

## **ATAGI recommendation for using 2 doses of currently approved rabies vaccines for rabies pre-exposure prophylaxis (PrEP) vaccination in people indicated to receive rabies PrEP vaccination**

### **Recommendation**

A 2-dose pre-exposure prophylaxis (PrEP) schedule of currently approved rabies vaccines is recommended as an alternative vaccination schedule to 3 doses of currently approved human diploid cell vaccine (HDCV) and purified chick embryo cell vaccine (PCECV) rabies vaccines in people indicated to receive rabies PrEP vaccination.

### *Additional considerations*

- There are four options for administering pre-exposure prophylaxis, varying by schedule length, number of doses and route of administration. There is no preferential recommendation for choosing a schedule and route of administration. Consideration should include a person's circumstances and personal preferences.
- The recommended 3-visit pre-exposure prophylaxis schedule comprises 3 vaccine doses, given at days 0, 7 and 21–28. These can be given by either the intramuscular or the intradermal route.
- The recommended 2-visit pre-exposure prophylaxis schedule given by the intramuscular route comprises 2 vaccine doses, given at days 0 and 7. The recommended 2-visit pre-exposure prophylaxis schedule given by the intradermal route comprises 4 vaccine doses, given as 2 × 0.1 mL injections given at different sites on both day 0 and day 7.
- Do not use 2-visit schedules in people who are immunocompromised, as the immune response may not be adequate. Do not use the 2-visit intradermal schedule in adults >50 years of age, because studies show that seroconversion is less likely to occur in this age group than in younger people.
- These 2-visit schedules provide short-term protection, which is particularly beneficial for travel to rabies-zoonotic areas. If further protection is required after 1 year, a single intramuscular booster dose should be given 1 year after the 1st dose of pre-exposure prophylaxis, regardless of the administration route for the original pre-exposure prophylaxis course.
- Recommendations and advice regarding booster doses of rabies vaccine remain unchanged.

### **Justification**

There is evidence that 2 doses of PrEP of currently approved HDCV and PCECV rabies vaccines are comparable to 3 doses of HDCV or PCECV rabies PrEP for both safety and immunogenicity outcomes.

2 doses of currently approved HDCV or PCECV rabies PrEP may result in little to no difference in rabies virus neutralising antibody (RVNA) seroconversion rates at 7 or more days after the last rabies vaccine PrEP dose, compared to 3 doses of HDCV or PCECV rabies PrEP. The evidence is very uncertain for RVNA seroconversion rates  $\geq 365$  days following rabies PrEP vaccination. Randomised controlled trials to measure the efficacy of rabies vaccines are not possible, and the evidence is therefore reliant on

immunogenicity outcomes. There may be an extent to which immunologic ‘correlates of protection’ may not fully predict protection.

There is likely little to no difference in the frequency of vaccine-related serious adverse events for 2 doses of currently approved HDCV or PCECV rabies PrEP, compared to 3 doses of HDCV or PCECV rabies PrEP. However, 2 doses of PrEP of currently approved HDCV or PCECV rabies vaccines likely slightly reduces total local and systemic adverse events compared to 3 doses of HDCV or PCECV rabies vaccines.

The certainty of evidence that 2 doses of PrEP of currently approved HDCV or PCECV rabies vaccines are comparable to 3 doses of HDCV or PCECV rabies vaccines is low overall, mainly due to imprecision from small study numbers and possible risk of bias in the observational studies. The body of evidence suggests that the overall balance of desirable and undesirable effects of 2 doses of PrEP of currently approved HDCV or PCECV rabies vaccines are comparable to 3 doses of HDCV or PCECV rabies vaccine PrEP schedules.

Incorporating a 2-dose rabies PrEP schedule of currently approved HDCV or PCECV rabies vaccines into the current rabies PrEP schedule is likely both acceptable and feasible to key stakeholders. In cases where it is difficult to ensure 3 doses are administered before travel or work, implementing a shorter 2-dose series will be easier to implement and is feasible. The simpler and less expensive 2-dose vaccine schedule may be more acceptable to populations recommended for rabies PrEP vaccination and clinical providers.