. The complete data package including the final CSR and the updated RMP is expected to be submitted by 31-Jul-2027.

Patient exposure

Safety analyses included all participants who received at least 1 dose of trial vaccine. This includes 230 children and 230 adults. All children received both vaccinations. Of the adults, 3 participants did not receive the second vaccination, due to loss to follow-up, pregnancy, or participant withdrawal (see Figure 1 above).

Adverse events

Results of safety reporting are available for:

- Solicited local and systemic AEs with an onset after each vaccination and for the 7 subsequent days;
- Unsolicited AEs with an onset after each vaccination and for the 28 subsequent days;
- SAEs and MAAEs reported until the time of database lock;
- AESIs from the time of vaccination through the time of database lock

An overview of treatment-emergent AEs is presented in Table 5. AEs were common, occurring in 87% of both children and adults participating in the trial. Solicited local AEs were reported in 69% of children and 77% of adults, and grade ≥3 solicited local AEs were reported in 2.6% of children and 3.9% of adults. Solicited systemic AEs considered to be related to trial vaccine occurred in 47% of children and 56% of adults, with grade ≥3 related solicited systemic AEs reported in 3.9% and 3.5%, respectively. Unsolicited AEs considered to be related to trial vaccine were uncommon, occurring in 0.9% of children and 3.5% of adults. None of the related unsolicited events were grade ≥3, and no unsolicited AE led to withdrawal from treatment or the trial.

Up to the time of database lock, 3 children (1.3%) and 8 adults (3.5%) experienced in total 16 SAEs, but none were considered related to trial vaccine. These included 2 deaths not related to trial vaccine, 1 in a child in the group aged 6 to 11 years and 1 in an adult.

There were no AESIs. Medically attended adverse events that were considered related to trial vaccine were uncommon, but 1 event occurred in a child in the group 6 to 11 years of age, and 5 events occurred in 3 adults.

Table 5: Overview of Treatment-emergent Adverse Events (Safety Population)

	MVA-BN (Children)			MVA-BN (Adults)
	2-5 yrs (N=73) n (%) [event]	6-11 yrs (N=157) n (%) [event]	Overall (N=230) n (%) [event]	Overall (N=230) n (%) [event]
Unsolicited or Solicited TEAEs (onset day up to 28 days after either vaccination)				
Any AE (grade ≥1)	62 (84.9) [271]	139 (88.5) [561]	201 (87.4) [832]	199 (86.5) [921]
Any Related AE (unsolicited or solicited systemic)	35 (47.9) [96]	75 (47.8) [215]	110 (47.8) [311]	130 (56.5) [409]
Any Grade ≥3 AE	9 (12.3) [13]	6 (3.8) [13]	15 (6.5) [26]	16 (7.0) [27]
Any Related Grade ≥3 AE (unsolicited or solicited systemic)	6 (8.2) [9]	3 (1.9) [8]	9 (3.9) [17]	6 (2.6) [13]
Solicited TEAEs (onset day of to 7 days after either vaccination)				
Any Solicited Local AE (grade ≥1)	44 (60.3) [110]	115 (73.2) [249]	159 (69.1) [359]	178 (77.4) [391]
Any Grade ≥3 Solicited Local AE	3 (4.1) [3]	3 (1.9) [4]	6 (2.6) [7]	9 (3.9) [11]
Any Solicited Systemic AE (grade ≥1)	36 (49.3) [98]	74 (47.1) [213]	110 (47.8) [311]	130 (56.5) [404]
Any Related Solicited Systemic AE	35 (47.9) [96]	74 (47.1) [213]	109 (47.4) [309]	129 (56.1) [398]
Any Grade ≥3 Solicited Systemic AE	6 (8.2) [9]	3 (1.9) [8]	9 (3.9) [17]	8 (3.5) [15]
Any Related Grade ≥3 Solicited Systemic AE	6 (8.2) [9]	3 (1.9) [8]	9 (3.9) [17]	6 (2.6) [13]
Unsolicited TEAEs (onset day of to 28 days after either vaccination)				
Any Unsolicited AE	36 (49.3) [63]	64 (40.8) [99]	100 (43.5) [162]	80 (34.8) [126]
Any Related Unsolicited AE	0	2 (1.3) [2]	2 (0.9) [2]	8 (3.5) [11]
Any Grade ≥3 Unsolicited AE	1 (1.4) [1]	1 (0.6) [1]	2 (0.9) [2]	1 (0.4) [1]
Any Related Grade ≥3 Unsolicited AE	0	0	0	0

	MVA-BN (Children)			MVA-BN (Adults)
	2-5 yrs (N=73) n (%) [event]	6-11 yrs (N=157) n (%) [event]	Overall (N=230) n (%) [event]	Overall (N=230) n (%) [event]
Any Unsolicited AE Leading to Withdrawal from Treatment	0	0	0	0
Any Unsolicited AE Leading to Withdrawal from Trial	0	0	0	0
Serious AEs (onset any time during the trial)				
Any SAE	1 (1.4) [1]	2 (1.3) [2]	3 (1.3) [3]	8 (3.5) [13]
Any Related SAE	0	0	0	0
Any Fatal SAE	0	1 (0.6) [1]	1 (0.4) [1]	1 (0.4) [1]
AEs of Special Interest (onset any time during the trial)				
Any AESI	0	0	0	0
Any Related AESI	0	0	0	0
Medically Attended AEs (Onset at Any Time during the Trial)				
Any MAAE	49 (67.1) [107]	84 (53.5) [163]	133 (57.8) [270]	109 (47.4) [262]
Any Related MAAE	0	1 (0.6) [1]	1 (0.4) [1]	3 (1.3) [5]

Solicited local AEs include erythema, swelling, induration, pruritus and pain at injection site with onset on the day of to 7 days after either vaccination.

Solicited systemic AEs include pyrexia, headache, myalgia, chills, nausea, and fatigue with onset on the day of or within 7 days after either vaccination.

Occurrence of AESIs for this trial are defined as any of: any cardiac sign or symptom developed since the first vaccination; electrocardiogram findings determined to be clinically significant; cardiac enzyme troponin I ≥2×upper limit of normal (grade ≥2).

Toxicity is graded according to the FDA Guidance for Industry: Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in preventive Vaccine Clinical Trials (September 2007).

Unsolicited or solicited systemic AEs are considered related when the causality of corresponding trial vaccine is recorded by the investigator as "Possible", "Probable" or "Definite". In the event of a missing causality, the AE was classified as related.

TEAEs are defined as all AEs with onset after the date/time of first vaccination.

Solicited Local Adverse Events

Injection site pain occurred in 69% of children 2-11 years of age and 74% of adults and pruritus in 24% and 37%, respectively. Injection site erythema occurred in 3.2% of children and 5.7% of adults when graded according to the standard scale; the frequency increased to 11% using the paediatric scale. Injection site swelling occurred in 5.2% of children and 4.4% of adults according to the standard scale but 16% of children according to the paediatric scale. For injection site induration, 3.5% of children and 4.8% of adults experienced this AE according to the standard grading scale, but when the paediatric scale was used, the frequency in children was 10%.

Frequency of AEs tended to decrease from the first to the second vaccination period in both children and adults.

Injection site pain was somewhat more common in the older compared to the younger children (73% and 59%, respectively). The frequency in older children (6-11 years of age) was similar to that in adults.

Grade 3 solicited local AEs were uncommon in both children and adults. For injection site pain, 4 children (1.7%) and 3 adults (1.3%) had grade 3 events after at least 1 of the 2 vaccination periods, and for pruritus, 3 children (1.3%) and 6 adults (2.6%). For injection site erythema, swelling, and induration according to the standard scale, no children had grade 3 events, and grade 3 swelling and induration were reported for 1 adult (0.4%) each after the second vaccination. When graded according to the paediatric scale, 1 child (0.4%) had grade 3 erythema after the first vaccination.

Solicited systemic AEs

Solicited systemic AEs were presented for both vaccination periods for all occurrences of the AEs and for those considered related to trial vaccine.

Vaccine-related headache was most common, occurring in 30% of children and 39% of adults. Myalgia considered related to trial vaccine was reported in 22% and 28% and fatigue in 18% and 31% of children and adults, respectively. Vaccine-related nausea was reported in 16% of children and 22% of adults, while chills occurred in 19% of both groups.

Frequency of AEs tended to decrease from the first to the second vaccination period.

Pyrexia and myalgia occurred with more frequency in the children 2 to 5 years of age (11% and 26%) than in children 6 to 11 years of age (3.8% and 20%). Otherwise, solicited systemic AEs appeared to occur with similar frequency in the younger and older age groups of children. The frequency of vaccine related pyrexia in the younger children was higher than that reported for adults (4.4%) as well.

Related grade 3 solicited systemic AEs were uncommon in both children and adults. The most frequent grade 3 event was chills, which occurred in 6 children (2.6%) and 2 adults (0.9%).

Unsolicited AEs

The SOC "Infections and infestations" was most frequently associated with unsolicited AEs. Upper respiratory tract infection occurred in 13% of children and 2.6% of adults; malaria occurred in 10% of both adults and children.

Three instances of fracture (radius fracture in a child 2 to <6 years of age, forearm fracture in a child 6 to <12 years of age, and ulna fracture in an adult) were considered grade ≥3, but none of the grade ≥3 events were considered related to trial vaccine.

Other than the difference in upper respiratory tract infection, frequencies of unsolicited events were similar between children and adults. There was no discernible pattern by age group of the children or by vaccination period.

Unsolicited AEs in the active trial phase thought to be related to trial vaccine were uncommon (see table 6). Decreased appetite was seen in children 6-11 yoa and adult groups; headache was only seen in children and Dizziness only in adults.

Table 6: Related Unsolicited Adverse Events in the Active Trial Phase by System Organ Class and Preferred Term (Safety Population)

	MVA-BN (Children)			MVA-BN (Adults)
System Organ Class Preferred Term	2-5 yrs (N=73) n (%) [event]	6-11 yrs (N=157) n (%) [event]	Overall (N=230) n (%) [event]	Overall (N=230) n (%) [event]
Any Related Unsolicited Adverse Events	0	2 (1.3) [2]	2 (0.9) [2]	8 (3.5) [11]
Metabolism and nutrition disorders	0	1 (0.6) [1]	1 (0.4) [1]	1 (0.4) [1]
Decreased appetite		1 (0.6) [1]	1 (0.4) [1]	1 (0.4) [1]
Nervous system disorders	0	1 (0.6) [1]	1 (0.4) [1]	4 (1.7) [4]
Headache	0	1 (0.6) [1]	1 (0.4) [1]	0
Dizziness	0	0	0	4 (1.7) [4]
Eye disorders	0	0	0	1 (0.4) [1]
Vision blurred	0	0	0	1 (0.4) [1]
Gastrointestinal disorders	0	0	0	1 (0.4) [1]
Vomiting	0	0	0	1 (0.4) [1]
General disorders and administration site conditions	0	0	0	1 (0.4) [1]
Injection site pruritus	0	0	0	1 (0.4) [1]
Investigations	0	0	0	1 (0.4) [1]
Heart rate decreased	0	0	0	1 (0.4) [1]
Skin and subcutaneous tissue disorders	0	0	0	1 (0.4) [1]
Pruritus	0	0	0	1 (0.4) [1]
Vascular disorders	0	0	0	1 (0.4) [1]
Hypertension	0	0	0	1 (0.4) [1]

Adverse Events of Special Interest

There were no AESIs that occurred through the time of database lock.

Medically Attended Adverse Events

Among the enrolled children, 133 (58%) had 270 MAAEs; 109 (47%) of the adult participants reported 262 MAAEs. Participants tended to come to the trial site for AEs, and thus they were frequently medically attended.

The MAAEs considered to be related to trial vaccine were 0.4% for children 2-11 years of age (i.e. headache) compared to 1.3% in adults (i.e. vision blurred, heart rate decreased, dizziness, headache and injection site pruritus). None of the related MAAEs were serious or resulted in interruption of trial vaccination.

Serious adverse event/deaths/other significant events

Serious adverse events

SAEs through the time of database lock were presented for both vaccinations periods. 1.3% of the children (2-11 years of age) reported SAEs compared to the 3.5% of the adults. None of the SAEs were related to trial vaccine.

Deaths

There were 2 deaths during the study, 1 in the group of children aged 6 to 11 years due to abdominal sepsis and 1 adult due to pulmonary tuberculosis. Neither death was assessed as related to the trial vaccine. Both deaths occurred more than 100 days after the second vaccination.

Other Serious Adverse Events

Fourteen non-fatal SAEs occurred in 9 participants (2 children and 7 adults). The non-fatal SAEs were radius fracture; forearm fracture; ulna fracture and inguinal hernia; alcohol poisoning, alcohol withdrawal syndrome, typhoid fever, and sepsis; appendicitis; appendicitis and ovarian cyst; spontaneous abortion; anembryonic gestation; and foetal growth restriction. None of these SAEs were related to trial vaccine as mentioned previously.

2.5.1. Discussion on clinical safety

Adverse events

The most common local reactions were injection site pain, pruritus and swelling in all age groups. The most common systemic reactions were headache, myalgia and fatigue in all age groups. The most frequent grade 3 event was chills.

Solicited systemic AEs considered to be related to trial vaccine occurred in 47% of children and 56% of adults, with grade ≥3 related solicited systemic AEs reported in 3.9% and 3.5%, respectively. The frequency of related ≥ grade 3 solicited systemic AEs was higher in the children 2-5 year of age (8.2%) than in the children 6-11 year of age (1.9%) and in the adults (3.9%). This difference was mainly driven by the number of related ≥ grade 3 pyrexia: 4.1% for the children 2-5 year of age versus none for the children 6-11 year of age (versus 1.3% for the adults).

Unsolicited AEs considered to be related to trial vaccine were uncommon. Decreased appetite was seen in children 6-11 yoa and adult groups; headache was only seen in children and dizziness only in adults. Decreased appetite is therefore being added with frequency rare to the SmPC section 4.8 and package leaflet.

None of the related unsolicited events were grade ≥3, and no unsolicited AE led to withdrawal from treatment or the trial.

SAEs

None of the SAEs (including 2 deaths) were considered related to trial vaccine. There were 3 SAEs in the context of pregnancies. The judgement for described SAEs of not being related to trial vaccine is agreed.

There were no AESIs. Medically attended adverse events that were considered related to trial vaccine were uncommon. All events resolved without sequalae.

The type and frequency of AEs and SAEs is similar to prior studies in other age groups. The relatedness as judged by the MAH is agreed upon by the assessor. No safety issues are seen in these data. The safety profile will be further characterised when the final CSR is submitted since the study is still ongoing. As a result, a new SOB regarding the ongoing study is requested.

2.5.2. Conclusions on clinical safety

In this interim analysis of safety and reactogenicity, the type and the frequency of AEs and SAEs reported were generally similar to those seen in adults.

The following measure (SOB) is considered necessary to further characterise the safety data once the final study results are available:

In order to further characterise the safety information of Imvanex in children 2 to 11 years of age, the MAH should submit by 31-Jul-2027 the final clinical study report of study POX-MVA-045:

- Open-label, Multicenter Immunogenicity and Safety Trial of MVA-BN Vaccine in Children From 2 Years to Less Than 12 Years of Age Compared to Adults for the Prevention of Smallpox, Mpox, and Related Orthopoxvirus Infections.

2.5.3. PSUR cycle

The requirements for submission of periodic safety update reports for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

2.6. Update of the Product information

The CHMP adopted an extension of indication (section 4.1) and the updated indication is now as follows:

> *"Active immunisation against smallpox, monkeypox and disease caused by vaccinia virus in individuals 2 ~~12~~ years of age and older adults (see sections 4.4 and 5.1)*
>
> *The use of this vaccine should be in accordance with official recommendations."*

As a consequence of this extension of indication, sections 4.2, 4.8 and 5.1 have also been updated. The Package Leaflet has been updated accordingly. Annex II is updated to refer to the new specific obligation.

Please refer to Attachment 1 which includes all agreed changes to the Product Information.

2.6.1. User consultation

No justification for not performing a full user consultation with target patient groups on the package leaflet has been submitted by the MAH. However, the changes do not require user consultation with target patient groups.

3. Benefit-Risk Balance

3.1. Therapeutic Context

3.1.1. Disease or condition

After smallpox has been eradicated, mpox has become the most significant orthopoxvirus that causes infection and disease in humans. The clinical course of mpox is similar to smallpox, although milder and with a significantly lower-case fatality rate. Mpox is endemic in Western and Central Africa.

Even if cases in children <12 years of age were uncommon during the global outbreak, they are occurring in substantial numbers in an ongoing outbreak in the DRC. In areas of the country where the disease is endemic, most suspected cases involve children under 15 years of age

Other related orthopoxviruses that are known to cause human infection and disease include cowpox and replicating vaccinia virus strains. The orthopoxviruses as such are generally less virulent, relative to smallpox and mpox viruses, and disease (pox lesions) caused by such orthopoxviruses may be less frequent and shows less spread across the body.

3.1.2. Available therapies and unmet medical need

In the EU, Imvanex is a vaccine approved to protect against smallpox (2013) and mpox and disease caused by the vaccinia virus (2022) in adults, then extended to individuals 12 years of age and older (2024). Currently, there is no vaccine licensed specifically for children below 12 years of age.

3.1.3. Main clinical studies

To support the current EoI, the MAH submitted interim results of the ongoing study POX-MVA-045. This is an open-label, multicentre immunogenicity and safety trial of the MVA-BN vaccine in children from 2 years to less than 12 years of age compared to adults for the prevention of smallpox, mpox, and related orthopoxvirus infections.

Participants received 2 SC injections of standard dose of IMVANEX 0.5 mL on study days 1 and 29 (28 days apart) and were followed for a total of 365 days after the second dose.

The primary endpoint was vaccinia-specific neutralising antibody titre by PRNT at 2 weeks after administration of the second dose of the vaccine.

At the time of this submission, the study is still ongoing. The MAH is requested to submit by 31-Jul-2027 the final CSR of study POX-MVA-045.

3.2. Favourable effects

The interim analysis showed that the GMTR in children versus adults of vaccinia-specific neutralizing antibody titers by PRNT at 2 weeks after the second MVA-BN vaccination was 2.552 (2-

sided 95% CI: 2.173, 2.998). Therefore, the immune response in enrolled children was non-inferior to those of the adult participants. The GMT ratio for the younger (2 to 5 years of age) and older (6 to 11 years of age) groups of children compared to the adults were 3.002 and 2.374, respectively, indicating a tendency of higher immunogenicity in the younger group.

3.3. Uncertainties and limitations about favourable effects

Study POX-MVA-045 was conducted in 460 trial subjects in 2 sites in Uganda and 1 site in DRC. While the trial population does not reflect the general population in the EU, it is not expected that the study conclusions based on these immunogenicity and safety results will vary substantially by ethnicity and race.

3.4. Unfavourable effects

In this interim analysis of safety and reactogenicity, the type and the frequency of AEs and SAEs reported were generally similar to those seen in adults. Decreased appetite with frequency rare is added to the SmPC section 4.8 and package leaflet due the cases seen in children 6-11 yoa and adult groups.

3.5. Uncertainties and limitations about unfavourable effects

This study was conducted in 460 trial subjects. Therefore, rare adverse events are not expected to be detected.

In order to further characterise the safety information of Imvanex in children 2 to 11 years of age, the final clinical study report will be submitted by 31-Jul-2027.

3.6. Effects Table

Table 7: *Effects Table for Imvanex for active immunisation against smallpox, monkeypox and disease caused by vaccinia virus in individuals 2 to 11 years of age*

Effect	Short description	Unit	Treatment	Control	Uncertainties / Strength of evidence	References
Favourable Effects						
Geometric Mean Titre Ratio (GMTR)	Vaccinia-specific neutralizing antibody titre by PRNT at 2 weeks after second vaccination	- fold	Imvanex	adults	2.552 [95% CI: 2.173, 2.998]	Study POX-MVA-045
Unfavourable Effects						
Not applicable.						

3.7. Benefit-risk assessment and discussion

3.7.1. Importance of favourable and unfavourable effects

The interim analysis showed that the GMTR in children versus adults of vaccinia-specific neutralizing antibody titers by PRNT at 2 weeks after the second MVA-BN vaccination was 2.552 (2-sided 95% CI:2.173, 2.998). This clearly demonstrated that the GMTR in children versus adults was non-inferior.

The type and frequency of AEs and SAEs is similar to prior studies in other age groups. No safety issues are seen in these data. In order to further characterise the safety information of Imvanex in children 2 to 11 years of age, the MAH will submit by 31-Jul-2027 the final clinical study report of study POX-MVA-045.

Clinical safety analysis did not detect new safety signals.

3.7.2. Balance of benefits and risks

Taking into account that the interim analysis showed that the GMTR in children versus adults of vaccinia-specific neutralizing antibody titers by PRNT at 2 weeks after the second MVA-BN vaccination was 2.552 (2-sided 95% CI:2.173, 2.998), and therefore non-inferior to adults, the benefit risk profile of Imvanex for prevention of smallpox, mpox and disease caused by vaccinia virus in individuals 2 to 11 years of age, is considered favourable.

3.8. Conclusions

The overall B/R of Imvanex is positive.

4. Recommendations

Outcome

Based on the review of the submitted data, the CHMP considers the following variation acceptable and therefore recommends, by consensus, the variation to the terms of the Marketing Authorisation, concerning the following changes:

Variation accepted		**Type**	**Annexes affected**
C.I.6.a	C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	Type II	I, II, IIIB

Extension of indication to include the active immunisation against smallpox, monkeypox and disease caused by vaccinia virus in individuals 2 years of age and older for IMVANEX, based on interim results from study POX-MVA-045; this is an open-label, multicenter immunogenicity and safety trial of the modified vaccinia Ankara-Bavaria Nordic (MVA-BN) vaccine in children from 2 years to less than 12 years of age compared to adults for the prevention of smallpox, monkeypox, and related orthopoxvirus infections. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Annex II and Package Leaflet are updated in accordance. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI.

The variation leads to amendments to the annexes I, II and IIIB.

Amendments to the marketing authorisation

In view of the data submitted with the variation, amendments to Annexes I, II and IIIB are recommended.

This recommendation is subject to the following new condition:

Specific Obligation to complete post-authorisation measures for the marketing authorisation under exceptional circumstances

This being an approval under exceptional circumstances and pursuant to Article 14(8) of Regulation (EC) No 726/2004, the MAH shall conduct, within the stated timeframe, the following measure:

Description	Due date
In order to further characterise the safety information of IMVANEX in children 2 to 11 years of age, the MAH shall submit the final clinical study report of study POX-MVA-045: • Open-label, Multicenter Immunogenicity and Safety Trial of MVA-BN Vaccine in Children From 2 Years to Less Than 12 Years of Age Compared to Adults for the Prevention of Smallpox, Mpox, and Related Orthopoxvirus Infections.	31 July 2027

Paediatric data

In this procedure, the CHMP reviewed the available data from the study conducted in accordance with the agreed PIP EMA/PE/0000223819, namely study *POX-MVA-045.* As part of a previous procedure, the CHMP also reviewed the data from the study conducted in accordance with the agreed PIP, namely study *DMID 22-0020.* The results of these studies are reflected in section 5.1 of the Summary of Product Characteristics (SmPC) and, as appropriate, the Package Leaflet. Further, these results were pivotal in supporting the new indication of active immunisation against smallpox, monkeypox and disease caused by vaccinia virus in individuals 2 years of age and older.

5. EPAR changes

The EPAR will be updated following Commission Decision for this variation. In particular the "EPAR-Procedural steps taken and scientific information after authorisation" will be updated as follows:

Scope

Please refer to the Recommendations section above.

Summary

Please refer to Scientific Discussion EMA/VR/0000337204

Attachments

1. Product information (changes highlighted) as adopted by the CHMP on 25 June 2026.