

Online supplementary material I

Table S1: Studies included for question 1: Which is the preferred first-line antiseizure medication in neonates requiring pharmacological treatment (specifically regarding cessation of seizures and adverse effects)?

First author, year	Design	N screened, included, received ASM	GA	Primary outcome measure	Diagnosis by	Efficacy by	ASM before	Dose	Efficacy	Safety
Phenobarbital										
Painter, 1999*	RCT	157, 59, 30	T & PT	Seizure cessation at 24 hrs	cEEG	cEEG	none	Titrated to plasma levels	43%	None observed
Sharpe, 2020*	RCT	280, 42, 30	T	Seizure cessation at 24 hrs	cEEG	cEEG	none	20-40 mg/kg	80%	Hypotension, respiratory suppression, sedation, and requirement for pressor support, were more common with phenobarbital
Boylan, 2002	Prospective observational	?, 33, 14	T & PT	EEG seizure cessation at 1, 2, and 24 hr	cEEG	cEEG	none	20-40 mg/kg	Seizure free at 24 hrs 3/14	None reported
Van den Broek, 2012	Prospective observational	?, ?, 31	T	Evaluation of PK and seizure cessation	aEEG	aEEG	none	20-40 mg/kg in 2 boluses	66%	None reported
Low, 2016	Prospective observational	35, 19, 19	T	Maximum seizure burden per hr	cEEG	cEEG	none	10-40 mg/kg	-14 min/h (-19.6,-85)	None reported
Glass, 2017	Prospective observational	611, 540, 540	T & PT	Seizure cessation after initial dose	cEEG	Unclear		Mean 19 mg/kg	T & PT: 36% (no difference between T and PT)	None reported
Connell, 1989	Prospective observational	31	T & PT	Seizure cessation	cEEG	cEEG	PB	20 mg/kg in single dose	2 / 31	20 of 31 included in study died, not specified for each AS
Spagnoli, 2016	Retrospective	154, 107, 91	T & PT	EEG Seizure cessation after initial dose (complete, partial, absent)	Intermittent EEG	Intermittent EEG	None	20-40 mg/kg in 2 boluses	47 complete response, 15 partial, 19 no response	None reported
Rao, 2018	Retrospective	78, 44, 24	T	Time to seizure freedom	EEG	EEG	none	15-20 mg/kg	Longer interval to seizure freedom in univariate analysis with PB	None reported
Thibault, 2020	Retrospective	700, 59, 31	T & PT	Seizure cessation	cEEG	cEEG	None	Not specified	18 / 31	Hypotension 16%, respiratory depression 2%
Phenytoin										
Painter, 1999*	RCT	157, 59, 29	T & PT	Seizure cessation at 24 hrs	cEEG	cEEG	None	Titrated to plasma levels	45%	None observed
Glass, 2017	Prospective observational	611, 4, 4	T & PT	Seizure cessation after initial dose	cEEG	cEEG	None	Not specified	T & PT: 0%	None reported
Levetiracetam										
Sharpe, 2020*	RCT	280, 64, 53	T	Seizure cessation at 24 hrs	cEEG	cEEG	None	40 - 60 mg/kg	28%	Less common than with phenobarbital but not specified, no SAE

Glass, 2017	Prospective observational	611, 33, 33	T & PT	Seizure cessation after initial dose	cEEG	cEEG	0 - 44 %	Not specified	T & PT: 42%	None reported
Abend, 2011	Retrospective	?, 23, 4	T & PT	> 50% seizure reduction in 24 hrs	cEEG	cEEG	none	Load. 5 - 22 mg/kg Maint. 20 - 80 mg/kg	1 / 4	None observed
Han, 2018	Retrospective	?, 37, 37	PT	Seizure cessation	EEG	EEG	none	Load 40-60 mg/kg Maint. 20-30 mg/kg/day	21 / 37	None observed
Rao, 2018	Retrospective	78, 44, 20	T	Time to seizure freedom	cEEG	cEEG	none	Load. 20-30 mg/kg Maint. 35-60 mg/kg/day	Significantly longer interval to seizure freedom in univariate analysis with LEV (Hazard ratio (HR)=2.58, P=0.007)	None reported
Kurtom, 2019	Retrospective	779, 61, 61	PT	Seizure cessation	EEG	EEG	none	Load. 40 mg/kg Maint. up to 80 mg/kg/day	16 / 61	None reported
Thibault, 2020	Retrospective	700, 59, 22	T & PT	Seizure cessation	cEEG	cEEG	none	Not specified	12 / 22	None observed

Legend: N=number, GA=gestational age, T= term, PT=preterm, ASM=anti-seizure medication, RCT=randomized controlled trial, EEG=electroencephalography, cEEG=continuous EEG, CHD=congenital heart disease, hrs=hours, Load.=loading dose, Maint.=maintenance dose. PB=phenobarbital. * Studies that went into the GRADE analysis.

Table S2: Studies included for question 2: Which is the preferred second-line anti-seizure medication in neonates requiring pharmacological treatment (specifically regarding cessation of seizures, mortality, and adverse effects)?

First author	Design	N included	GA	Primary outcome measure	Diagnosis by	Efficacy by	ASM before	Dose	Efficacy	Safety
Phenobarbital										
Sharpe, 2020*	RCT	37	T	Seizure cessation at 24 hrs	cEEG	cEEG	LEV	20 - 40 mg/kg	20/37 seizure free	Respiratory insufficiency, not quantified
Painter, 1999*	RCT	13	T & PT	Seizure cessation at 24 hrs	cEEG	cEEG	PHT	Titrated according to plasma level	5/13 seizure free	None observed
Phenytoin										
Painter, 1999*	RCT	15	T & PT	Seizure cessation at 24 hrs	cEEG	cEEG	PB	Titrated according to plasma level	4/15 seizure free	None observed
Glass, 2017 ¹⁻⁷	Prospective observational	4 (out of 611)	T & PT	Further seizures before discharge	cEEG	cEEG	N/A	N/A		None reported
Pisano, 2015	Retrospective	8 KCNQ2 DEE	?	Seizure cessation	Intermittent EEG [^]	Intermittent EEG [^]	variable	Load. 18 mg/kg Maint. 5-7 mg/kg/day	5 / 8	None observed
Connell, 1989	Prospective observational	6	T & PT	Seizure cessation	cEEG	cEEG	PB	20 mg/kg single dose	0 / 6	20 of 31 included in study died, not specified for each AS
Midazolam										
Boylan, 2004	RCT not blinded	3	T	>80% reduction at 6 hr	cEEG	cEEG	PB	Load. 0.06 mg/kg Maint. 0.15-0.3 mg/kg/h	0/3	None reported
Van Den Broek, 2015	Prospective observational	22	T	>80% reduction and no need for 3 rd line	aEEG	aEEG	PB	Load. 0.05 mg/kg Maint. 0.05-0.6mg/kg/h	5 / 22	Hypotensive episodes in 50%
Sheth, 1996	Retrospective	6	T	Seizure cessation at 12 hours	EEG	EEG	PB or PB&PHT	0.1-0.4mg/kg/h	4/6	None reported
Weeke, 2016	Retrospective	165	T	Seizure free for 4 hr	aEEG or EEG	aEEG	PB	Load. 0.05 mg/kg Maint. 0.15-0.5mg/kg/h	21 / 165	None reported
Shany, 2007	Retrospective	8	T	Seizure cessation for at least 6 hr	aEEG	aEEG	PB	0.06-0.2mg/kg/h	4/8 partial response	None reported
Castro Conde, 2005	Retrospective	13	T	Seizure cessation at 24 hr	EEG	EEG	PB in 9, PB & PHT in 4	Load. 0.15 mg/kg Maint. 0.06-1 mg/kg/h	13/13	None reported
Lidocaine										
Boylan, 2004	RCT not blinded	5	T	>80% reduction	cEEG	cEEG	PB	Load. 4mg/kg Maint. 2mg/kg/h for 48 hr	3/5	None reported
Weeke, 2016	Retrospective	186	T&PT	Seizure cessation for 4 hr or partial response	aEEG or EEG	aEEG	PB	Load. 2mg/kg Maint. 6mg/kg/h for 6 -24 hr	Seizure free: 37 / 186 Partial response 90 / 186	None reported
Shany, 2007	Retrospective	22	T	Seizure cessation or partial response at 6 hr	aEEG	aEEG	PB	Load. 2mg/kg Maint. 4-6mg/kg/h for 48 hr	17/22 seizure free or partial response	None reported
Van Rooij, 2004	Retrospective	207	T&PT	Safety (arrhythmias)	aEEG	aEEG	PB in 169, PB&PHT in 41	Load. 2mg/kg Maint. 6mg/kg/h for 48 hr	N/A	Cardiac arrhythmias in 4.8%
Shany, 2007	Retrospective	22	T	Seizure cessation or partial response at 6 hr	aEEG	aEEG	PB	Load. 2mg/kg Maint. 4-6mg/kg/h	17/22 seizure free or partial response	None reported

									for 48 hr		
Clonazepam											
Boylan, 2004	RCT not blinded	3**	T	>80% reduction	cEEG	cEEG	PB	N/A		0/3	None reported
Bumetanide											
Pressler, 2015	Prospective observational, combined dose finding and efficacy	14	T	>80% reduction and no need for secure medication	EEG	EEG	PB	Load. 0.05-0.2 mg/kg with 2 nd dose of PB Maint. 0.05-0.2 mg/kg for 2 days		2 / 14	Dehydration in 1/14, hypotension in 7/14, electrolyte disturbances in 11/14, hearing loss in 3 /11 surviving infants
Topiramate											
Courchia, 2018	Retrospective	10	PT	Safety	EEG	EEG	N/A	10mg/kg		N/A	40% develop NEC
Paraldehyde											
Connell, 1989	Prospective observational	15	T & PT	Seizure cessation	cEEG	cEEG	PB	0.3 ml/kg per rectum, or 1-3 ml/kg/hr of a 5% intravenous infusion in 5% dextrose)		0 seizure free 4 partial	20 of 31 included in study died, not specified for each ASD
Diazepam											
Connell, 1989	Prospective observational	7	T & PT	Seizure cessation	cEEG	cEEG	PB	0.25 mg/kg single dose		0 / 7	20 of 31 included in study died, not specified for each AS
Carbamazepine											
Sands, 2016	Retrospective	19 SLFNE			Intermittent EEG^	Intermittent EEG^	variable	10 mg/kg /day		17/19	None observed
Pisano, 2015	Retrospective	6 KCNQ2 DEE			Intermittent EEG^	Intermittent EEG^	variable	15-20 mg/kg /day		6	None observed
Levetiracetam											
Sharpe, 2020	RCT	6	T	Seizures cessation at 24 hrs	cEEG	cEEG	PB	20 mg/kg		1/6 seizure free	No serious AE, systematic adverse event assessment
Yau, 2015	Retrospective	12	T & PT	Seizure cessation	EEG	EEG	PB	Load. 7.5-20mg/kg Maint. 5-60mg/kg/d		7/12 day 1 9/12 day 3	None reported
Rakshasbhuvankar, 2013	Retrospective	8		> 80% seizure reduction	aEEG	aEEG	PB/PHT/MZ	Load. 5 or 10 mg/kg; Maint. 10-35 mg/kg/day		6/8 good response	No serious AE
Khan, 2013	Retrospective	12	Preterm	Seizure cessation	EEG	EEG	PB in 9, none in 3	Load. 25 or 50 mg/kg Maint. 25mg/kg		9/11 seizure free by 24 hr	None observed
Khan, 2011	Retrospective	22	T	Seizure cessation	EEG	EEG	PB /PHT /LOR/MZ / none in 3	Load. 10-50 mg/kg Maint. 20-75 mg/kg/day		19 / 22 by 24 hr 22 / 22 by 48 hr	None observed
Abend, 2011	Retrospective	2nd line in 14 3rd line in 5	T	> 50% seizure reduction within 24 hours	cEEG	cEEG	PB or PB&PHT	Load. 5-22 mg/kg Maint. 10-80 mg/kg/day		7/19	None observed

Legend: N=number, GA=gestational age, T= term, PT=preterm, ASM=anti-seizure medication, RCT=randomized controlled trial, EEG=electroencephalography, cEEG=continuous EEG, CHD=congenital heart disease, hrs=hours, Load.=loading dose, Maint.=maintenance dose, PB=phenobarbital, PHT=(fos)phenytoin. LEV=levetiracetam, LOR=Lorazepam, MZ=midazolam* Studies that went into the GRADE analysis. ^ intermittent EEG considered acceptable in epilepsy syndromes (KCNQ2).

Table S3: Studies included for question 3: Will continuation of anti-seizure medication improve neurodevelopmental outcome and reduce subsequent epilepsy?

First author	Design	N included in study	GA	Outcome measure Epilepsy	Outcome measure Development	Diagnosis by	Efficacy by	Comparator	Efficacy (quantitatively, dose-response relationship)	Safety
Nunes et al. 2008	Prospective observational	104 43 on PB	T & PT	Epilepsy	Developmental delay	clinical	mixed	21 not on PB	Risk of epilepsy overall 30%, not different if ASM at discharge	N/A
Fitzgerald et al. 2017	Retrospective	35 with acute symptomatic or electrographic seizures	T	Epilepsy in patients on ASM at discharge	N/A	Clinical and/or EEG	mixed	patients without acute symptomatic seizures, and not on ASM	Epilepsy in 4/35 who had acute symptomatic seizures	No adverse events observed
Guillet et al. 2007	Retrospective	146 33 on PB at discharge	>34 w	Epilepsy	Telephone interview (CP, WeeFim)	Mostly clinical	mostly clinical	99 not on PB at discharge	Epilepsy in 8/33 vs 13/99 (ns) CP in 27% (PB) vs 17% (no ASM) (ns) WeeFim abnormal in 58 (PB) vs 52 (no ASM) (ns)	N/A

Legend: N=number, GA=gestational age, T= term, PT=preterm, ASD=anti-seizure drug, EEG=electroencephalography, PB=phenobarbital, N/A not available, CP=cerebral palsy, WeeFim Functional Independence Measure for Children, ns=not significant.

Table S4: Studies included for question 4: In neonates with hypoxic-ischaemic encephalopathy, does therapeutic hypothermia reduce seizure burden (min/hr)?

First author	Year	Design	Intervention	Comparator	N screen / included	Primary outcome measure	Secondary outcome measure	Seizure diagnosis (EEG / aEEG)	Efficacy (quantitatively)	Safety
Yap	2009	Prospective observational	TH (head cooling)	No control	20 TH	Clinical and electrographic seizures	MRI Magnesium levels	aEEG	Clinical seizures 18/20 19/20 electrographic seizures No association between degree of MRI abnormality and abnormal EEG.	hypomagnesemia in nine (45%) infants
Wusthoff	2011	Prospective observational	TH (whole body)	No control	26 TH	Clinical and electrographic seizures	MRI	cEEG	Electrographic seizures 17/26 Nonconvulsive 8/17 Status epilepticus 4/17 MRI and seizures could not be correlated	N/A
Srinivasakumar*	2013	Prospective observational	TH (whole body)	18 neonates no TH – 11/18 historical (before 2008). 7/18 outside the 6-hour eligibility window for TH.	51 TH 18 no TH	Seizure burden	Compared to mod HIE to severe HIE outcomes	cEEG	Seizure incidence higher no-TH 16/18, 88% vs TH 19/51, 37%, of Seizure burden significant reduction TH 2.9±0.6 vs. no TH 6.2±0.9, p=0.003, especially with moderate HIE - TH 2.2±0.6 vs noTH 7.0±1.0, p=0.001. But not evident for severe HIE – TH 7.6±2.5 vs noTH 8.4±3.8, p=0.800.	N/A
Shah	2014	Prospective observational	TH (whole body)	No controls	85	Occurrence of seizure	MRI features	aEEG	52% had seizures on aEEG/EEG. 35% high seizure burden , 49% had abnormal aEEG background in the first 24 h 36% had severe injury on MRI.	N/A
Nash	2011	Retrospective	TH (whole body)	No control	41/49 TH	Background EEG Occurrence of seizures	MRI	cEEG	EEG background improved 49%, remaining static 38%, and worsened in 13%. Burst suppression and extremely low voltage patterns held the greatest prognostic value (specificity 81% start TH and 100% at later time points). Electrographic seizures in 34% (14/41) 10% (4/41) status epilepticus. Correlations in MRI and background EEG.	5 neonates died (4 severe HIE, 1 moderate HIE)
Low*	2012	Retrospective	TH (whole body)	Historical HIE group previously managed without cooling	15 TH 16 non-TH	Seizure burden		aEEG and cEEG	Median seizure burden significantly less in TH: 60 (39-224) vs non-TH 203 (141-406) min; p=0.027. TH significant reduction seizure burden moderate HIE (non-TH: 162 (97–262) vs TH: 49 (26–89) min; p=0.020) but not with severe HIE (non-TH: 223 (172–720) vs TH: 224 (60–289) min; p=0.558).	N/A
Lynch	2015	Retrospective	TH (whole body)	Historical HIE group previously managed without cooling	23 TH	Seizure burden	Difference in seizure burden with or without PB	Continuous video EEG	seizure burden was 4.0 min/h (IQR: 2.0 to 7.0). Limited effect With TH alone but increased with addition of PB	N/A
Guidotti*	2016	Retrospective	TH (whole body)	Historical HIE group previously managed without cooling	33 TH 39 non-TH	Seizures Status epilepticus Duration of sz Seizure burden	Number of ASMs Long term outcome for development and epilepsy	cEEG	TH group fewer sz (14/39 v 20/33 p=0.036) less status epilepticus (7/39 v 13/33, p=0.043), and a lower mean duration of seizures (18mins vs 133mins, p=0.026). Seizure burden in TH with moderate (0.0 vs 0.1;	N/A

									<p>p=0.045) and severe HIE (0.3 vs 4.9; p=0.018) lower than non-TH. ASMs for sz control less in TH (median 0 vs 1, p=0.045). Long term outcome (24 months) better in TH. Normal / mild motor impairment in 32/39 TH v 16/33 non-TH, p=0.003. Cerebral palsy in 14 non-TH and 3 TH. Development of epilepsy 7 non-TH and 2 TH.</p>	
Ghosh	2017	Retrospective	TH (head cooling)	Historical HIE group previously managed without cooling	33 TH 39 non-TH	Seizure burden after discharge	Number of ASMs Long term developmental outcome	aEEG/clinical	<p>Seizure burden in TH groups for moderate (0.0 vs 0.1; p=0.045) and severe HIE (0.3 vs 4.9; p=0.018) was lower than in non-TH patients</p>	N/A

Legend: EEG=electroencephalography, aEEG=amplitude integrated EEG, TH=therapeutic hypothermia, HIE-hypoxic ischemic encephalopathy, GA=gestational age, T= term, PT=preterm, RCT=randomized controlled trial, ASM=anti-seizure medication, MRI=magnetic resonance tomography, N/A= not available.

Table S5: Studies included for question 5: Is a reduction of electro-clinical and/or electrographic seizure burden associated with improved neurodevelopmental outcome and reduction of subsequent epilepsy?

First author	Design	Case definition	N screen / included	GA	Intervention	Outcome measures	Seizure verification by EEG	MRI	Outcome - Neurodevelopmental	Outcome - Epilepsy
Van Rooij, 2010	RCT	HIE and subclinical seizures	42/138	T	ASM	Bayley and MRI	aEEG	Yes	Worse MRI scores (short term outcome N/A)	N/A
Srinivasakumar, 2015	RCT	Neonates with seizures or at risk	91/72	T	ASM	Bayley and MRI	cEEG	yes	All grouped together, high seizure burden	N/A
McBride, 2000	Prospective observational	Neonate at risk	68/ 40 treated	T & P T	ASM (PB)	Long term neurodevelopmental outcome	cEEG	N/A	Higher seizure burden associated with worse outcome	N/A
Toet, 2005	Prospective observational	Term with seizures	169	T	ASM	Post-neonatal epilepsy	aEEG	In part of cohort		Epilepsy in 12/126 survivors, all requiring >2 ASM
Payne, 2014	Prospective observational	Neonates and children on PICU	259 total (93 with seizures)	T	Not specified	PCPC score Mortality	cEEG	No	Higher seizure burden associated with worse short term outcome	N/A
Glass, 2016	Prospective observational	neonates with seizures and at risk	426	T & PT	ASM	Short-term neurological exam, mortality	cEEG	N/A	Higher seizure burden associated with mortality and worse outcome	N/A
Pisani, 2009	Retrospective	Term with seizures	106	T & PT	ASM	Mortality, Griffith at 2 y	cEEG	No	Nonresponses had worse Griffith scores	N/A
Kharoshankaya, 2016	Retrospective	HIE	47	T	ASM	Compound score incl mortality, CP, epilepsy, Bayley at 24-48 mon	cEEG	No	Higher seizure burden associated with worse outcome	same
Guidotti , 2016	Retrospective	HIE	72	T	ASM	Compound score incl Touwen, Amiel-Tisor, Griffith, Gross motor function, epilepsy, mortality	cEEG	No	Lower seizure burden associated with better outcome	same
Fitzgerald, 2018	Retrospective,	HIE with therapeutic hypothermia	116	T	ASM	Motor and language abnormality at 12-36 mon, MRI	cEEG	yes	Higher seizure burden associated with abnormal outcomes	N/A

Legend: N=number, GA=gestational age, T= term, PT=preterm, EEG=electroencephalography, cEEG=continuous EEG, aEEG=amplitude integrated EEG, N/A= not available, PICU pediatric intensive care unit, ASM=anti-seizure medication, HIE-hypoxic ischemic encephalopathy, PCPC=????, mon=months, y=years

Table S6: Studies included for question 6: In neonates with seizures, is the use of pyridoxine or pyridoxal 5'-phosphate effective and safe?

First author	Design	N included	GA	EEG	Genetics	Dose of pyridoxine	Concomitant ASD	Efficacy (quantitatively, dose-response relationship)	Safety (narrative and quantitative if available)
Pyridoxine									
Schmitt, 2010	Retrospective	4	T & PT	suppression-burst and discontinuity	ALHD7A1	pyridoxine	N/A		Respiratory depression in 1/4, somnolence in 2/4, drop in arterial blood pressure in 1/4
Bok, 2010	Retrospective	6	---	conventional in 5, aEEG in 1	Antiquitin gene	100 mg iv	PB, PHT, MZ, CLB lidocaine,	Decline of aEEG amplitude	Not reported
Mills, 2014	Retrospective	pyridoxine dependent presenting with NS 8/15	T & PT	N/A	PNPO gene variants in 3	pyridoxine in 8, 2-26 mg/kg*d		Pyridoxine: immediate response in 8/8	Not reported
Plecko, 2014	Retrospective	11	T & PT	EEG in 9/11: (BG: suppression-burst 5, discontinuous 4)	PNPO gene	100 mg iv - 400 mg iv	not given	4/11 immediate cessation 2/11 seizure reduction 2/11 improvement of EEG 2/11 no improvement	None observed
Coughlin, 2015	Retrospective	6	---	unclear	Antiquitin gene	15-40 mg/kg*d	PB, PHT, CLB	No further seizures in 5/6	Sensorimotor neuropathy in 1/6
Xue, 2015	Retrospective	8 (6 presenting with NS)	---	standard EEG abnormal in 6/8	ALDH7A1 gene	10 - 30 mg/kg*d	PB, VPA, TOP, LEV, CZB, OXC	6/6 became seizure free	None observed
Darin, 2016	Retrospective	NS in 6/7	T & PT	standard EEG, suppression-burst 5/7	PROSC gene	not specified	additional ASM in five/six survivors	Pyridoxine: partial response	Respiratory depression in 2/7
Falsaperla, 2018	Retrospective	NS in 12/16	---	standard EEG, suppression burst in 7	ALDH7A1 gene in 8/16, PROSC in 2, PNPO in 3, neg in 3	100 mg iv in 9, 10-50 mg/kg in 7	PB, benzodiazepines, LEV, VPA, VGB, PHT, ACTH in 15/16	Improvement of seizures in all, immediate response in 8	None observed
Pyridoxal phosphate									
Schmitt, 2010	Retrospective	1	T	suppression-burst and discontinuity	ALHD7A1, PNPO	pyridoxine	NA		Somnolence
Plecko, 2014	Retrospective	2	---		PNPO gene				2 patients showed deterioration when switched to PLP
Mills, 2014	Retrospective	PLP-dep. NS in 5/15 (+1sib)	T & PT	NA	PNPO gene	PLP in 5 (+1sib), 10-85 mg/kg*d		PLP: immediate response in 3/5,	3 patients showed deterioration with switch from pyridoxine to PLP hepatotoxicity 2/15

Legend: N=number, GA=gestational age, T= term, PT=preterm, EEG=electroencephalography, cEEG=continuous EEG, aEEG=amplitude integrated EEG, NS=neonatal seizures, N/A= not available, ASM=anti-seizure medication, PB=phenobarbital, PHT=(fos)phenytoin, MZ=midazolam, CLB=clobazam, VPA=sodium valproate, LEV=levetiracetam, CBZ=carbamazepine, OXC=oxcarbazepine, PLP=pyridoxal 5'-phosphate, PNPO=pyridox(am)ine 5'-phosphate oxidase, PLPBP=pyridoxal 5'-phosphate binding protein (former PROSC)