

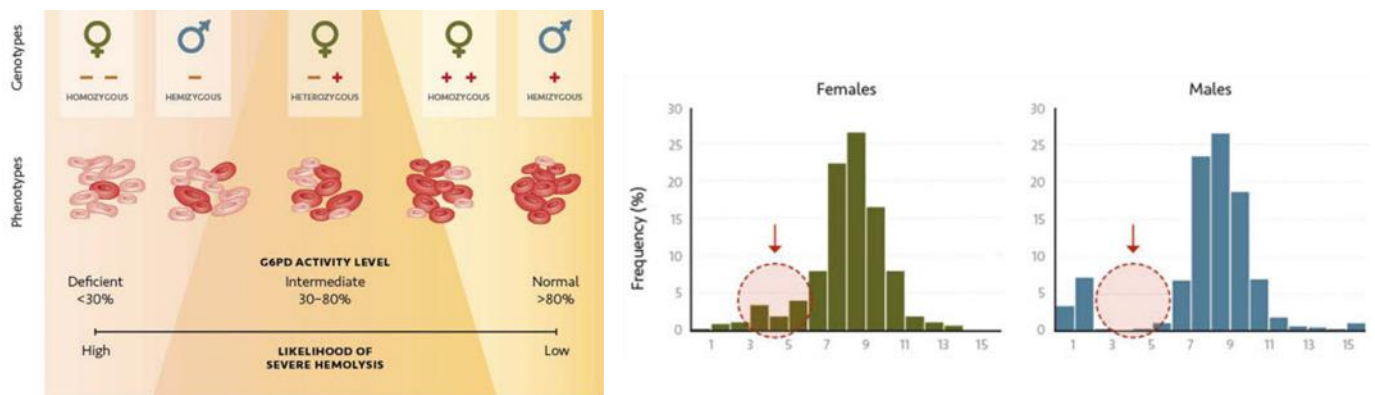
**FACTSHEET**

**Focus on: G6PD risk**

G6PD is an X-linked trait. Males (XY) have only one X chromosome and females have two (XX). Males only need one copy of a G6PD-deficient X chromosome to express this trait (hemizygotes), whereas females need to have inherited two copies of the mutant gene, one on each X chromosome (homozygotes).<sup>1</sup> Thus, male G6PD-deficient hemizygotes are more common than female homozygotes. Both will have low levels of G6PD enzyme expression, usually below 30% of normal levels.<sup>2</sup>

Females who have one X chromosome with the G6PD-deficient gene and the other X chromosome with the G6PD normal gene are termed heterozygotes. In female heterozygotes, the average G6PD activity across the red blood cell population can range from that of hemizygous males to that of G6PD-normal individuals. This is because in female heterozygotes a process called lyonization (somatic cell mosaicism) occurs whereby either the G6PD-deficient or the G6PD-normal allele on the X chromosome can be silenced, i.e. each individual red blood cell can either be G6PD normal or deficient in the same person.<sup>3</sup> X-chromosome inactivation is fixed embryonically in each individual and the average G6PD enzyme activity of their red cell population will depend on the proportion of cells that express each allele. There will be extreme phenotypes that resemble G6PD-deficient homozygote females or G6PD-normal females. However, the majority of female heterozygotes will have G6PD enzyme activities  $\geq 30\%$  but  $< 80\%$  of normal.<sup>1</sup> Thus, heterozygote females are the most at risk to be treated by mistake with 8-aminoquinolines.

**Figures 1 & 2: Female heterozygotes will have varying levels of expression of either the G6PD-deficient allele or the G6PD-normal allele and this will determine their phenotypic G6PD enzyme level<sup>4</sup>**



For more information please visit [www.vivaxmalaria.org](http://www.vivaxmalaria.org)

<sup>1</sup>Domingo et. al (2018) Addressing the gender-knowledge gap in glucose-6-phosphate dehydrogenase deficiency: challenges and opportunities, International Health; 11(1).

<sup>2</sup> Ibid.

<sup>3</sup> Wy et al. (2007) G6PD deficiency from lyonization after hematopoietic stem cell transplantation from female heterozygous donors, International Health; 11.

<sup>4</sup>Ibid