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Yellow fever vaccine: stronger precautions in people with weakened immunity and those aged 60 years or older

This letter informs you of the recommendations of a Commission on Human Medicines (CHM) review of serious and fatal reactions following yellow fever vaccine and strengthened measures to minimise risk in those with weakened immune systems, and in particular those aged 60 years or older and anyone who has had their thymus removed.

Two risks unique to yellow fever vaccine are viscerotropic disease (YEL-AVD) and neurotropic disease (YEL-AND), which both resemble yellow fever infection. These are very rare but can be fatal. These side effects are more likely to occur in certain groups, particularly people with a weakened immune system and people aged 60 years or older. The risks of YEL-AND and YEL-AVD are estimated to be up to 1 per 100,000 primary vaccinees, although this risk is may be 4 or more-fold greater in those aged 60 years or older.

The CHM convened a Yellow Fever Vaccine Expert Working Group to re-evaluate the benefit-risk balance of yellow fever vaccine. The CHM found the balance between benefits and risks of yellow fever vaccine remains favourable for most travellers when used as indicated but updated its recommendations to minimise risks to vaccinees.

- **In people aged 60 years or older**, due to a higher risk of life-threatening side effects, the vaccine should be given only when there is a **significant and unavoidable risk** of acquiring yellow fever infection, such as travel to an area where there is a current or periodic risk of yellow fever transmission
 - this would exclude travel to areas in which vaccination is 'generally not recommended' by WHO
- **Only healthcare professionals specifically trained** in benefit-risk evaluation of yellow fever vaccine should administer the vaccine, following their individualised assessment of a person's travel itinerary and suitability to receive the vaccine
- **Do not administer** the vaccine to people:
 - who have had their thymus gland removed for any reason
 - who are taking biological drugs that are immunosuppressive or immunomodulating
 - who have a first-degree family history of YEL-AVD or YEL-AND following vaccination that was not related to a known medical risk factor (i.e. in case of an unidentified genetic predisposition).

Thoroughly inform vaccinees about the early signs and symptoms of these side effects and to urgently seek medical attention if these side effects are suspected – this will support rapid identification and referral for treatment of YEL-AND and YEL-AVD. **The manufacturer's patient information leaflet** should be given to everyone receiving a yellow fever vaccine as part of the travel consultation.

The above recommendations are in addition to the full list of contraindications and precautions described in the current Summary of Product Characteristics and patient information leaflet, which will be updated in due course. Standardised pre-vaccination screening checklists are also being produced, along with a patient group direction (PGD) template. A further communication will be issued when these are ready to ensure they are implemented in clinical practice. An article will be published in the MHRA's Drug Safety Update (<https://www.gov.uk/drug-safety-update>) with a detailed assessment report and more information about the risks and manifestation of YEL-AVD and YEL-AND.

Reporting incidents

Any suspected adverse reactions associated with the yellow fever vaccine should be reported to the Yellow Card Scheme (<https://www.gov.uk/yellowcard>). The batch number should be included in any reports about a vaccine.

The batch number, in addition to the statutory patient information leaflet, should be provided to all patients receiving a yellow fever vaccine to ensure they are able to report suspected adverse drug reactions to the Yellow Card Scheme directly.

Other incidents, including medication errors should be reported via local reporting methods. Incidents involving the yellow fever vaccine in England, Wales and Northern Ireland should be reported to NaTHNaC and incidents in Scotland should be reported to Health Protection Scotland.

Dr June Raine

CEO, Medicines & Healthcare products
Regulatory Agency (MHRA)

Dr Dipti Patel

Director, National Travel Health Network and Centre
(NaTHNaC)

Dr Mary Ramsay

Head of Immunisation
Public Health England

Dr Kali Perrow

Medical Lead, Travel and International Health
NHS National Services Scotland, Health Protection Scotland