

Revised advisory on the use of Hydroxychloroquine (HCQ) as prophylaxis for COVID-19 infection (in supersession of previous advisory dated 23rd March, 2020)

1. Background

The Joint Monitoring Group under the Chairmanship of DGHS and including representatives from AIIMS, ICMR, NCDC, NDMA, WHO and experts drawn from Central Government hospitals reviewed the prophylactic use of Hydroxychloroquine (HCQ) in the context of expanding it to healthcare and other front line workers deployed in non-COVID and COVID areas, respectively.

The National Task force (NTF) for COVID-19 constituted by Indian Council of Medical Research also reviewed the use of HCQ for prophylaxis of SARS-CoV-2 infection for high risk population based on the emerging evidence on its safety and efficacy. The NTF reviewed the data on in-vitro testing of HCQ for antiviral efficacy against SARS-CoV-2, safety profile of HCQ reported to the pharmacovigilance program of India, and data on the use of HCQ for the prophylaxis of SARS-CoV-2 infection among health care workers (HCWs) and reported its findings as detailed below:

1.1 In-vitro study

At NIV, Pune, the report of the in-vitro testing of HCQ for antiviral efficacy showed reduction of infectivity /log reduction in viral RNA copy of SARS-CoV2.

1.2 Safety Profile of HCQ

The data on assessment of HCQ prophylaxis among 1323 HCWs indicated mild adverse effects such as nausea (8.9%), abdominal pain (7.3%), vomiting (1.5%), hypoglycemia (1.7%) and cardio-vascular effects (1.9%). However, as per the data from the Pharmacovigilance program of India, there have been 214 reported instances of adverse drug reactions associated with prophylactic HCQ use. Of these, 7 were serious individual case safety reports with prolongation of QT interval on ECG in 3 cases.

1.3 Studies on prophylaxis of SARS-CoV-2 infection

- A retrospective case-control analysis at ICMR has found that there is a significant dose-response relationship between the number of prophylactic doses taken and frequency of occurrence of SARS-CoV-2 infection in symptomatic healthcare workers who were tested for SARS-CoV-2 infection.
- Another investigation from 3 central government hospitals in New Delhi indicates that amongst healthcare workers involved in COVID-19 care, those on HCQ prophylaxis were less likely to develop SARS-CoV-2 infection, compared to those who were not on it. The benefit was less pronounced in healthcare workers caring for a general patient population.
- An observational prospective study of 334 healthcare workers at AIIMS, out of which 248 took HCQ prophylaxis (median 6 weeks of follow up) in New Delhi also showed that those taking HCQ prophylaxis had lower incidence of SARS-CoV-2 infection than those not taking it.

2. Eligibility criteria for HCQ prophylaxis

The Advisory earlier issued (dated 23rd March, 2020; available at: <https://www.mohfw.gov.in/pdf/AdvisoryontheuseofHydroxychloroquinasprouphylaxisforSARSCoV2infection.pdf>), provided placing the high risk population (asymptomatic Healthcare Workers involved in the care of suspected or confirmed cases of COVID-19 and asymptomatic household contacts of laboratory confirmed cases of COVID-19) under chemoprophylaxis with HCQ.

In light of all of the above, the Joint Monitoring Group and NTF have now recommended the prophylactic use of HCQ in the following categories:

1. All asymptomatic healthcare workers involved in containment and treatment of COVID19 and asymptomatic healthcare workers working in non-COVID hospitals/non-COVID areas of COVID hospitals/blocks
2. Asymptomatic frontline workers, such as surveillance workers deployed in containment zones and paramilitary/police personnel involved in COVID-19 related activities.
3. Asymptomatic household contacts of laboratory confirmed cases.

3. Exclusion/contraindications

- The drug is contraindicated in persons with known case of:
 1. Retinopathy,
 2. Hypersensitivity to HCQ or 4-aminoquinoline compounds
 3. G6PD deficiency
 4. Pre-existing cardiomyopathy and cardiac rhythm disorders
- The drug is not recommended for prophylaxis in children under 15 years of age and in pregnancy and lactation.

Rarely the drug causes cardiovascular side effects such as cardiomyopathy and rhythm (heart rate) disorders. In that situation the drug needs to be discontinued. The drug can rarely cause visual disturbance including blurring of vision which is usually self- limiting and improves on discontinuation of the drug. For the above cited reasons the drug has to be given under strict medical supervision with an informed consent.

4. Dosage

S. No.	Category of personnel	Dosage
1	<ul style="list-style-type: none"> • Asymptomatic household contacts of laboratory confirmed cases 	400 mg twice a day on Day 1, followed by 400 mg once weekly for next 3 weeks; to be taken with meals
2	<ul style="list-style-type: none"> • All asymptomatic healthcare workers involved in containment and treatment of COVID-19 and asymptomatic healthcare workers working in non-COVID hospitals/non-COVID areas of COVID hospitals/blocks • Asymptomatic frontline workers, such as surveillance workers deployed in containment zones and paramilitary/police personnel involved in COVID-19 related activities 	400 mg twice a day on Day 1, followed by 400 mg once weekly for next 7 weeks; to be taken with meals

5. Use of HCQ prophylaxis beyond 8 weeks [in categories 4 (2) above]

In clinical practice HCQ is commonly prescribed in a daily dose of 200mg to 400mg for treatment of diseases such as Rheumatoid Arthritis and Systemic Lupus Erythematosus for prolonged treatment periods with good tolerance. With available evidence for its safety and beneficial effect as a prophylactic drug against SARS-COV-2 during the earlier recommended 8 weeks period, the experts further recommended for its use beyond 8 weeks on weekly dosage with strict monitoring of clinical and ECG parameters which would also ensure that the therapy is given under supervision.

Based on the available evidence, it has been opined that HCQ is relatively safe, when certain contraindications are avoided, and has some beneficial effect as a prophylactic option.

6. Monitoring

- An ECG (with estimation of QT interval) may be done before prescribing HCQ prophylaxis.
- An ECG should be done in case any new cardiovascular symptoms occurs (e.g., palpitations, chest pain syncope) during the course of prophylaxis.
- An ECG (with estimation of QT interval) may be done in those who are already on HCQ prophylaxis before continuing it beyond 8 weeks.
- One ECG should be done anytime during the course of prophylaxis.

7. Key considerations

While following above recommendations, it should be noted that:

- 1) The drug has to be given under strict medical supervision with an informed consent.
- 2) The drug has to be given only on the prescription of a registered medical practitioner.
- 3) Advised to consult with a physician for any adverse event or potential drug interaction before initiation of medication. The contraindications mentioned in the recommendations should strictly be followed.
- 4) Health care workers and other frontline workers on HCQ should be advised to use PPE. Front line workers should use PPEs in accordance with the guidelines issued by this Ministry (available at: <https://www.mohfw.gov.in/pdf/GuidelinesonrationaluseofPersonalProtectiveEquipment.pdf> and <https://www.mohfw.gov.in/pdf/UpdatedAdditionalguidelinesonrationaluseofPersonalProtectiveEquipmentsettingapproachforHealthfunctionariesworkinginnonCOVID19areas.pdf>) or by their respective organization.
- 5) They should be advised to consult their physician (within their hospital/surveillance team/security organization) for any adverse event or potential drug interaction before initiation of medication. The prophylactic use of HCQ to be coupled with the pharmacovigilance for adverse drug reactions through self-reporting using the Pharmacovigilance Program of India (PvPI) helpline/app. (available at: https://play.google.com/store/apps/details?id=com.vinfotech.suspectedadversedrugreaction&hl=en_IN)
- 6) If anyone becomes symptomatic while on prophylaxis, he/she should immediately contact the health facility, get tested as per national guidelines and follow the standard treatment protocol. Apart from the symptoms of COVID-19 (fever, cough, breathing difficulty), if the person on chemoprophylaxis develops any other symptoms, he should immediately seek medical treatment from the prescribing medical practitioner.
- 7) All asymptomatic contacts of laboratory confirmed cases should remain in home quarantine as per the National guidelines, even if they are on prophylactic therapy.
- 8) Simultaneously, proof of concept and pharmacokinetics studies should be continued/ taken up expeditiously. Findings from these studies and other new evidence will guide any change further in the recommendation.
- 9) They should follow all prescribed public health measures such as frequent washing of hands, respiratory etiquettes, keeping a distance of minimum 1meter and use of Personal protective gear (wherever applicable).

Note: It is reiterated that the intake of above medicine should not instil a sense of false security.