Date: 15 November 2024

DIRECT HEALTHCARE PROFESSIONAL COMMUNICATION

IMVANEX suspension for injection
Smallpox and mpox vaccine (Live Modified Vaccinia Virus Ankara)
Modified Vaccinia Ankara – Bavarian Nordic Live virus no less than 5 x 10^7 Inf.U
Interim Supply of EU Stock to Mitigate Supply Disruption

Dear Healthcare Professional,

Summary: Bavarian Nordic A/S is currently experiencing a supply disruption with Imvanex (MVA-BN, 0.5 ml suspension for injection) in the UK (Great Britain and Northern Ireland).

To ensure continuity of supply, Bavarian Nordic A/S has obtained approval from the MHRA to supply EU Imvanex product (batch number FDP00624; batch size: 50,000 doses), which is expected to be on the UK market from 30-Nov-2024 to 31-Aug-2033 (when stored at -80°C)

Please note the following:

- This product is considered licensed in the UK.
- The product from EU has the same **formulation** as the UK product.
- The product from EU is manufactured according to the same **manufacturing process and quality controls** as the UK product.
- There are **differences in labelling** between the EU and UK product information.
  Key differences are:
  SmPC:
  section 4.1: Active immunisation against smallpox, monkeypox and disease caused by vaccinia virus in individuals 12 years of age and older (see sections 4.4 and 5.1).
  section 4.2: *Paediatric population*
  The safety and efficacy of IMVANEX in children below 12 years have not been established. No data are available.
  section 4.8: *Paediatric population*
  Adolescents 12-18 years
  Interim data from the currently ongoing study DMID 22-0020 suggest a mainly similar safety-profile in adolescents as in adults. The study enrolled 315 adolescents. Data up to Study Day 57 are considered clean. More than 99% received two vaccination doses.

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According to the current database, the most frequent injection site reaction was injection site pain (> 70%), and the most frequent systemic adverse reactions were fatigue (> 50%) and headache (50%).

Section 5.1:

Table 1 Seroconversion rates by PRNT in Vaccinia-naïve healthy (including adults and adolescents aged 12 to 17 years) and special populations

SCR - PRNT			Day 7/14[1]	Day 28[1]	Day 42[1]
Studies in adults					
Study	**Health Status**	**N**	**SCR % (95% CI)**	**SCR % (95% CI)**	**SCR % (95% CI)**
POX-MVA-005[2]	Healthy	183	45.1 (37.7, 52.6)	56.7 (49.1, 64.0)	89.2 (83.7, 93.4)
POX-MVA-008[3]	Healthy	194	5.4 (2.6, 9.8)	24.5 (18.6, 31.2)	86.6 (81.0, 91.1)
	Atopic Dermatitis	257	5.6 (3.1, 9.3)	26.8 (21.4, 32.7)	90.3 (86.0, 93.6)
POX-MVA-009[4]	Healthy	66	12.1 (5.4, 22.5)	10.6 (4.4, 20.6)	82.5 (70.9, 90.9)
POX-MVA-011[2]	Healthy	88	11.1 (5.2, 20.0)	20.9 (12.9, 31.0)	77.2 (66.4, 85.9)
	HIV	351	15.7 (11.9, 20.1)	22.5 (18.1, 27.4)	60.3 (54.7, 65.8)
POX-MVA-013[2]	Healthy	2119[6]	N/A[5]	N/A[5]	99.8 (99.5; 99.9)
Study in adolescents (12 to 17 years) and aduls (18 to 50 years) – data from interim analysis					
DMID 22-0020[7]	Adolescents (Arm 5)	310	N/A[5]	82.6 (77.9, 86.6)	99.0 (97.1, 99.8)
	Healthy adults (Arms 3 and 4) [8]	210	N/A[5]	75.2 (68.8, 80.9)	97.6 (94.5, 99.2)
	Healthy adults (Arm 4 only) [8]	134	N/A[5]	76.9 (68.8, 83.7)	97.7 (93.5, 99.5)

[1]Day 7/14 corresponding to 1 or 2 weeks after the first IMVANEX dose (analysis time point at day 7 only in studies POX-MVA-008 and POX-MVA-011; POX-MVA-005 had the first post vaccination analysis at day 14); day 28 corresponding to 4 weeks after the first IMVANEX dose; day 42 corresponding to 2 weeks following the second dose of IMVANEX; SCR = Seroconversion rate; PRNT = plaque reduction neutralisation test; ELISA = enzyme-linked immunosorbent assay using MVA as an antigen [2]

Full Analysis Set (FAS) (for POX-MVA-013: Immunogenicity Analysis Set; IAS); [3] Per Protocol Analysis Set (PPS), [4] seropositivity rates, [5] no immunogenicity sample taken, [6] combined Groups 1-3; [7] Number of participants in the mITT population [8] Arms 3 and 4 were combined as a comparator group in the primary analysis.

Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with IMVANEX in one or more subsets of the paediatric population for prevention of smallpox, monkeypox and disease caused by vaccinia virus by active immunisation against smallpox, monkeypox and disease caused by vaccinia virus infection and disease (see section 4.2 for information on paediatric use).

A study in adolescents (DMID 22-0020[7]) is currently ongoing with immunogenicity data up to Study Day 43 (14 days Post Dose 2) already available. The results of the primary endpoint show non-inferiority regarding antibody response of adolescents to adults in the vaccinia specific neutralization assay.

Table 2 Vaccinia Virus Specific PRNT Primary Hypothesis Testing, mITT Population

Hypothesis	Statistic	Adolescents (N=313)	Adults[c] (N=211)	Adults - Arm 4 Only (N=135)
At Day 43 the humoral immune response in adolescents is non-inferior to adults, as assessed by Vaccinia specific PRNT GMT	n	304	208	132
	GMT (95% CI)	470.3 (422.3, 523.8)	293.2 (249.8, 344.2)	295.7 (240.8, 363.2)
	GMTR (95% CI)	N/A	1.60 (1.32, 1.95)	1.59 (1.26, 2.00)
	p-value[a]	N/A	<0.001	<0.001
	Non-inferiority result[b]	N/A	Yes	Yes

N = Number of participants in the mITT Population; n = Number of participants with data at time point;
GMT = Geometric mean titer; GMTR = Geometric mean titer ratio of adolescents to adults;
CI = Confidence Interval, calculated using Student's t distribution for GMT and Welch-Satterthwaite t test for GMTR.
[a] Two-sample t-test with unequal variance, non-inferiority (NI) margin of 0.67 and two-sided type I error rate of 0.05 to test the null hypothesis that humoral immune response in adolescents will be noninferior to adults.
[b] If the lower bound of the GMTR 95% CI is greater than or equal to 0.67 (NI=0.174 log10 scale) prior to rounding, the result is "Yes".
[c] Arms 3 and 4 were combined as a comparator group in the primary analysis. Arm 3 participants were excluded for a sensitivity analysis.

PIL:

Section 1: IMVANEX is a vaccine used to prevent smallpox, monkeypox and disease caused by vaccinia virus in adults and adolescents aged 12 years and older.

- Please refer to the UK-Imvanex Patient Information Leaflet (PIL) supplied together with each vial.
- In addition, you can access the EU-Imvanex PIL in English electronically via QR-code on the EU outer cartons.
- The UK SmPC and PIL is also available on the MHRA website: https://products.mhra.gov.uk/product/
- For additional copies of the UK-leaflet, please use the one on the MHRA side or contact the company contact point (see below).
- The MHRA has agreed to an exemption granted in accordance with regulation 266(4)(a) and (b) of the Human Medicines Regulations (HMR) 2012 and Article 63(3) of Council Directive 2001/83/EC, from the obligation that certain particulars should appear on the outer and immediate packaging of Imvanex suspension for injection and that the information must be given in English.

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Please ensure all relevant staff are made aware of the content of this letter and that the information is communicated to the patients.

Call for reporting
Please continue to report suspected adverse drug reactions (ADRs) to the MHRA through the Yellow Card scheme.

Please report:

- all suspected ADRs that are serious or result in harm. Serious reactions are those that are fatal, life-threatening, disabling or incapacitating, those that cause a congenital abnormality or result in hospitalisation, and those that are considered medically significant for any other reason
- all suspected ADRs associated with new drugs and vaccines identified by the black triangle ▼

You can report via:

- the Yellow Card website
- the free Yellow Card app available from the Apple App Store or Google Play Store
- some clinical IT systems (EMIS/SystmOne/Vision/MiDatabank) for healthcare professionals

Alternatively, you can report a suspected side effect to the Yellow Card scheme by calling 0800 731 6789 for free, Monday to Friday between 9am and 5pm.

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, timing onset, treatment dates, and product brand name.

- Imvanex▼ is subject to additional monitoring. This will allow quick identification of new safety information
- Please report ANY suspected adverse drug reactions (ADRs) to drugs and vaccines identified by the black triangle▼ to the MHRA through the Yellow Card Scheme.

Additionally, when providing patients with details of the vaccine administered, it is good practice to give them details of the brand and batch number. This will allow patients and carers to more accurately report suspected ADRs to the Yellow Card scheme.

Company contact point

If you have any questions about this letter or require more information about Imvanex please contact Bavarian Nordic Philip Heymans Alle 3, 2900 Hellerup Denmark, Service Tel.: 004533268383, Email: medical.information_eu@bavarian-nordic.com or https://www.bavarian-nordic.com/.

Signed by:

Yours faithfully,

Signer Name: Ralph Torgler
Signing Reason: I approve this document
Signing Time: 10-Jan-2025 | 07:38 CET

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