The National Task Force on COVID-19
Considerations for Exclusion of Ivermectin and Hydroxychloroquine from the
"CLINICAL GUIDANCE FOR MANAGEMENT OF ADULT COVID-19 PATIENTS"

The ‘Clinical guidance for management of adult COVID-19 patients’ version dated 19th May, 2021 prepared jointly by AIIMS, ICMR-National Task Force of COVID-19 and Joint Monitoring Group was reviewed on 20th August 2021 in the context of emerging evidence for ivermectin and hydroxychloroquine.

It was recommended that these medicines may be removed from the guidance document after reviewing the current evidence.

I. The summary of the evidence that led to recommendation of removal of Hydroxychloroquine is given below:

- Many ongoing clinical trials (n=339).
- 13 systematic reviews and meta-analysis since Jan 2021 were discussed during the meeting.
  - 2/13 - Mortality benefit (in severe cases and low dose), 10/13 no mortality benefit or increases mortality, 3/13 increases mortality when co-administered with Azithromycin
  - Other outcomes –
    - Faster viral clearance – 1/13, no faster viral clearance – 2/13
    - Non progression to severe disease - 2/13, no benefit 1/13
    - Adverse events more – 6/13, no increased ADE – 1/13.
  - Risk of bias – many of the studies showed moderate-high risk of bias and moderate-high certainty of evidence.
- Recommendation: HCQ may be considered for removal from guideline, with recommendation to use with caution only in clinical trial setting (since there is some genuine uncertainty regarding the possible benefit for severe cases and in low dose).
  - Considering moderate-high certainty of evidence for no mortality benefit
  - Many studies showing increased mortality risk (10/13) and low mortality benefit of HCQ (2/13)
  - Considering evidence for increased ADE (6/13), especially with azithromycin; and only one study showed no increase in ADE (1/13)

II. The summary of the evidence that led to recommendation of removal of ivermectin is given below:

- Many ongoing clinical trials (n=62, 16 complete)
- 13 Systematic reviews and meta-analysis since Jan 2021 were included in this review
  - 7/13 showed mortality benefit, 4/13 no mortality benefit, 2/13 inconclusive/unclear
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- Other outcomes —
  - no effect on length of stay (1),
  - no effect on clinical recovery (1),
  - no difference in ADE (1)
- Risk of bias — High risk of bias in many studies (especially with the ones showing benefit), level of certainty for mortality benefit is low.

*Recommendation:* Ivermectin may be considered for removal from the guideline, with recommendation to use only in clinical trial setting until warranted by more conclusive large-scale randomized controlled trials due to the following reasons
- Many studies show mortality benefit, and no evidence for increased mortality
- High risk of bias in many studies (especially with the ones showing benefit), level of certainty for mortality benefit is low

These recommendations are also in the context of having effective vaccines that are known to be effective in preventing progression of disease. The guideline shall be revised periodically based on emerging evidence as well as inputs from the ICMR-National Clinical Registry on COVID-19. The treatment of mild COVID-19 may be mostly symptomatic.

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