



C_{max}* is the maximum drug concentration in human plasma after one dose. IC₅₀ is the drug concentration in vitro which yields 50% inhibition of a given cell function after one dose. All drugs were tested using 1x drug treatment followed by a 24-hour readout.

Mitochondrial toxicity was predicted based on the drug label/box insert and post-marketing reports. For some drugs such as kinase inhibitors, the benefits outweigh the risks. These drugs are approved, but require regular monitoring of liver enzymes to prevent drug-induced liver injury in patients.

*C_{max} and IC₅₀ are the total drug concentrations (bound plus unbound).

	Drug	Approval status	DILI status	DILI type	Mitochondrial toxicity IC ₅₀ /C _{max}	Predicted
Structurally similar	Troglitazone	Withdrawn	Positive	Idiosyncratic	0.09	Yes
	Pioglitazone	✓	Negative/low DILI	Intrinsic	> 34	Yes
Structurally similar	Tolcapone	Withdrawn†	Positive	Idiosyncratic	0.06	Yes
	Entacapone	✓	Positive/lower DILI	Unknown	9.47	Yes
Structurally similar	Sitax(s)entan	Withdrawn	Positive	Intrinsic	4.15	Yes
	Ambrisentan	✓	Negative	Intrinsic	> 1025	Yes
Structurally similar	Clozapine	✓	Positive	Idiosyncratic	11.41	Yes
	Olanzapine	✓	Negative	Intrinsic	> 625	Yes
Kinase inhibitors	Sorafenib	Box Warning	Positive	Intrinsic	0.19	Yes
	Ceritinib	Box Warning	Positive	Unknown	1.34	Yes
	Crizotinib	Box Warning	Positive	Unknown	8.02	Yes
	Ruxolitinib	✓	Lower DILI	Unknown	19.30	Yes
NSAIDs	Diclofenac	Box Warning	Positive	Intrinsic	8.49	Yes
	Lumiracoxib	Withdrawn	Positive	Idiosyncratic	3.81	Yes
	Celecoxib	✓	Positive	Idiosyncratic	12.12	Yes
	Valdecoxib	Withdrawn††	Negative/rare DILI	Unknown	145	Yes
	Rofecoxib	Withdrawn††	Negative/rare DILI	Unknown	> 490	Yes
	Zileuton	Box Warning	Positive	Intrinsic	14.91	Yes
	Telithromycin	Box Warning	Positive	Unknown	16.30	Yes
	Asunaprevir	Withdrawn NDA	Positive	Unknown	16.84	Yes
Structurally similar	Trovaflaxacin	Withdrawn	Positive	Idiosyncratic	1.48	Yes
	Levofloxacin	✓	Negative/low DILI	Hypersensitivity	> 32	Yes
Structurally similar	Nefazodone	Withdrawn†	Positive	Intrinsic	1.84	Yes
	Trazodone	✓	Negative/low DILI	Intrinsic	32.93	Yes
	Buspirone	✓	Negative	Intrinsic	26010	Yes

† Later approved with patient monitoring

†† The cause of withdrawal is not related to DILI

DILI positive:

IC₅₀/C_{max} < 25

Definitions

Intrinsic:

Idiosyncratic:

Dose-dependent

Patient-dependent