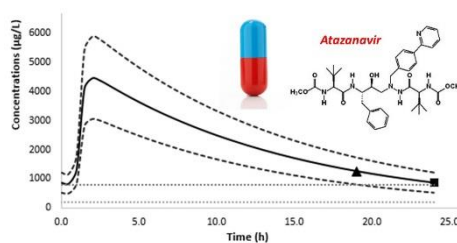


## User Guide for Individual Atazanavir Dose Adjustment (IADAv<sub>1</sub>) June 2014



# User Guide

Three files are given with the Excel program entitled *Individual Atazanavir Dose Adjustment (IADAv1)*:

- 1°) this pdf file entitled “Installation Guide for IADA” that contains an explanation of the procedure to activate the macros and load the Solver.
- 2°) a pdf file “User Guide for IADA” explains how to use and interpret the results given by IADA. One example is proposed.
- 3°) a TextEdit file entitled « LicenceEN” containing a licence.

IADAv1 only works on Microsoft Excel 2013 or later versions. Using incompatible versions of Microsoft leads to error messages and incorrect estimation. This is due to differences in the Solver.



Don't forget to activate the macros and to load the Solver (see “Installation Guide for IADA”) before using IADAv1.

***Individual Atazanavir Dose Adjustment (IADAv1) is free software exploitable only for patients receiving repeated oral route administration of ritonavir-boosted atazanavir.***

***If you need to contact me :***

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## How to use IADAv1

### **Step 1: Insertion of clinical data**

The file entitled “Clinical data” has to be completed.

Insert information into the green boxes:

- Name of the patient
- Date (dd/mm/yy) of the last drug administration (respect cell format)
- Date (dd/mm/yy) of the blood sample (respect cell format)
- Dose (mg) of atazanavir and ritonavir
- Number of administrations *per* day (1 or 2)
- Drug administration time (hh:mm; respect cell format)
- Blood sample time (hh:mm; respect cell format)
- Concentration of atazanavir and ritonavir

Step 1: Insertion of clinical data in green boxes

Name of the patient	TOTO	
	Atazanavir	Ritonavir
Last drug-administration date (dd/mm/yy)	03/06/14	
Blood sample date (dd/mm/yy)	04/06/14	
Time elapsed (d)	1	
Dose per administration (mg)	300	100
Number of administration per day	1	
Last drug-administration time (hh:mm)	8:00	
Blood sampling time (hh:mm)	6:00	
Time elapsed (h)	22.00	
Measured concentration (µg/L = ng/ml)	1204	100

If information is lacking or incorrect, warning messages appear.

Step 1: Insertion of clinical data in green boxes

Name of the patient	TOTO	
	Atazanavir	Ritonavir
Last drug-administration date (dd/mm/yy)	06/06/14	
Blood sample date (dd/mm/yy)	08/06/14	
Time elapsed (d)	2	
Dose per administration (mg)	800	100
Number of administration per day	5	
Last drug-administration time (hh:mm)	21:10	
Blood sampling time (hh:mm)	6:30	
Time elapsed (h)	9.33	
Measured concentration (µg/L = ng/ml)		11000

Time elapsed between administration and sampling can not exceed 1 day

invalid dose

invalid value

Elapsed time between administration and sampling is incorrect: Check dates and times

check the concentration

Insert a concentration

### **Step 2: Estimation of atazanavir trough concentration**

Click on the box entitled “Estimation”. Estimation of atazanavir trough concentration (concentration obtained just before the next administration: 12 hours after the last administration if 2 administrations *per* day; 24 hours after the last administration if 1 administration *per* day) takes 3-4 seconds. atazanavir trough concentration is estimated at the steady-state (repeated oral route administration).

## Step 2: Pharmacokinetic estimation

Estimation

### Step 2: Viewing results

Click on the box entitled “Viewing”: results appear in a new file with the clinical data, the estimated steady-state trough concentration and a proposition for dose adjustment if necessary.

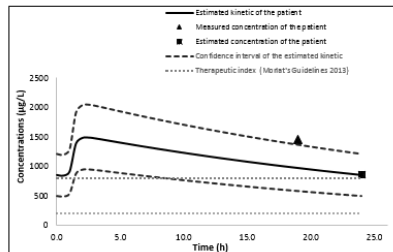
## Step 3: View results

View

If the dose adjustment leads to a dose of atazanavir lower or higher than 100 mg and 400 mg respectively, warning messages appear.

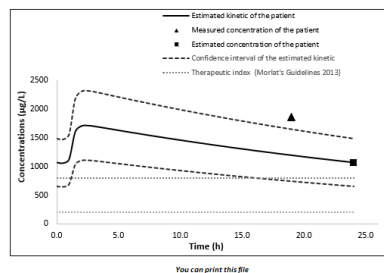
Estimated steady-state concentration : 850 µg/L at 24 h  
Therapeutic index (Morlat's Guidelines 2013) : 200-800 µg/L at 24 h  
Dose adjustment is required

Warning!!! Recommended dose is lower than 100 mg



If the estimated kinetic of the patient is not consistent with the one of the applied PK-POP models (Schipani et al. JAIDS 2013; Dickinson et al. JAC 2009), a warning message appears.

Warning!! Patient's pharmacokinetics are different from those of the PK-POP model. No pharmacokinetic interpretation can be done. A new blood sample would allow verifying this result.



This file can be printed in A4 or in US letter format.

## Examples and pharmacological interpretation

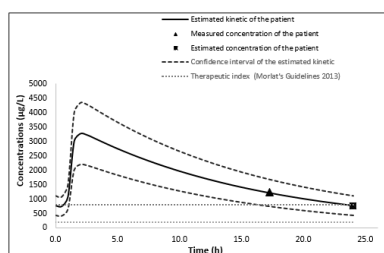
### Example 1

M. POPE takes atazanavir/ritonavir (300 mg/100 mg) once a day. The last drug-administration was on 06/06/14 at 21h15. A blood sample was taken on 07/06/14 at 14h30. Measured concentrations were 1250 ng/mL and 120 ng/mL for atazanavir and ritonavir, respectively.

Step 1: Insertion of clinical data in green boxes		
Name of the patient	POPE	
	Atazanavir	Ritonavir
Last drug-administration date (dd/mm/yy)	06/06/14	
Blood sample date (dd/mm/yy)	07/06/14	
Time elapsed (d)	1	
Dose per administration (mg)	300	100
Number of administration per day	1	
Last drug-administration time (hh:mm)	21:15	
Blood sampling time (hh:mm)	14:30	
Time elapsed (h)	17.25	
Measured concentration (µg/L = ng/mL)	1250	120

Estimation of atazanavir trough concentration (24h post-administration) leads to a value of 772 ng/mL. This concentration is within the therapeutic index (Morlat's Guidelines). No dose adjustment is required.

Estimated concentration [from the PK-POP models published by Dickinson et al. JAC 2009 and Schijns et al. JAIDS 2013]			
Estimated steady-state concentration :	772	µg/L	at 24 h
Therapeutic index (Morlat's Guidelines 2013) :	200-800	µg/L	at 24 h
No dose adjustment is required			



### Example 2

M. POPE takes atazanavir/ritonavir (400 mg/100 mg) twice a day. The last drug administration was on 06/06/14 at 21h10. A blood sample was taken on 07/06/14 at 6h30. Measured concentrations were 1680 ng/mL and 100 ng/mL for atazanavir and ritonavir, respectively.

Step 1: Insertion of clinical data in green boxes		
Name of the patient	POPE	
	Atazanavir	Ritonavir
Last drug-administration date (dd/mm/yy)	06/06/14	
Blood sample date (dd/mm/yy)	07/06/14	
Time elapsed (d)	1	
Dose per administration (mg)	400	100
Number of administration per day	2	
Last drug-administration time (hh:mm)	21:10	
Blood sampling time (hh:mm)	6:30	
Time elapsed (h)	9.33	
Measured concentration (µg/L = ng/mL)	1680	100

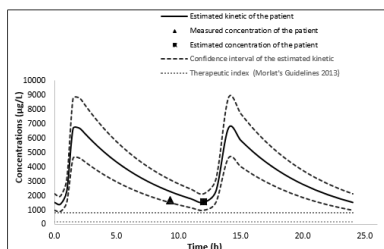
Estimation of atazanavir trough concentration (12h post-administration) leads to a value of 1556 ng/mL. This concentration is outside the therapeutic index (Morlat's Guidelines). Dose adjustment is required with two possible doses.

**Estimated concentration** (from the PK-PDP models published by Dickinson et al. JAC 2009 and Schipani et al. JAIDS 2013)

Estimated steady-state concentration :	1556	µg/L	at 12 h
Therapeutic index (Morlat's Guidelines 2013) :	200-800	µg/L	at 12 h

**Dose adjustment is required**

With 100 mg per administration, the concentration will be :	389	µg/L	at 12 h
With 200 mg per administration, the concentration will be :	778	µg/L	at 12 h



STOP.