

IM = intermediate metaboliser (gene dose 0.25-1) (decreased CYP2D6 enzyme activity), NM = normal metaboliser (gene dose 1.25-2.5) (normal CYP2D6 enzyme activity), NS = non-significant, PM = poor metaboliser (gene dose 0) (absent CYP2D6 enzyme activity), UM = ultra-rapid metaboliser (gene dose ≥ 2.75) (increased CYP2D6 enzyme activity)

Justification of choices:

The enzymes involved in flupentixol metabolism are unknown. It was believed that CYP2D6 plays an important role. However, Waade 2021 showed that CYP2D6 phenotype does not affect flupentixol exposure, making involvement of CYP2D6 in flupentixol metabolism unlikely. For this reason, the KNMP Pharmacogenetics Working Group decided that there is no CYP2D6-flupentixol interaction, and thus no reason to recommend dose adjustment or selection of an alternative in patients with a CYP2D6 IM, PM or UM phenotype (no/no-interactions).

The available kinetic data per phenotype are provided in the background information text of the phenotype-drug combinations in the KNMP Kennisbank. You may also have access to this background text via your pharmacy or physician electronic decision support system.

The table below follows the KNMP definitions for NM, PM, IM and UM. The definitions of NM, PM, IM and UM used in the table below may therefore differ from the definitions used by the authors in the article.

[illegible]

Risk group	--
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Comments:

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Date of literature search: 28 July 2021.

	Phenotype	Code	Gene-drug interaction	Action	Date
KNMP Pharmacogenetics Working Group decision	PM	4 AA	no	no	13 September 2021
	IM	4 AA	no	no	
	UM	--	no	no	

Mechanism:

The enzymes involved in flupentixol metabolism are unknown. It was believed that CYP2D6 played an important role. However, a study showed that CYP2D6 phenotype does not affect flupentixol exposure in patients, making involvement of CYP2D6 in flupentixol metabolism unlikely.