

Supplementary Information for:

**'Physiologically Based Pharmacokinetic (PBPK) Model-Informed Dosing Guidelines
for Pediatric Clinical Care: A Pragmatic Approach for a Special Population'**

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Pediatric Drugs, 2022

Supplementary Information

Online Resource 1: List of drugs relevant for pediatric PBPK modeling

On WHO list* and included in European pediatric formularies	On BPCA list [#]	Potential value of pediatric PBPK modeling ^{\$}	
abacavir	-		
acetylcysteine	-		
acetylsalicylic acid	-		
aciclovir	yes	4 - Moderate	
adalimumab	-		
albendazole	yes	5 - Low	
allopurinol	-		
all-trans retinoid acid (tretinoin)	-		
amikacin	yes	2 - High	
amitriptyline	-		
amoxicillin	-		
ampicillin	yes	4 - Moderate	Written request received from the FDA
aprepitant	-		
artemether	-		
artesanate	-		
asparaginase	-		
atazanavir	-		
atropine	yes	2 - High	
avibactam	-		
azathioprine	-		
azithromycin	yes	2 - High	Written request received from the FDA
bedaquiline	-		
benzathine benzylpenicillin	-		
benzoyl peroxide	-		
benzylpenicillin	-		
betamethasone	yes	3 - Moderate	
bleomycin	-		
budesonide	-		
bupivacaine	-		
caffeine	yes	4 - Moderate	
calcium folinate (folinic acid)	-		
calcium gluconate	-		
carbamazepine	-		
cefalexin	-		
cefazolin	-		
cefixime	-		
cefotaxime	-		
ceftazidime	yes	2 - High	

ceftriaxone	-		
chloroquine	-		
ciclosporin	-		
ciprofloxacin	yes	2 - High	
clarithromycin	-		
clavulanic acid	-		
clindamycin	yes	4 - Moderate / 2 - High / 5 - Low	Skin and soft tissue infections / Infections in neonates / Exposure of medication in breastmilk
coagulation factor IX	-		
coagulation factor VIII	-		
colistin	-		
cyclizine	-		
cyclophosphamide	-		
cytarabine	-		
dapsone	yes, as chlorproguanil- dapsone	5 - Low	
darunavir	-		
dasatinib	-		
daunorubicin	-		
deferoxamine	-		
desmopressin	-		
dexamethasone	yes	2 - High	
diazepam	yes	2 - High	
diazoxide	-		
digoxin	yes	2 - High	
dihydroartemisinin (artemimol)	-		
docusate	-		
dolutegravir	-		
dopamine	yes	5 - Low	
doxorubicin	-		
doxycycline	yes	4 - Moderate	
efavirenz	-		
enalapril	-		
enoxaparin	-		
entecavir	-		
epinephrine (adrenaline)	yes	2 - High	
erythromycin	-		
ethambutol	-		
ethosuximide	-		
etoposide	-		
filgrastim	-		
fluconazole	yes	2 - High	

flucytosine	-		
fludrocortisone	-		
fluorouracil	-		
fluoxetine	-		
fomepizole	-		
fosfomycin	yes	2 - High	
furosemide	yes	2 - High	
gentamicin	-		
glucagon	-		
griseofulvin	yes	2 - High	
haloperidol	yes	2 - High	
heparin	yes	5 - Low	
hydrochlorothiazide	yes	2 - High / 2 - High	Pediatric hypertension / Neonatal bronchopulmonary dysplasia/lung development
hydrocortisone	yes	2 - High	
hydroxycarbamide	-		
hydroxychloroquine	-		
hyoscine hydrobromide (scopolamine)	-		
ibuprofen	-		
ifosfamide	-		
imatinib	-		
insulin	-		
irinotecan	-		
isoflurane	-		
isoniazid	yes	5 - Low	
itraconazole	-		
ketamine	yes	2 - High / 2 - High	Anesthesia/sedation / Neonatal pain
lactulose	-		
lamivudine	-		
lamotrigine	-		
levamisole	-		
levofloxacin	yes	2 - High	
levothyroxine	-		
lidocaine	yes	2 - High	
linezolid	-		
lopinavir	-		
loratadine	-		

lorazepam	yes	4 - Moderate / 3 - Moderate	Seizures / Anesthesia/sedation, both: Written request received from the FDA
lumefantrine	-		
mannitol	-		
mebendazole	-		
mefloquine	yes	5 - Low	
mercaptopurine	yes	5 - Low	
meropenem	yes	4 - Moderate	Written request received from the FDA
mesna (mercaptoethanesulphonic acid)	-		
metformin	yes	5 - Low / 1 - High	Exposure of medication in breastmilk / Metabolic syndrome
methadone	yes	2 - High	
methimazole (thiamazole)	-		
methotrexate	yes	5 - Low / 2 - High / 5 - Low	Leukemias and solid tumours (WR received from the FDA) / Severe inflammatory infections / Pediatric formulations
methylprednisolone	yes	2 - High	
metoclopramide	-		
metronidazole	yes	2 - High / 2 - High	Infections in neonates (abdominal infections) / Infections in neonates (various infections, also preterm neonates)
miconazole	-		
midazolam	yes	2 - High	
morphine	yes	2 - High	Written request received from the FDA
moxifloxacin	-		
mupirocin	-		
naloxone	-		
neostigmine	-		
nevirapine	-		
niclosamide	-		
nilotinib	-		
nitrofurantoin	-		
nystatin	-		
ofloxacin	-		
omeprazole	-		
ondansetron	yes	5 - Low / 2 - High	Exposure of medication in breastmilk / Nausea and vomiting
oseltamivir	yes	5 - Low	

paracetamol	-		
paromomycin	-		
pegaspargase	-		
pentamidine	-		
permethrin	-		
phenobarbital	-		
phenoxymethylpenicillin	-		
phenytoin	yes, as fosphenytoin	2 - High	
piperacillin-tazobactam	yes	2 - High / 2- High	Infections in neonates / Opportunistic study of drugs used in children (not previously listed)
piperaquine	-		
polymyxin B	-		
praziquantel	-		
prednisolone	-		
procarbazine	-		
proguanil	-		
propofol	yes	2 - High	
propranolol	-		
propylthiouracil	-		
prostaglandin E (alprostadil)	-		
protamine	-		
pyrantel	-		
pyrazinamide	-		
pyridostigmine	-		
pyrimethamine	yes, as sulfadoxine-	5 - Low	
quinine	-		
raltegravir	-		
ranitidine	-		
ribavirin	-		
rifampicin	yes	2 - High	
ritonavir	-		
rituximab	-		
salbutamol	-		
salicylic acid	-		
senna	-		
silver sulfadiazine	-		
spironolactone	yes	1 - High	
sulfadiazine	-		
suxamethonium	-		
terbinafine	-		
tetracaine	-		
tetracycline	-		

tioguanine	-		
trimethoprim-sulfamethoxazole	yes	2 - High	
tropicamide	-		
valganciclovir	yes	1 - High	
valproic acid	yes	2 - High	
vancomycin	yes	2 - High	
vecuronium	yes	2 - High	
vinblastine	-		
vincristine	yes	2 - High	Written request received from the FDA
voriconazole	-		
xylometazoline	-		
zidovudine	-		

* Model List of Essential Medicines for Children from the World Health Organization (WHO)

Priority List of Needs in Pediatric Therapeutics from the Best Pharmaceuticals for Children Act (BPCA), 2020-2021

§ Five categories defined as follows:

Category	Gaps in knowledge/labeling	Status	Value of pediatric PBPK modeling
1	Related to PK and/or dosing	<u>Under consideration</u>	High
2	Related to PK and/or dosing	<u>Ongoing</u> Clinical trial(s) and/or analysis ongoing and/or awaiting final disposition	High
3	Related to PK and/or dosing	<u>No label change</u> : Clinical trial(s) conducted and analysis completed, no label change anticipated or waiver received from FDA	Moderate
4	Related to PK and/or dosing	<u>Label change</u> Clinical trial(s) conducted and analysis completed, resulted in label change	Moderate
5	Unrelated to PK and/or dosing	<u>Not applicable</u>	Low