

**Table II.** Reported elimination half-life ( $t_{1/2}$ ) and population pharmacokinetic (PopPK) parameters for monoclonal antibodies (mAbs)<sup>a</sup>

Generic name	$t_{1/2}$	PopPK model	$k_a$ (d <sup>-1</sup> )	CL (L/d)	$V_{max}$ (mg/d)/ Km (mg/L)	$V_d$ (L)	Q (L/d)	$V_2$ (L)	Covariates	Reference
Abciximab	30 min									21
Adalimumab	14 d			0.288		4.7–6.0 <sup>b</sup>			(AA + AGE + DOSE + RF + CRP) – CL	22
Alemtuzumab	6 d	2-comp, NLE			24.48/0.338	11.3	25.2	41.5	(WBC) – $V_{max}$	23
Basiliximab	7.2 d	2-comp, LE		0.881		3.6		4.4	(WT, AGE) – CL	24
Bevacizumab	20 d	2-comp, LE		0.207		2.66	0.593	2.76	(WT, SEX, ALB, AP, SGOT, CHEM) – CL; (SEX, WT, ALB) – $V_d$	25
Canakinumab	26 d			0.174 <sup>c</sup>		6.01 <sup>c</sup>				26
Catumaxomab	2.5 d									27
Certolizumab pegol	14 d			0.408		6.4 <sup>b</sup>			AA + ADM + WT + IMM	28
Cetuximab	70–100 h	2-comp, NLE			105.1/74	2.83	2.472	2.43		29
Daclizumab	20 d								(WT, AGE, SEX, PU, RACE) – CL	30
Eculizumab	11.3 d	1-comp, LE		0.528		7.7				31
Efalizumab	5.5–10.5 d	1-comp; LE, LA	0.191	1.29		9.13			(WT, OBS, PASI, LYM, AGE, DOSE) – CL	32
Gemtuzumab ozogamicin	1.9 d									33
Golimumab	12.5 d	1-comp; LE, LA	0.908	0.68 <sup>c</sup>		12.5			MTX	34
Ibritumomab tiuxetan	28 h									35
Infliximab	8–9.5 d	2-comp, LE		0.273		3.06	1.72	2.94	(WBC, AA) – CL; (BSA, SEX) – $V_d$	36
Natalizumab	16 d			0.314					(WT + AA) – CL	37
Ofatumumab	14 d					1.7–5.1			SEX – CL	38
Omalizumab	26 d	Mechanistic, nonlinear							WT – (CL + $V_d$ )	39
Palivizumab	18 d					3.99 <sup>c</sup>				40
Panitumumab	7.5 d	2-comp, LE + NLE		0.269	10.6/0.401	3.66	0.389	2.58	WT – CL + $V_{max}$ + $V_d$ ; CANC – CL; AGE – $V_{max}$	41
Ranibizumab	9 d <sup>d</sup>									42
Rituximab	8.6 d	2-comp, LE		0.257		2.98	0.656	3.64	(BSA, SEX) – CL + $V_d$	43
Tocilizumab	14–8 d <sup>e</sup>	2-comp, LE + NLE		0.30		3.5		2.9	(TB + SPL + BM) – CL	44
Tositumomab (I-131)	2.8 d			1.636					TB	45

**Table II. Contd**

Generic name	$t_{1/2}$	PopPK model	$k_a$ (d <sup>-1</sup> )	CL (L/d)	$V_{max}$ (mg/d)/ Km (mg/L)	$V_d$ (L)	Q (L/d)	$V_2$ (L)	Covariates	Reference
Trastuzumab	28.5 d	2-comp, LE		0.254		3.02	0.452	3.10	(AP, SHED, WT) – CL; WT – $V_d$	46
Ustekinumab	15–32 d	1-comp; LE, LA	0.354	0.465		15.7			(WT, DIA, IMR, ALB, CRE, SEX, AP) – CL; (WT, DIA, RACE) – $V_d$	47

a Only PopPK data from journal publications are reported here, since, in most instances, meeting abstracts did not provide sufficient information on model parameters or model structure. If those data are not available, pharmacokinetic parameters from the SPC or prescribing information are reported.

b  $V_{ss}$ .

c For a person weighing 70 kg.

d Vitreous  $t_{1/2}$ .

e Reported as the initial and final  $t_{1/2}$  within a dosing interval.

AA=formation of anti-mAb antibodies; ADM=repeated administration; AGE=age; ALB=serum albumin concentration; AP=alkaline phosphatase; BM=bone marrow involvement; BSA=body surface area; CANC=cancer type; CHEM=chemotherapy; CL=apparent total clearance; comp=compartment; CRE=serum creatinine; CRP=C-reactive protein; DIA=diabetes mellitus; DOSE=dose of the drug; IMM=immunosuppressant use; IMR=immune response;  $k_a$ =absorption rate constant; Km=Michaelis-Menten constant; LA=linear absorption; LE=linear elimination; LYM=baseline lymphocyte counts; MONO=monocyte count; MTX=methotrexate use; NLE=nonlinear elimination; OBS=obesity; PASI=Psoriasis Area and Severity Index score; PU=proteinuria; Q=intercompartmental clearance; RACE=race or ethnicity; RF=rheumatoid factor; SEX=sex (male or female); SGOT=serum glutamic oxaloacetic transaminase (now called AST); SHED=shed antigen; SPC=summary of product characteristics; SPL=splénomegaly; TB=tumour burden;  $V_2$ =peripheral volume of distribution;  $V_d$ =volume of distribution;  $V_{max}$ =maximum rate of NLE;  $V_{ss}$ =volume of distribution at steady state; WBC=white blood cell count; WT=bodyweight.

21. Reopro 2mg/mL solution for injection or infusion: summary of product characteristics. Basingstoke: Eli Lilly and Company Limited, 2009 Aug 7 [online]. Available from URL: [http://www.medicines.org.uk/emc/medicine/610/spc/reopro+2mg-ml+solution+for+injection+or+infusion./#pharmacokinetic\\_props](http://www.medicines.org.uk/emc/medicine/610/spc/reopro+2mg-ml+solution+for+injection+or+infusion./#pharmacokinetic_props) [Accessed 2010 May 27]
22. Humira pen and syringe: summary of product characteristics. Maidenhead: Abbott Laboratories Limited, 2010 May 18 [online]. Available from URL: <http://www.medicines.org.uk/emc/medicine/21201/SPC/Humira+Pen+and+Syringe/> [Accessed 2010 May 27]
23. Mould DR, Baumann A, Kuhlmann J, et al. Population pharmacokinetics-pharmacodynamics of alemtuzumab (Campath) in patients with chronic lymphocytic leukaemia and its link to treatment response. *Br J Clin Pharmacol* 2007; 64: 278-91
24. Kovarik JM, Kahan BD, Rajagopalan PR, et al. Population pharmacokinetics and exposure-response relationships for basiliximab in kidney transplantation. The US Simulect Renal Transplant Study Group. *Transplantation* 1999; 68: 1288-94
25. Lu J, Bruno R, Eppler S, et al. Clinical pharmacokinetics of bevacizumab in patients with solid tumors. *Cancer Chemother Pharmacol* 2008; 62: 779-86
26. Novartis Pharmaceuticals Corporation. Ilaris (canakinumab) injection for subcutaneous use: US prescribing information. East Hanover (NJ): Novartis Pharmaceuticals Corporation, 2009 Jun [online]. Available from URL: [http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2009/125319s000lbl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2009/125319s000lbl.pdf) [Accessed 2010 Jun 11]
27. Removab 10 microgram concentrate for solution for infusion: summary of product characteristics. Graefelfing: Fresenius Biotech GmbH, 2010 Feb 1 [online]. Available from URL: <http://www.ema.europa.eu/humandocs/PDFs/EPAR/removab/emea-combined-h972en.pdf> [Accessed 2010 Jun 11]
28. Cimzia 200 mg solution for injection: summary of product characteristics. Slough: UCB Pharma Limited, 2009 Oct 12 [online]. Available from URL: <http://www.medicines.org.uk/emc/medicine/22323/SPC/Cimzia+200+mg+solution+for+injection> [Accessed 2010 May 27]
29. Dirks NL, Nolting A, Kovar A, et al. Population pharmacokinetics of cetuximab in patients with squamous cell carcinoma of the head and neck. *J Clin Pharmacol* 2008; 48: 267-78
30. Zenapax 5 mg/mL concentrate for solution for infusion: summary of product characteristics. Welwyn Garden City: Roche Registration Limited, 2004 [online]. Available from URL: <http://www.ema.europa.eu/humandocs/PDFs/EPAR/Zenapax/H-198-PI-en.pdf> [Accessed 2010 May 27]
31. Soliris: summary of product characteristics. Weybridge: Alexion Pharma UK Ltd, 2009 Sep 23 [online]. Available from URL: [http://www.medicines.org.uk/EMC/medicine/19966/SPC/Soliris/#pharmacokinetic\\_props](http://www.medicines.org.uk/EMC/medicine/19966/SPC/Soliris/#pharmacokinetic_props) [Accessed 2010 May 27]
32. Sun Y, Lu J, Joshi A, et al. Population pharmacokinetics of efalizumab (humanized monoclonal anti-CD11a antibody) following long-term subcutaneous weekly dosing in psoriasis subjects. *J Clin Pharmacol* 2005; 45: 468-76
33. Mylotarg<sup>®</sup> (gemtuzumab ozogamicin for injection): US prescribing information. Philadelphia (PA): Wyeth Pharmaceuticals Inc., 2009 Sep [online]. Available from URL: <http://www.wyeth.com/content/showlabeling.asp?id=119> [Accessed 2010 May 27]

34. Xu Z, Vu T, Lee H, et al. Population pharmacokinetics of golimumab, an anti-tumor necrosis factor- $\alpha$  human monoclonal antibody, in patients with psoriatic arthritis. *J Clin Pharmacol* 2009 Sep; 49: 1056-70
35. Zevalin 1.6mg/mL, kit for radiopharmaceutical preparation for infusion: summary of product characteristics. Newbury: Bayer plc, 2009 Oct 16 [online]. Available from URL: [http://www.medicines.org.uk/emc/medicine/14048/spc/zevalin+1.6+mg+ml%2c+kit+for+radiopharmaceutical+preparation+for+infusion/#pharmacokinetic\\_props](http://www.medicines.org.uk/emc/medicine/14048/spc/zevalin+1.6+mg+ml%2c+kit+for+radiopharmaceutical+preparation+for+infusion/#pharmacokinetic_props) [Accessed 2010 May 27]
36. Xu Z, Seitz K, Fasanmade A, et al. Population pharmacokinetics of infliximab in patients with ankylosing spondylitis. *J Clin Pharmacol* 2008; 48: 681-95
37. Tysabri 300mg concentrate for solution for infusion: summary of product characteristics. Maidenhead: Biogen Idec Ltd, 2010 May 25 [online]. Available from URL: [http://www.medicines.org.uk/EMC/medicine/18447/SPC/tysabri+300+mg+concentrate+for+solution+for+infusion/#pharmacokinetic\\_props](http://www.medicines.org.uk/EMC/medicine/18447/SPC/tysabri+300+mg+concentrate+for+solution+for+infusion/#pharmacokinetic_props) [Accessed 2010 May 27]
38. Coiffier B, Losic N, Rønn BB, et al. Pharmacokinetics and pharmacokinetic/pharmacodynamic associations of ofatumumab, a human monoclonal CD20 antibody, in patients with relapsed or refractory chronic lymphocytic leukaemia: a phase 1-2 study. *Br J Haematol*. Epub 2010 Apr 16
39. Hayashi N, Tsukamoto Y, Sallas WM, et al. A mechanism-based binding model for the population pharmacokinetics and pharmacodynamics of omalizumab. *Br J Clin Pharmacol* 2007; 63: 548-61
40. Synagis: summary of product characteristics. Maidenhead: Abbott Laboratories Limited, 2010 Jan 12 [online]. Available from URL: <http://www.medicines.org.uk/EMC/medicine/5676/SPC/Synagis/> [Accessed 2010 May 27]
41. Ma P, Yang BB, Wang YM, et al. Population pharmacokinetic analysis of panitumumab in patients with advanced solid tumors. *J Clin Pharmacol* 2009; 49: 1142-56
42. Lucentis 10 mg/ml solution for injection: summary of product characteristics. Camberley: Novartis Pharmaceuticals UK Ltd, 2009 Feb 9 [online]. Available from URL: <http://www.medicines.org.uk/EMC/medicine/19409/SPC/Lucentis+10+mg+ml+solution+for+injection/> [Accessed 2010 May 27]
43. Ng CM, Bruno R, Combs D, et al. Population pharmacokinetics of rituximab (anti-CD20 monoclonal antibody) in rheumatoid arthritis patients during a phase II clinical trial. *J Clin Pharmacol* 2005; 45: 792-801
44. RoActemra 20 mg/mL concentrate for solution for infusion: summary of product characteristics. Welwyn Garden City: Roche Products Ltd, 2010 Jun 9 [online]. Available from URL: <http://www.medicines.org.uk/EMC/medicine/22311/SPC/RoActemra+20mg+ml+Concentrate+for+Solution+for+Infusion/> [Accessed 2010 Jun 11]
45. Bexxar (tositumomab and iodine I 131 tositumomab): US prescribing information. Research Triangle Park (NC): GlaxoSmithKline, 2005 [online]. Available from URL: [http://us.gsk.com/products/assets/us\\_bexxar.pdf](http://us.gsk.com/products/assets/us_bexxar.pdf) [Accessed 2010 May 27]
46. Fukushima Y, Charoin J-E, Brewster M, et al. Population pharmacokinetic analysis of trastuzumab (Herceptin<sup>®</sup>) based on data from three different dosing regimens [abstract no. 1121]. Sixteenth Meeting of the Population Approach Group in Europe; 2007 Jun 13-17; Copenhagen [online]. Available from URL: <http://www.page-meeting.org/default.asp?abstract=1121> [Accessed 2010 May 27]
47. Zhu Y, Hu C, Lu M, et al. Population pharmacokinetic modeling of ustekinumab, a human monoclonal antibody targeting IL-12/23p40, in patients with moderate to severe plaque psoriasis. *J Clin Pharmacol* 2009; 49: 162-75