National Immunisation Advisory Committee

MONKEYPOX VACCINATION

NIAC | 27.05.2022

About NIAC

NIAC membership includes nominees from the RCPI, its Faculties and Institutes, the RCSI, the ICGP, the National Immunisation Office, the Nursing and Midwifery Board of Ireland, the Infectious Diseases Society of Ireland, the Travel Medicine Society, the National Virus Reference Laboratory and lay members. Meetings are attended by representatives from the Department of Health and the HSE. Representatives of the Health Products Regulatory Agency attend to provide regulatory advice in relation to vaccines.

NIAC considers new evidence about vaccines and provides advice to the Chief Medical Officer and the Department of Health. The Department and the Minister for Health make policy decisions on vaccines which are implemented by the HSE.

RECOMMENDATIONS

a) Pre exposure prophylaxis for healthcare workers (including domestic staff etc.)

All healthcare workers (including domestic staff etc.) should follow recommended infection protection control (IPC) measures. Where possible, healthcare workers (including domestic staff etc.) who are immunocompromised or pregnant should not directly care for suspected or confirmed monkeypox cases.

Whilst the priority is to ensure appropriate IPC measures are followed, Imvanex may provide additional protection depending on the nature and timing of exposure risk. Designated healthcare and laboratory staff (including domestic staff etc.) who will be involved in the management of monkeypox cases or their samples should be offered two 0.5 ml doses of Imvanex 28 days apart. Those who have had previous smallpox vaccination only require one 0.5 ml dose.

b) Post exposure prophylaxis for contacts

High and intermediate risk contacts (as defined by HPSC) within four days of exposure to a laboratory confirmed case should be offered one 0.5 ml dose of Imvanex. This may include healthcare workers (including domestic staff, etc.) caring for the case, and other contacts who have not previously been vaccinated.

If there is a likelihood of ongoing exposure, a second dose should be given at least 28 days after the first.

c) Prioritisation

If vaccines supplies are sufficient, pre and post exposure prophylaxis should be offered as above.

If vaccine supplies are limited, priority should be given to the groups in the following order:

i. High risk contacts within 4 days of exposure
ii. Intermediate risk contacts within 4 days of exposure
iii. High and intermediate risk contacts between 5 and 14 days of exposure
iv. Pre-exposure prophylaxis following individual risk assessment.

d) Prior to vaccination

Vaccine recipients should be informed that this vaccine is being used off label and given comprehensive information about the disease, the risks of contracting it, and the benefits and risks of the vaccine. They should also be informed that they may develop adverse reactions similar to the prodromal symptoms of monkeypox infection during the first 48 hours after vaccination.

e) Children

As monkeypox may cause severe disease in children, the vaccine may be considered for use in children at increased risk following an individual risk assessment.

1. EXECUTIVE SUMMARY

These recommendations reflect a dynamic vaccination programme strategy. Scientific evidence about the use of vaccines in the 2022 monkeypox outbreak is emerging and being refined. Recommendations may be updated when more information becomes available.

- The epidemiology of monkeypox has been changing with an increase in detected cases, possibly contributed to by the cessation of smallpox vaccination with subsequent waning of immunity, and other factors including deforestation, disruption of animal habitats, increase in population mobility and possible genetic evolution of the virus.
- The 2022 outbreak involving many countries is under investigation. While the index case in the UK had a travel history, linkage to other cases is not clear although linked cases within the outbreak have been identified.
- The majority of cases have been mainly, but not exclusively, in those who have self-identified as gay, bisexual or men who have sex with men (gbMSM).
- While most cases in this outbreak have been mild and self limited, severe disease and death can occur. The disease may be more severe in young children, pregnant women, older persons and those with severe immunocompromise, especially if related to HIV.
- Smallpox (vaccinia) vaccines are effective against monkeypox. Imvanex, an attenuated non-replicating vaccinia virus is licensed in the US and Canada for prevention of smallpox and monkeypox, and in Europe by the EMA for prevention of smallpox.
- Imvanex has been used in Europe for pre and post exposure prophylaxis against monkeypox. The vaccine can prevent the onset of symptoms if given within four days of exposure. If given between 5-14 days after the date of exposure, it may reduce the symptoms but may not prevent the disease.
- Monkeypox in pregnancy can be associated with adverse outcomes including fetal death.
- Consideration may be given to using Imvanex, a non replicating vaccine, in pregnancy and during breastfeeding for those at increased risk following individual benefit risk assessment.
- As monkeypox may cause severe disease in children, Imvanex may be considered for use in children at increased risk following an individual risk assessment. Although the vaccine is not authorised for use in those aged under 18 years, adverse events are expected to be similar to those in adults based on clinical trials of vaccines using similar platforms.

2. BACKGROUND

Monkeypox is a zoonotic disease caused by an orthopoxvirus that results in a smallpox-like disease in humans. Monkeypox virus belongs to the *Orthopoxvirus* genus in the family *Poxviridae*. The *Orthopoxvirus* genus also includes variola virus (which causes smallpox), vaccinia virus (used in the smallpox vaccine), and cowpox virus.

Monkeypox was first discovered in 1958 when two outbreaks of a pox-like disease occurred in monkeys kept for research.[1] The first human case was recorded in 1970 in the Democratic Republic of the Congo (DRC), and since then the infection has been reported in a number of central and western African countries Most cases are reported from the DRC and Nigeria.

Monkeypox cases have occurred outside of Africa, generally related to international travel. In 2003, monkeypox was recorded in the US when an outbreak occurred in humans and pet prairie dogs following importation of rodents from Africa.[2] The human infections followed contact with an infected pet and all patients recovered. No other country outside West and Central Africa has reported similar outbreaks.

On 7 May 2022, monkeypox was identified in the UK in a person with a recent travel history to Nigeria. Since then, more than 100 cases have been reported in non-endemic countries without a history of travel to Africa. Subsequently the majority of cases in the UK have been mainly but not exclusively in those who have self-identified as gay, bisexual or other man who has sex with men (gbMSM). It is likely that cases will become more widespread and involve more countries.

These recommendations are made in anticipation that there may be individuals in Ireland who have contracted or been exposed to the virus and health care workers at risk of occupational exposure.

3. EPIDEMIOLOGY

Monkeypox is indigenous to the rainforests of Central and West Africa. The number of human monkeypox cases has been increasing since the 1970s, with the most dramatic increases occurring in the DRC where it is now endemic.[3] This is possibly due to the cessation of smallpox vaccination and subsequent waning of immunity and other factors including deforestation, disruption of animal habitats, increase in population mobility and possible genetic evolution of the virus.

There are two clades (strains) of monkeypox, i.e., Central African and West African strain. A recent systematic review reported a case fatality rate of 10.6% for the Central African strain and 3.6% for the West African strain in a Nigerian population.[3] The West African lineage is generally associated with milder disease and is responsible for the 2022 outbreak.

Males are more commonly affected and the median age at presentation had increased from 4 (1970s) to 21 years (2010-2019). Commonly reported occupations included traders, students,

artisans, healthcare professionals, farmers, hunters and transport workers. Eating inadequately cooked meat and other animal products of infected animals is a possible risk factor.

The natural reservoir of monkeypox has not yet been identified, though rodents are the most likely hosts.

While most cases in this outbreak have been mild and self limited, severe disease and death can occur. The disease may be more severe in young children, pregnant women, older persons and those with severe immunocompromise, especially if related to HIV.

Transmission

Monkeypox is not very infectious – it usually requires close unprotected physical contact with a symptomatic individual for transmission to occur. Transmission can occur through direct contact with the virus from an animal human or other source, e.g., preparation or ingestion of bush meat or contact with bedding contaminated with the virus. The virus enters the body through broken skin, respiratory tract, or mucous membranes (eyes, nose, or mouth).

Person-to-person transmission is thought to occur primarily through large respiratory droplets that generally cannot travel more than one to two metres, or close household or sexual contact. Close household or sexual contact poses the greatest risk of person-to-person spread, particularly direct contact with skin lesions. Transmission can also occur from mother to fetus. The risk of spread within the community is very low. For further information refer to the HPSC guidance.

4. CLINICAL FEATURES

The incubation period is 6-14 days (range 5-21 days). Initial symptoms include fever (38.5-40.5^{o}C), malaise, intense headache, lymph node enlargement, back pain, myalgia and intense weakness.[4] The rash appears within 1 to 10 days of development of fever, usually beginning on the face and then spreading to other parts of the body.[4] The lesions seen in monkeypox are similar to those of chickenpox. The whole process can last for 2-4 weeks. For further information refer to the HPSC guidance.

5. VACCINE

Imvanex is authorised by the European Medicines Agency for active immunisation against smallpox in adults. Smallpox is caused by the vaccinia virus. Imvanex contains a live non-replicating form of vaccinia called ‘vaccinia Ankara’. It does not cause disease in humans and cannot replicate in human cells.

This vaccine is authorised in the US (as JYNNEOS) and in Canada (as Imvamune)[5] for the prevention of smallpox and monkeypox disease in adults aged 18 years and older determined to be at high risk for smallpox or monkeypox infection.

Previous smallpox vaccines have been shown to be 85% effective in preventing monkeypox in close contacts.[6] Because monkeypox virus is closely related to smallpox virus, Imvanex can protect people from monkeypox. Data from animal models shows high efficacy of Imvanex against monkeypox and high immunogenicity in humans compared to another smallpox vaccine.[7] Vaccination with Imvanex after monkeypox exposure may help prevent the disease or make it less severe. Imvanex has been used in Europe for pre and post exposure prophylaxis against monkeypox. The vaccine can prevent the onset of symptoms if given within four days of exposure. If given between 5-14 days after the date of exposure, it may reduce the symptoms but may not prevent the disease.[8]

Imvanex is given subcutaneously in the deltoid region. The authorised schedule is two 0.5 ml doses 28 days apart for those who have not had smallpox vaccination. Those who have had previous smallpox vaccination only require one 0.5 ml dose. A person is fully immunised two weeks after the second dose. The most common side effects (which may affect 1 in 10 people or more) are fatigue, injection site erythema, pain, induration, pruritus, redness and swelling, headache, myalgia and nausea. Similar rates of side effects are seen after either dose. Those with atopic dermatitis develop more local and general symptoms after vaccination. Details of all side effects can be found in the Summary of Product Characteristics.

Imvanex is contraindicated in those who have had anaphylaxis to previous doses of the vaccine and any of the vaccine constituents.

There are limited data on the use of Imvanex in pregnancy. However, animal studies do not indicate harmful effects regarding reproductive toxicity. There is no theoretical reason for concerns in pregnancy and the adverse events profile would be expected to be similar to that in non-pregnant vaccinees. A benefit risk assessment should be carried out prior to vaccination.

The use of this vaccine during breast-feeding is not contraindicated. Individuals who are breast feeding and who may have significant exposure should be offered vaccination, after a benefit risk assessment.

The vaccine can be used for vaccination of people 18 years and older with certain immune deficiencies or conditions, such as HIV or atopic dermatitis although the immune response may be lower.

6. INTERNATIONAL RECOMMENDATIONS

Recommendations regarding the use of Imvanex for monkeypox in this outbreak have been made by the WHO[9,10], ECDC[11], UK[12] and others.

7. DISCUSSION

The first case of monkeypox has been confirmed in Northern Ireland. Further cases in Ireland are anticipated. It is very early in this outbreak and the evolution is uncertain. Human to human transmission of monkeypox can occur and while in most cases disease is mild and self-limited, there is potential for serious morbidity and death. Thus, when possible, those who have had a high/intermediate risk exposure and those at occupational risk of exposure should be offered Imvanex vaccination following benefit risk assessment.

8. RECOMMENDATIONS

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