



Direct Healthcare Professional Communication

13-Feb-2025

Hydroxychloroquine sulfate (PLAQUENIL): Potential risk of major congenital malformations associated with use of Hydroxychloroquine sulfate among pregnant women

Dear Healthcare professional,

SANOFI Saudi Arabia in agreement with the Saudi Food and Drug Authority (SFDA) would like to inform you of the following about risk of major congenital malformations and new risks association with use of Hydroxychloroquine sulfate among pregnant women:

Summary

- **The Data from a population-based cohort study (Huybrechts et al.) published in 2021 suggested a small increase in the relative risk of major congenital malformations (including, but not limited to major disorders such as oral clefts, cardiac issues, respiratory conditions, gastrointestinal disorders, genital abnormalities, urinary defects, musculoskeletal issues, and limb defects) associated with use of hydroxychloroquine in the first trimester of pregnancy, especially when used at high daily dosage (greater than or equal to 400 mg daily).**
- **At daily doses greater than or equal to 400 mg, hydroxychloroquine should be avoided in the first trimester of pregnancy except when, in the judgment of the physician, the individual benefits outweigh the risks.**
- **Close monitoring during the pregnancy, especially during the first trimester, is recommended for early detection of major congenital malformations.**
- **If there is no alternative treatment to hydroxychloroquine during the first trimester of pregnancy, the lowest effective dose should be used.**

Background on the product and safety concern

PLAQUENIL® is indicated for the treatment of rheumatoid arthritis, discoid and systemic lupus erythematosus, and dermatological conditions caused or aggravated by sunlight.

Animal studies with the structurally related chloroquine, have shown reproduction toxicity at high maternal exposure. In humans, hydroxychloroquine crosses the placenta and blood concentrations in the foetus are similar to maternal blood concentrations.

Data from a population-based cohort study including 2045 hydroxychloroquine exposed pregnancies suggests a small increase in the relative risk (RR) of congenital malformations associated with hydroxychloroquine exposure in the first trimester (n = 112 events). For a daily dose of **greater than or equal to 400 mg** the RR was 1.33 (95% CI, 1.08 – 1.65). For a daily dose of < 400 mg the RR was 0.95 (95% CI, 0.60 – 1.50).

As a consequence of this study results the “Fertility, pregnancy and lactation” section of the Product Information has been updated as follows:

- Hydroxychloroquine should generally be avoided during pregnancy unless the physician determines that the benefits outweigh the risks.
- Close monitoring during the pregnancy, especially during the first trimester, is recommended for early detection of major congenital malformations.



Further to the above Product Information update the following is recommended:

- If there is no alternative treatment to hydroxychloroquine during the first trimester of pregnancy, the lowest effective dose should be used.

Call for reporting

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to National Pharmacovigilance Centre (NPC- Saudi Food and Drug Authority (SFDA):

Website: <https://ade.sfda.gov.sa/>



E-mail: npc.drug@sfda.gov.sa

SFDA call center: 19999

SANOFI contact point:

SANOFI Saudi Arabia Pharmacovigilance department contact information:

Email: Ksa_pharmacovigilance@sanofi.com

Mobile: + 966-54-428-4797

For Medical Information enquiries, please contact:

Phone: +966 12 669 3318 | **Email:** ksa.medicalinformation@sanofi.com

Annexes

European Medicines Agency Hydroxychloroquine Procedure No.: DK/H/PSUFU/00001693/202104

Huybrechts KF, Bateman BT, Zhu Y, Straub L, Mogun H, Kim SC, Desai RJ, Hernandez-Diaz S.

Hydroxychloroquine early in pregnancy and risk of birth defects. Am J Obstet Gynecol. 2021 Mar;224(3): 290.e1-29

Best regards,

Mossab Shafy

Country Safety Head & Local QPPV