

Table 2 Overview of published methods for nitrosamine impurities analysis in APIs and drug products

Method name	Technique	Ionisation	Impurity	Sample	Column	LOQ
LGL method	LC-MS/MS	Q-Trap	NMBA	Losartan-K (API)	C8	NMBA 28.6 ppb
LGL method	GC-HS-MS	EI/CI	NDMA, NDEA	Valsartan, Losartan, Candesartan, Irberatan, Olmesartan (APIs)	Rtx-624	NDMA 0.10 ppm NDEA 0.080 ppm
LGL method	GC-MS (direct injection)	EI/CI	NDMA	Ranitidine (API and DPs)	Rtx-624	NDMA 19.8 ppb
LGL method	LC-MS/MS	Q-Trap	NDEA, NMDA	Valsartan, Irbesartan, Losartan (APIs and DPs)	C18	NDMA 79 (Irbesartan), 236 (Valsartan), 492 (Losartan) ppb NDEA 19.5 (Irbesartan), 61 (Valsartan), 149 (Losartan) ppb
Swissmedic method	GC-MS (direct injection)	EI	NDMA, NDEA	Various "sartans" (APIs and DPs)	DB-624	Not provided
CVUA Karlsruhe	UHPLC-MS/MS	APCI	NDMA, NDEA	Various "sartans" (APIs and DPs)	C18	NDMA 0.1 (all DPs), 0.1 (Valsartan API), 0.2 (other APIs) ppm NDEA 0.04 (all DPs), 0.04 (Valsartan API), 0.08 (other APIs) ppm
CVUA Karlsruhe	UHPLC-MS/MS	APCI	NDMA	Ranitidine (API and DPs)	C18	NDMA 0.12 ppm
PALG method	GC-HS-MS	Single Quad	NDMA	Various "sartans" (APIs and DPs)	Restek Rtx-624	LOD 0.04 ppm
ANSM method	HPLC-UV	Not applicable	NDMA, NDEA	Various "sartans" (APIs and DPs)	ODS-3	NDMA 0.04 (Valsartan), 0.05 (Losartan), 0.04 (Irbesartan), 0.25 (Candesartan), 0.25 (Olmesartan) ppm NDEA 0.08 (Valsartan), 0.10 (Losartan), 0.09 (Irbesartan), 0.40 (Candesartan), 0.50 (Olmesartan) ppm
ANSM method	HPLC-UV	Not applicable	NDMA	Valsartan (API and DP)	ODS-3	NDMA 0.3ppm
FDA method	GC-MS (direct injection)	Triple Quad	NDMA, NDEA, NDIPA, NEIPA, NDBA	Valsartan (API and DP)	VF-WAXms	NDMA 0.008 (API), 0.013 (DP), NDBA 0.025 (API), 0.040 (DP), 0.005 (other impurities in APIs), 0.008 (other impurities in DPs) ppm
FDA method	GC-HS-MS	Quadrupole	NDMA, NDEA, NDIPA, NEIPA	Valsartan (API and DP)	DB-WAX	LOQ for APIs 0.05 (all impurities) LOQ for DPs 0.05 (all impurities)
FDA method	LC-MS/MS	HR or Triple Quad	NDMA	Ranitidine (API and DPs)	C18	NDMA 0.033 ppm
Health Canada method	GC-MS/MS (direct injection)	EI	NDMA, NDEA	Various "sartans" (APIs and DPs)	DB-624	NDMA 0.0054 ppm NDEA 0.0073 ppm
HSA method	LC-MS/MS	Q-Trap	NDMA	Ranitidine (API and DPs)	C18	LOD 0.09 ppm