

**Title:** Population pharmacokinetic model of irinotecan and its four main metabolites in patients treated with FOLFIRI or FOLFIRINOX regimen

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## Structural model code– CPT-11 and its four main metabolites : SN38, SN38G, APC and NPC

[LONGITUDINAL]

input = {V1, V3a, V5a, V6a, V7, k12, k21, ke, Vmax, Km, k34, k43, k35, k5, k6, k7, tau, fa}

PK:

depot(target=C1,p=1/V1)

EQUATION:

odeType=stiff

t\_0 = 0

C1\_0 = 0

C2\_0 = 0

C3\_0 = 0

C5\_0 = 0

C6\_0 = 0

C7\_0 = 0

ddt\_C1 = k12\*(C2-C1) - ke\*C1 - (Vmax\*C1/(Km+C1))

ddt\_C2 = k21 \* (C1-C2)

ddt\_C3 = ke \* V1/V3a \* C1 - k35 \* C3 + k34 \* (C4-C3) + k7\*fa\*V7/V3a \*delay(C7,tau)

ddt\_C4 = k43 \* (C3-C4)

ddt\_C5 = k35\*V3a/V5a\*C3 - k5\*C5

ddt\_C6 = ke\*V1/V6a\*C1 - k6\*C6

ddt\_C7 = V1/V7 \* (Vmax \* C1/(Km+C1)) - k7\*C7

CcIrinu = C1

CcSN38 = C3

CcSN38G = C5

CcAPC = C6

CcNPC = C7

OUTPUT:

output = {CcIrinu, CcSN38, CcSN38G, CcAPC, CcNPC}