



Conditions for use of long-lasting insecticidal nets treated with a pyrethroid and piperonyl butoxide

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RECOMMENDATIONS

BACKGROUND

Long-lasting insecticidal nets (LLINs) treated with a pyrethroid insecticide and the synergist piperonyl butoxide (PBO) have become available. Two of these nets (Olyset®Plus and PermaNet®3.0) have a WHO Pesticide Evaluation Scheme (WHOPES) interim recommendation as LLINs.¹ These nets are now undergoing WHOPES phase III evaluation to inform a decision on giving full recommendation of their use. One of these nets (Permanet®3.0) was reviewed by the WHO Vector Control Advisory Group.²

PBO is not an insecticide by itself, but acts by inhibiting certain metabolic enzymes (e.g. mixed-function oxidases) within the mosquito. These enzymes detoxify or sequester insecticides before they can have a toxic effect on the mosquito. Therefore, a PBO LLIN would in theory have an increased killing effect on malaria vectors that harbour such resistance mechanisms compared to a pyrethroid treated LLIN. However, the entomological and epidemiological impact of PBO LLINs is expected to vary according to the bioavailability and retention of PBO,³ and the level, intensity and mechanisms of insecticide resistance for local vectors, as well as across different transmission settings.

The evidence base of PBO LLINs, and the conditions that govern their use under field conditions, was recently reviewed by a WHO/GMP Evidence Review Group (ERG), with input from the Malaria Vector Control Technical Expert Group and the WHO's Malaria Policy Advisory Committee. Details of the review process, quality of the evidence, outstanding questions, and efforts to further strengthen the current evidence, are found in the ERG meeting report.⁴

RECOMMENDATIONS

On the basis of the current evidence, WHO concludes and recommends the following:

1. While PBO LLINs appear to have an increased efficacy in certain settings, at this point, the evidence is still limited to justify a complete switch from pyrethroid-only LLINs to PBO LLINs across all settings.
2. PBO LLINs with a WHOPES interim or full recommendation can be considered to be at least an equivalent option to other LLINs in all settings, and probably superior in some settings. However, there is neither evidence to assume their higher efficacy nor greater utility in a resistance management strategy in all settings.
3. PBO LLINs should be used only where universal coverage with effective vector control (LLINs and/or indoor residual spraying – IRS) of populations at risk of malaria will not be reduced, as PBO LLINs may be more expensive than pyrethroid-only LLINs.
4. Due to the potential for an antagonistic effect between PBO and organophosphates, PBO LLINs should not be used in areas programmed for IRS with pirimiphos-methyl CS. Further data to confirm or disprove any antagonistic effect should be collected promptly.
5. In order to build the evidence base that would support accelerated deployment of PBO LLINs, pilot “exploratory” implementation is necessary. However, it should only be undertaken in areas where prevalence of malaria in children aged 2–10 years is > 20% and mosquito mortality in bioassay with pyrethroids is < 80%. Pilot implementation should not be undertaken unless it is accompanied by robust evaluation.
6. In order to guide potential deployment of PBO LLINs, countries considering pilot exploratory implementation should be supported to:
 - (i) collect data on the presence, level, intensity and mechanisms of resistance to all insecticide classes at representative sentinel sites;
 - (ii) design an evaluation with appropriate indicators based on detailed guidance.
7. To manage insecticide resistance, in addition to the rotational use of insecticides with different modes of action in IRS, WHO urgently calls for the development and evaluation of non-pyrethroid LLINs and other innovative vector control tools for use across all settings.

These recommendations will be revised periodically, on the basis of emerging evidence.

ENDNOTES

The mention of specific companies or of certain manufacturers’ products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

1. WHO recommended long-lasting insecticidal nets (http://who.int/whopes/Long-lasting_insecticidal_nets_November_2015.pdf).
2. WHO (2014) Second meeting of the Vector Control Advisory Group. Summary report. Geneva (http://apps.who.int/iris/bitstream/10665/137318/1/9789241508025_eng.pdf)
3. In one product (PermaNet®3.0), in WHOPES studies, PBO was no longer bioavailable after 10 washes, although high content of PBO was retained by the net fibres after up to 20 washes. (http://apps.who.int/iris/bitstream/10665/69986/1/WHO_HTM_NTD_WHOPES_2009_1_eng.pdf)
4. WHO (2015). Report of evidence review group to define the conditions for deployment of long-lasting insecticidal nets treated with a pyrethroid and the synergist piperonyl butoxide, 21–23 September 2015. Geneva, Switzerland (<http://www.who.int/malaria/publications/atoz/use-of-pbo-treated-llins/en>).



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