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Supplementary Tables and Figures

Table S1: Use/consumption data of anticancer drugs in hospitals in NW England as well as selected studies

Drug name	Consumption for NW England hospitals shown in g/year and (µg/capita/d)						Average (range) for NW hospitals (g/yr)	International studies	
	University hospitals of Morecombe Bay[2]	Lancashire teaching hospitals[3]	Blackpool teaching hospitals NHS foundation[4]	East Lancashire teaching hospitals[5]	Greater Manchester & Cheshire cancer network[6]	Clatterbridge centre for oncology[7]		France, 2008 [14] (kg/yr)	University Hospital, Geneva Switzerland [64] (g/yr)1
Cyclophosphamide	1300 (9.8)	610 (4.3)	1900 (15.8)	1300 (7.1)	1400 (2.6)	71000 (84.5)	12918(310-71000)	310	610
Chlorambucil	12 (0.1)	-	10 (0.1)	-	12 (0.0)	-	6 (10-12)	8	-
Melphalan	1 (0.0)	-	20 (0.2)	-	1 (0.0)	-	4 (1-20)	5	-
Ifosfamide	150 (1.1)	-	-	-	120 (0.2)	1000 (1.2)	423 (120-1000)	100	450
Bendamustine	-	-	1 (0.0)	-	91 (0.2)	-	15 (1-91)	-	-
Busulfan	<1	-	30 (0.2)	-	-	-	5 (<1-30)	-	-
Treosulfan	200 (1.5)	860 (6.0)	400 (3.3)	100 (0.5)	-	-	260 (100-860)	-	-
Carmustine	-	-	6 (0.0)	-	-	-	1 (6)	2	-
Lomustine	-	-	6 (0.0)	-	-	42 (0.0)	8 (6-42)	3	-
Temozolomide	-	120 (0.8)	-	-	-	900 (1.1)	170 (120-900)	54	-
Dacarbazine	83 (0.6)	36 (0.3)	64 (0.5)	60 (0.3)	50 (0.1)	460 (0.5)	126 (36-460)	29	-
Methotrexate	12 (0.1)	-	130 (1.1)	7 (0.0)	260 (0.5)	900 (1.1)	218 (7-	75	410

							900)		
Pemetrexed	160 (1.2)	150 (1.1)	130 (1.1)	140 (0.8)	35 (0.1)	870 (1.0)	248 (35-870)	37	-
Mercaptopurine	16 (0.1)	-	26 (0.2)	-	90 (0.2)	-	22 (16-90)	95	-
Tioguanine	-	-	-	-	2 (0.0)	-	<1 (2)	2	-
Cladribine	<1	1 (0.0)	<1	-	<1	-	<1 (<1-1)	-	-
Fludarabine	11 (0.1)	-	9 (0.1)	-	16 (0.0)	-	6 (9-16)	6	6
Cytarabine	8 (0.1)	-	940 (7.8)	64 (0.4)	970 (1.8)	-	330 (8-970)	130	670
5-Fluorouracil	2500 (18.9)	3100 (21.8)	1800 (14.9)	790 (4.3)	1800 (3.4)	13000 (1.5)	3832 (790-13000)	1700	3100
Tegafur	-	58 (0.4)	-	-	-	58 (0.0)	19 (58)	37	-
Gemcitabine	1300 (9.8)	2300 (16.1)	860 (7.1)	1600 (8.8)	110 (0.2)	6800 (0.8)	2162 (110-6800)	380	660
Capecitabine	29000 (218.8)	64000 (449.3)	34000 (282.1)	-	-	230000 (27.4)	59500 (29000-230000)	5100	-
Azacitidine	18 (0.1)	-	11 (0.1)	28 (0.2)	17 (0.0)	-	12 (11-28)	-	-
Vinblastine	2 (0.0)	-	2 (0.0)	<1	1 (0.0)	-	1 (<1-2)	1	-
Vincristine	1 (0.0)	1 (0.0)	1 (0.0)	<1	1 (0.0)	<1	1 (<1-1)	<1	1
Vinorelbine	13 (0.1)	19 (0.1)	45 (0.4)	-	1 (0.0)	220 (0.0)	50 (1-220)	13	-
Etoposide	190 (1.4)	90 (0.6)	210 (1.7)	3 (0.0)	38 (0.1)	700 (0.1)	205 (3-700)	41	110
Paclitaxel	35 (0.3)	200 (1.4)	39 (0.3)	57 (0.3)	140 (0.3)	390 (0.0)	144 (35-390)	39	79
Docetaxel	58 (0.4)	74 (0.5)	44 (0.4)	53 (0.3)	43 (0.1)	260 (0.0)	89 (44-260)	27	43
Trabectedin	-	-	-	-	-	6 (0.0)	1 (6)	-	-
Dactinomycin	-	-	-	-	-	72 (0.0)	12 (72)	-	-

Doxorubicin	26 (0.2)	6 (0.0)	14 (0.1)	27 (0.1)	32 (0.1)	88 (0.0)	32 (6-88)	17	30
Daunorubicin	-	-	15 (0.1)	-	11 (0.0)	-	4 (11-15)	1	-
Epirubicin	87 (0.7)	95 (0.7)	70 (0.6)	96 (0.5)	61 (0.1)	44 (0.0)	76 (44-96)	18	41
Idarubicin	<1	-	1 (0.0)	-	1 (0.0)	-	<1 (<1-1)	<1	-
Mitoxantrone	<1	-	1 (0.0)	-	<1	-	<1 (<1-1)	<1	-
Bleomycin	1 (0.0)	4 (0.0)	2 (0.0)	<1	2 (0.0)	7 (0.0)	3 (<1 -4)	1	-
Mitomycin C	16 (0.1)	<1	11 (0.1)	13 (0.1)	3 (0.0)	<1	8 (<1-16)	3	9
Cisplatin	45 (0.3)	190 (1.3)	39 (0.3)	43 (0.2)	16 (0.0)	370 (0.0)	117 (16-370)	23	67
Carboplatin	320 (2.4)	950 (6.7)	540 (4.5)	600 (3.3)	15 (0.0)	2800 (0.3)	871 (15-2800)	84	330
Oxaliplatin	96 (0.7)	130 (0.9)	110 (0.9)	89 (0.5)	74 (0.1)	510 (0.1)	168 (74-510)	33	64
Procarbazine	24 (0.2)	-	-	-	3 (0.0)	120 (0.0)	25 (3-120)	35	-
Rituximab	-	120 (0.8)	320 (2.7)	-	310 (0.6)	18 (0.0)	128 (18-320)	72	-
Trastuzumab	250 (1.9)	370 (2.6)	160 (1.3)	260 (1.4)	-	2000 (0.2)	507 (160-2000)	56	-
Alemtuzumab	-	-	-	-	30 (0.1)	-	5 (30)	-	-
Cetuximab	17 (0.1)	110 (0.8)	57 (0.5)	-	-	270 (0.0)	76 (17-270)	55	-

"-" = not recorded

[1] Calculated using the average dose (mg) from NW hospital survey

[2] Comprising of Furness general hospital, Royal Lancaster Infirmary, Westmorland general hospital, Queen Victoria hospital, Ulverston community health centre. Population served 363,000

[3] Comprising of Royal Preston hospital (Rosemere cancer foundation) and Chorley and South Ribble hospital. Population served 390,000

[4] Comprising of Blackpool Victoria hospital, Clifton hospital, Fleetwood hospital and three elderly rehabilitation hospitals. Population served 330,000

[5] Comprising of Burnley general hospital, Royal Blackburn hospital and Inpatient rehabilitation services are also provided at Pendle community hospital and the Rakehead unit at Burnley general hospital. Outpatient and diagnostic services are also provided at the Accrington Victoria, Clitheroe hospital, Rossendale and St Peters Primary health care centre's. Population served 500,000

[6] Comprising of NHS Trafford (Trafford general hospital host to the Trafford Macmillan care centre); Bolton NHS Foundation trust (Royal Bolton hospital); Salford Royal NHS Foundation trust (Salford Royal hospital); Mid Cheshire hospitals NHS foundation trust (Leighton hospital, Victoria Infirmary and Elmhurst intermediate care centre); Wrightington, Wigan and Leigh NHS foundation trust (Royal Albert Edward Infirmary, Leigh Infirmary, Wrightington hospital and Thomas Linacre centre (provides the majority of out-patient services for the Trust). Population served 1,463,000

[7] Comprising of outpatient clinics at Linda McCartney centre (Royal Liverpool University hospital), the Countess of Chester, Southport hospital, Halton general hospital, Aintree University hospital, Broadgreen hospital and The Liverpool Woman's. Population served 2,300,000

Table S2: Average urinary excretion rates of the unchanged parent drug

% of administered drug excreted (i.e. not metabolized)					
<5%	5-15%	15-25%	25-45%	45-75%	>75%
Chlorambucil[1, 2, 3, 4] [1] Busulfan[1, 2, 5] [2] Lomustine[1, 2] Capecitabine[1, 2] [3] Trabectedin[1, 2] [4] Idarubicin[2] [5] Gefitinib[1, 2] Sorafenib[1, 2] Dasatinib[1] Laptinib[1] [6] Nilotinib[2, 5] Temsirolimus[1, 2] Everolimus[1, 2] Pazopanib[1, 2] Bortezomib*** Trastuzumab*** Alemtuzumab*** Rituximab*** Cetuximab*** Bevacizumab***	Temozolomide[1, 2] [7, 8] Mercaptopurine[1, 2] Cytarabine[2] Gemcitabine[1] [9] Vinblastine[2] [10] Vincristine[2,] [11] Vinorelbine[1, 2] Paclitaxel[1, 2] Docetaxel[1, 2] Doxorubicin[1, 2, 3] [12] Epirubicin[1, 2] [12] Mitoxantrone[1, 2] Mitomycin[1, 2] Procarbazine[2, 4] Imatinib[1, 2] Erlotinib[1, 2] Mitotane[1, 2, 4, 6] [13] Eribulin[1]	Cyclophosphamide[1, 2, 3] [12, 14-17] Melphalan[1, 2] [18] Bendamustine[1] Treosulfan [19-22] Tioguanine [23, 24] 5-Fluorouracil[1, 2] [3, 9, 12] Tegafur[1] Dactinomycin[1] Sunitinib[1, 2] [25] Irinotecan[1, 2]	Ifosfamide[2, 3] [17, 26, 27] Dacarbazine[1, 2] Cladribine[1, 2] Fludarabine[1, 2] Etoposide[1, 2, 3] Daunorubicin[1, 2] [28] Cisplatin[1] [8] Oxaliplatin[1, 2] [8] Topotecan[1, 2]	Carmustine[1, 2] Azacitidine[2] Bleomycin[1, 2] Carboplatin[1, 2] [8] Hydroxyurea[1, 2] Tretinoin[1, 2]	Methotrexate[2, 3] [29] Pemetrexed[1, 2, 3] [30]

[1] electronic Medicines Compendium (eMC) (http://www.medicines.org.uk/EMC)
[2] Product monograph (http://www.bccancer.bc.ca/HPI/DrugDatabase/DrugIndexPro/default.htm)
[3] RxList (http://www.rxlist.com/script/main/hp.asp)
[4] Drugs.com (http://www.drugs.com/)
[5] Ema (http://www.ema.europa.eu/ema/)
[6] ToxNet (http://toxnet.nlm.nih.gov/)
*** No available data (Urinary excretion data was not available for six L01X anticancer drugs)

Table S3: Physiochemical properties of selected cytotoxic drugs and their classification according to the Anatomical Therapeutic Classification (ATC) system.

ATC	Drug name	pKa	Charge at pH 7.4	Weak acid/weak base	Log Kow	Log Dow at pH 7.4	Koc[4]	BCF[4]	Solubility in water (mg/L) at 25°C[4]
L01AA01	Cyclophosphamide	2.84, 6.00 [31, 32]	Neutral	Acid [32]	0.63		44	3	4.00E+04
L01BC06	Capecitabine	8.8 [33]	Neutral	Acid	0.96*		8	3	8.23E+02
L01BC02	5-Fluorouracil	7.6-8.0, 13.0 [32-34]	Neutral	Acid [32]	-0.93		4	3	1.11E+04
L01XX05	Hydroxyurea	10.6*	Neutral	Acid	-1.27		3	3	7.91E+04
L01XE01	Imatinib	8.07, 3.73, 2.56, 1.52*	Positive	Base		0.19	16	3	6.48E+01
L01BA01	Methotrexate	3.80, 4.8, 5.6 [33]	Negative	Acid		-1.41	20	3	4.98E+03
L01XA02	Carboplatin	0.24, 3.55*		Base	-1.78	0.01	891 [35]		
L01BC05	Gemcitabine	3.6 [34]	Neutral	Base	-1.24		1	3	1.53E+04[6]
L01CB01	Etoposide	9.8 [36]	Neutral	Acid	0.60		19	3	5.87E+01
L01AA05	Ifosfamide	1.45-4.0 [31, 32]	Neutral	Base [32]	0.86		51	3	3.78E+03
L01AX04	Dacarbazine	4.42*	Neutral	Base	-0.24		15	10	4.22E+03
L01AB02	Treosulfan	12.36*	Neutral	Acid	-2.09*		1	3	7.00E+04[8]
L01XX23	Mitotane	N/A	Neutral	N/A	6.11*		154882	4989	1.00E-01
L01XE07	Lapatinib	3.80, 7.20[2]*	Positive	Base		4.72	426580	1127	9.06E-02
L01CD01	Paclitaxel	11.99	Neutral	Zwitterion [32]	5.25		58884	750	1.07E-04
L01AA03	Melphalan	1.83, 9.13 [37]	Neutral	Acid [38]	-0.52		14	3	2.71E+02
L01AA09	Bendamustine	0.88, 4.17, 6.94[5]	Negative	Zwitterion/Acid		2.84	977	3	2.69E+01
L01AD01	Carmustine	12.27*	Neutral	Acid	1.53		89	5	1.83E+03
L01AX03	Temozolomide	N/A [39]	Neutral	Base	1.15		29	3	1.81E+03
L01BA04	Pemetrexed	3.6, 4.4 [33]	Negative	Acid		-2.43	60	3	1.84E+02

L01BB02	Mercaptopurine	7.9 [40]	Neutral	Acid [40]	0.67 [40]		40	3	1.98E+04
L01BB05	Fludarabine	3.2, 5.8*	Negative	Acid		-1.22	2	3	1.44E+04
L01BC01	Cytarabine	4.2 [34]	Neutral	Base	-2.15		1	3	8.66E+04
L01BC03	Tegafur	7.98[1]	Neutral	Acid	-0.27		6	3	3.64E+03
L01BC07	Azacitidine	2-3 [41]	Neutral	Base	-2.17		1	3	8.89E+04
L01CA04	Vinorelbine	7.4, 5.4 [42, 43]	Positive	Base	4.72*	4.57	30200	604	9.86E-03
L01CD02	Docetaxel	12.02*	Neutral	Acid	3.64*		27	65	5.17E-03
L01DA01	Dactinomycin	8.06 [44]	Neutral	Acid	1.42*				
L01DB01	Doxorubicin	7.34, 8.3, 9.46 [31, 33, 45]	Positive	Base [32]		-1.93	389	3	5.34E+02
L01DB02	Daunorubicin	8.4 [31, 45]	Positive	Base [32]		-0.14	490	1	1.23E+02
L01DB03	Epirubicin	7.7 [31]	Positive	Base*		-0.30	372	4	6.25E+02
L01DC01	Bleomycin	7.3 [46]	Positive	Base		-0.47			
L01DC03	Mitomycin C	3.2	Neutral	Base	-0.38		76	3	8.11E+03
L01XA01	Cisplatin	6.6, 5.5, 7.3 [47]			-2.40	-2.19	12589 [35]		
L01XA03	Oxaliplatin	7.35, 9.99*		Base	-1.63	-1.42			
L01XB01	Procarbazine	6.8*	Neutral	Base	-0.82*		18	3	8.32E+03
L01XE03	Erlotinib	5.42*	Neutral	Base	2.96*		2188	42	9.97E+00
L01XE04	Sunitinib	8.95*	Positive	Base		0.76	891	29	1.52E+01
L01XE05	Sorafenib	11.55, 2.03[2]*	Neutral	Base/Acid	4.39*		2884	366	2.14E-01
L01XE08	Nilotinib	2.1, 5.4[1]	Neutral	Base	3.60		79433	110	3.90E-01
L01XE11	Pazopanib	2.1, 6.4, 10.2[3]	Neutral	Base/Acid	3.38*		12023	79	2.32E+00
L01XX14	Tretinoin	5.0*	Negative	Acid		4.30			
L01XX17	Topotecan	0.60, 6.99, 10.50 [48]	Positive	Base/Acid		-3.13	107	3	3.30E+02
L01XX19	Irinotecan	8.1*	Positive	Base		3.24	2818	355	3.64E-02
L01XX32	Bortezomib	13.82*	Neutral	Acid	1.47*		766	4	2.13E+02
L01XX41	Eribulin	9.59[2]	Positive	Base		-0.34	1288	14	2.70E+00

[1] www.ema.europa.eu/docs/en_GB/.../WC500034398.pdf
[2] *ACD properties calculator (*http://www.chemicalize.org/structure*)*
[3] http://www.medicines.org.au/files/gwpvotri.pdf
[4] BCF predicted with EPI SUITE: linear relationship with kow does not hold for many compounds with high polarity (see text)
[5] http://www.faqs.org/patents/app/20090264488
[6] MSDS gemcitabine (http://ehs.lilly.com/msds/Gemzar.pdf)
[7] MSDS imatinib (http://export.fass.se/pdfprint/servlet/se.itsip.pdfprint.servlets.ConvertServlet?nplId=20031111000058&docTypeId=78&userType=2&paraImported=null&orgNplId=null&showParaLink=null&hasEnvSection=yes&paraInfo=null&orgCompany=null&docId=ID18IILYT1XUZ1XGCS_IDX0000000180&fontSize=standard)
[8] MSDS treosulfan (http://www.medac.de/medac_international/data/SDS/treosulfan_E.pdf)
*From predicted data
** Calculated as an average, with consideration to dastinib a similar compound to basic ionization

Table S4: Degradative loss processes: biodegradation and hydrolysis

Drug Name	Biodegradation				Hydrolysis			% STP total removal (EPI suite)	Ref.
	Test	Incubation (days)	Initial conc.	Results	Log k_{OH} (L/mole.s)[1]	% loss in 5days			
						at pH 7.0	at pH 8.1		
Cyclophosphamide	ZWT[2] (OECD 302B)	28	51.7mg/L	No degradation	-8.458	Neg.	Neg.	1.86	[49]
	OECD confirmatory	10	375, 750mg/L	0±5% degradation					[50]
	CBT[3] (OECD 1992)	40	4.3mg/L	28-66% degradation in 40 days. Chemical structurally related to CP					[51]
	ZWT[2] (OECD 1992)	40	200mg/L	5-72% degradation in 28 days. Chemical structurally related to CP					[51]
	AS incubation	1	90, 900ng/L	No degradation					[52]
Ifosfamide	ZWT[2] (OECD 302B)	42	51.7mg/L	No degradation	-7.397	Neg.	Neg.	1.88	[53]
	STP simulation	42	11.4µg/L	Negligible					[53]

	test (OECD 1992)								
	CBT[3] (OECD 1992)	40	4.3mg/L	28-66% degradation in 40 days. Chemical structurally related to IF					[51]
	ZWT[2] (OECD 1992)	40	200mg/L	5-72% degradation in 28 days. Chemical structurally related to IF					[51]
Treosulfan	CBT[3] (OECD 301D)	40	5mg/L	30% degradation in the first 28 days (40% in 40 days)	N/A	N/A	N/A	1.85	[54]
Methotrexate	OECD confirmatory (AS incubation)	10	10, 20mg/L	98±6% degradation. > 10% in the first four days	N/A	N/A	N/A	1.85	[50]
Pemetrexed	Ready biodegradability	29	N/A	20% was released as CO^2	N/A	<10% (at 50°C)[4]	N/A	1.85	MSDS[4]
	Biodegradation (sludge)	1	N/A	>99% disappearance when incubated with 1.5g/L					MSDS[4]

				sludge solids. After 1 hour incubation 90% of pemetrexed had degraded					
Fludarabine	N/A	N/A	N/A	N/A	-4.097	Neg.	Neg.	1.85	N/A
Cytarabine	OECD confirmatory AS incubation	10	12.5, 25mg/L	60±8% degradation, 2 days = ~10%	N/A	N/A	N/A	1.85	[50]
	CBT[3] (OECD 301D)	40	N/A	50% degradation after 20days					[55]
	ZWT[2] (OECD 302B)	40	N/A	>95% degradation HOW MANY DAYS?					[55]
5-fluorouracil	CBT[3] (OECD 301D)	28 and 40	9.02mg/L	No degradation	N/A	N/A	N/A	1.85	[55]
	ZWT[2] (OECD 302B)	28	854mg/L	2% degradation					[55]
	OECD 303A confirmatory AS incubation	10	5, 10, 20mg/L	100±4% (15% after 1 day and a sharp increase to 100% on day 2) Higher degradation rate with lower concentrations					[50]
	AS incubation	50	50ug/L	<60% removal					[56]

				after 50 days					
	AS incubation	1	5, 500ug/L	Complete degradation					[57]
	ZWT[2] (0ECD 302B)	21	270mg/L	No degradation, using pre-adapted AS					[3]
	Inherent biodegradation test, 4g AS/L and closed test vessels	14	0.2, 11.4mg/L	97.5->100% degradation. > 25% Biodegradation in 1day					[3]
	OECD 303A	3	10mg/L	38-92% biodegradation					[3]
Gemcitabine	CBT[3] (OECD 301D)	40	1660mg/L	45% Degradation	N/A	Neg.[5]	N/A	1.85	[55]
	ZWT[2] (OECD 302B)	40	1660mg/L	50% degradation					[55]
	Aerobic biodegradation	28		30% degradation					MSDS[5]
Capecitabine	ZWT[2] (OECD 303B)	28	N/A	58% degradation (15% removed in 7 days)	N/A	N/A	N/A	1.85	[3]
	Like OECD 302C	21	30mg/L	41% mineralization, 27% mineralization in 14 days					[3]
	Like OECD	84		55-66%					[3]

	302C			mineralization, 29% mineralization in 28 days					
Vinblastine	CBT[3]	28	N/A	10% Degradation	0.016/-0.835/-1.261	0.63-4.48	7.95-56.40	NOT ON LIST	[58]
	ZWT[2]	40	N/A	18% degradation					[58]
Vincristine	CBT[3]	28	N/A	30% degradation	-0.788/0.149	0.70-6.09	8.86-76.60	NOT ON LIST	[58]
Vinorelbine	N/A	N/A	N/A	N/A	-0.844/0.004/-1.261	0.24-4.36	2.98-54.90	66.90	N/A
Etoposide	N/A	N/A	N/A	N/A	-2.689	0.01	0.11	1.86	N/A
Paclitaxel	N/A	N/A	N/A	N/A	-0.297/-1.669/0.000/-0.433	0.09-4.32	1.17-54.40	84.19	N/A
Docetaxel	N/A	N/A	N/A	N/A	-0.317/-1.689/-0.452/4.667	0.00-2.08	0.00-26.20	16.63	N/A
Doxorubicin	AS incubation	1	2500ug/L	48-74% degradation (20-40% recovered in sludge, 6-12% recovered in liquid phase). Degraded mainly due to adsorption to	N/A	N/A	N/A	1.85	[57]

				sludge					
Epirubicin	CBT[3] (OECD 301D)	N/A	5mg/L	No degradation	N/A	N/A	N/A	1.85	[59]
	ZWT[2] (OECD 302B)	N/A	N/A	Degraded, mainly due to adsorption to sludge					[59]
	ZWT[2] (OECD 302B) CBT[3] (OECD 301D)	N/A	N/A	Eliminated in ZWT but not in CBT					[57]
Mitoxantron	CBT[3] (OECD 301D)	40	5mg/L	No degradation	N/A	N/A	N/A		[54]
Mitomycin	N/A	N/A	N/A	N/A	-2.218	0.03	0.33	1.85	N/A
Cisplatin	OECD screening test	21	0, 0.32, 1.6mg/L	0±2% Degradation	N/A	N/A	N/A	N/A	[50]
Imatinib	Aerobic, 92/69/EC (L383) C.4-C	28	N/A	9-12%; not readily biodegradable	N/A	N/A	N/A	1.85	MSDS[6]
Topotecan	N/A	N/A	N/A	N/A	-0.986	0.45	5.62	1.85	N/A
Irinotecan	N/A	N/A	N/A	N/A	-1.127/0.000	0.32-4.32	4.06-54.40	8.33	N/A

Neg. – negligible
N/A – not available
AS – activated sludge
STP – sewage treatment plant
[1] Second order rate constant estimated using the SPARC model (http://archemcalc.com/sparc/test/login.cfm?CFID=250050&CFTOKEN=79322869)
[2] ZWT - Zahn-Wellens Test (test for inherent biodegradability – OECD302)

[3] CBT – Closed Bottle Test (OECD 301)
[4] MSDS pemetrexed (http://ehs.lilly.com/msds/Alimta.pdf)
[5] MSDS gemcitabine (http://ehs.lilly.com/msds/Gemzar.pdf)
[6] MSDS imatinib (http://export.fass.se/pdfprint/servlet/se.itsip.pdfprint.servlets.ConvertServlet?nplId=20031111000058&docTypeId=78&userType=2&paraImported=null&orgNplId=null&showParaLink=null&hasEnvSection=yes&paraInfo=null&orgCompany=null&docId=ID18IILYT1XUZ1XGCS_IDX0000000180&fontSize=standard)

Table S5: Consumption and predicted fate of anticancer drugs likely to be present in sewage effluent based on 2010-2012 consumption in NW England. Values assume excretion of the unchanged drug based on Table S2 (Supplementary information) and 'best values' for estimated removal rates in STPs.

ATC Drug	Consumption (kg/year)[1]	Consumption (µg/capita/d)[2]	Excretion of original drug %[3]	Influent load (µg/capita/d)	% of intact drug after STP biodegradation[4]	Load after STP biodegradation (µg/capita/d)	Predicted effluent conc. (ng/L)[5]	Predicted river water conc. (ng/L)[6]	Discussion
L01AA01*** Cyclophosphamide	77.51	40	21	8.4	98.1*	8.3	41.3	4.1	- Continuous diffusive discharge[7] - Persistence in the environment confirmed (hospital effluents, STP wastewaters and surface waters)
L01BC06*** Capecitabine	357.00	183	3	5.4	85.0	4.6	23.1	2.3	- Pro-drug of 5-FU (may contribute to 5-FU load) - Continuous diffusive discharge[7] - No biodegradation studies: used a predicted biodegradation rate similar to 5-FU (85% loss) – at present this is highly uncertain.
L01BC02*** Fluorouracil	22.99	12	18	2.1	85.0	1.8	8.9	0.9	- No evidence of abiotic degradation is apparent. - 5-FU has only been detected in hospital effluents, presence in surface waters needs confirming.

L01XX05*** Hydroxyurea	64.00	33	58	18.8	5.0	0.9	4.7	0.5	- By far the most consumed anticancer drug[8] - No biodegradation studies: model predictions possibly underestimate its loss, particularly when incubated with activated sludge. - Urease catalyses the hydrolysis of urea, it also catalyses the hydrolysis of HU. - Due to hydrolysis the environmental persistence of this chemical is likely to be low relative to other L01 drugs. - Presence in the environment needs confirming
L01XE01*** Imatinib	20.40	10	9	0.9	98.2*	0.9	4.6	0.5	- Concern for contamination of soils (if sludge is dispersed onto fields) and water phase. - Presence in the environment needs confirming
L01BA01*** Methotrexate	1.31	1	83	0.6	90.0	0.5	2.5	0.2	- Point discharge (Primarily used to treat inpatients and administered 7days/week). Diffusive discharge (outpatient clinics) - Consumption underestimated[8] - Methotrexate not marked for environmental concern in other studies [ref] (removal rate of 95%), however, only 10% was removed in first four days akin to incubation time at STPs - Confirmed detection in sewage effluent at 12.9ng/L
L01XA02*** Carboplatin	5.23	3	54	1.4	30.0	0.4	2.2	0.2	- No other biodegradation studies are available for carboplatin and this assessment is based on the results from a pilot membrane bioreactor system [ref].
L01BC05*** Gemcitabine	12.97	7	8	0.5	70.0	0.4	1.8	0.2	- Persistence in the environment confirmed (hospital effluents, STP wastewaters and surface waters)
L01CB01*** Etoposide	1.23	1	43	0.3	98.1*	0.3	1.3	0.1	- No biodegradation data - Persistence in the environment confirmed (hospital effluents and STP wastewaters)

L01XA03 Oxaliplatin	1.01	1	40	0.2	100.0**	0.2	1.0	0.1	
L01AA06*** Ifosfamide	1.27	1	26	0.2	98.1*	0.2	0.8	0.1	- Point discharge (used to treat inpatients and administered 7days/week). Continuous diffusive discharge[7] - Persistence in the environment confirmed (hospital effluents and STP wastewaters and surface waters)
L01AX04*** Dacarbazine	0.75	0	36	0.1	98.2*	0.1	0.7	0.1	- 58% increased consumption from 2004 to 2008 [ref]. - No biodegradation data available - Presence in the environment needs confirming
L01AB02*** Treosulfan	1.56	1	22	0.2	70.0	0.1	0.6	0.1	- Administered at high doses (1-5g) - Expect periodic detection or detection near hospitals that utilise this specialist chemotherapy.
L01XA01 Cisplatin	0.70	0	33	0.1	98.2*	0.1	0.6	0.1	
L01XE03 Erlotinib	4.14	2	6	0.1	94.6*	0.1	0.6	0.1	
L01BC01 Cytarabine	1.98	1	10	0.1	90.0	0.1	0.5	0.0	
L01BA04 Pemetrexed	1.49	1	80	0.6	10.0	0.1	0.3	0.0	
L01XE04 Sunitinib	0.70	0	16	0.1	98.1*	0.1	0.3	0.0	
L01XX19 Irinotecan	0.56	0	16	0.0	91.7*	0.0	0.2	0.0	
L01AX03 Temozolomide	1.02	1	7	0.0	98.1*	0.0	0.2	0.0	
L01BC07 Azacitidine	0.07	0	68	0.0	98.2*	0.0	0.1	0.0	

L01DB03 Epirubicin	0.45	0	11	0.0	98.2*	0.0	0.1	0.0	
L01CD02 Docetaxel	0.53	0	7	0.0	83.4*	0.0	0.1	0.0	
L01BC03 Tegafur	0.12	0	20	0.0	98.2*	0.0	0.1	0.0	
L01DB01 Doxorubicin	0.19	0	14	0.0	80.0	0.0	0.1	0.0	
L01XX23**** Mitotane	4.50	2	6	0.1	7.4*	0.0	0.1	0.0	- High dose (2-10g/day) only used at specialist hospitals - High bioaccumulation potential (log K_{oc} > 5)
L01XE07**** Lapatinib	4.60	2	1	0.0	33.1*	0.0	0.1	0.0	- 92% of lapatinib seen in fecal excretion - High bioaccumulation potential (log K_{oc} > 5) - 116% increased consumption from 2004 to 2008 [ref].
L01AA09 Bendamustine	0.09	0	20	0.0	95.5*	0.0	0.0	0.0	
L01XB01 Procarbazine	0.15	0	11	0.0	98.2*	0.0	0.0	0.0	
L01CA04 Vinorelbine	0.30	0	13	0.0	33.1*	0.0	0.0	0.0	
L01DA01 Dactinomycin	0.07	0	17	0.0	100.0**	0.0	0.0	0.0	
L01BB05 Fludarabine	0.04	0	34	0.0	98.2*	0.0	0.0	0.0	
L01XE08 Nilotinib	0.57	0	2	0.0	84.5*	0.0	0.0	0.0	
L01DC01 Bleomycin	0.02	0	62	0.0	100.0**	0.0	0.0	0.0	
L01XX17 Topotecan	0.03	0	33	0.0	98.2*	0.0	0.0	0.0	

L01CD01**** Paclitaxel	0.86	0	7	0.0	15.8*	0.0	0.0	0.0	- 61% of paclitaxel seen in fecal excretion - High bioaccumulation potential (log K_{oc} > 5)
L01XX14 Tretinoin	0.02	0	63	0.0	54.5*	0.0	0.0	0.0	
L01DB02 Daunorubicin	0.03	0	25	0.0	98.2*	0.0	0.0	0.0	
L01XX41 Eribulin	0.06	0	9	0.0	98.2*	0.0	0.0	0.0	
L01XE05 Sorafenib	10.28	5	0	0.0	49.9*	0.0	0.0	0.0	
L01XX32 Bortezomib	0.00	0	100	0.0	98.0*	0.0	0.0	0.0	
L01DC03 Mitomycin	0.04	0	10	0.0	98.2*	0.0	0.0	0.0	
L01AA03 Melphalan	0.02	0	20	0.0	98.2*	0.0	0.0	0.0	
L01AD01 Carmustine	0.01	0	57	0.0	98.0*	0.0	0.0	0.0	
L01XE11 Pazopanib	0.05	0	4	0.0	89.4*	0.0	0.0	0.0	
L01BB02 Mitoxantrone	0.00	0	7	0.0	100.0**	0.0	0.0	0.0	

[1] Consumption total of NW survey

[2] Based on NW population of 5,346,000 from the populations each hospital serves

[3] Mean excretion rate taken from *n* clinical studies

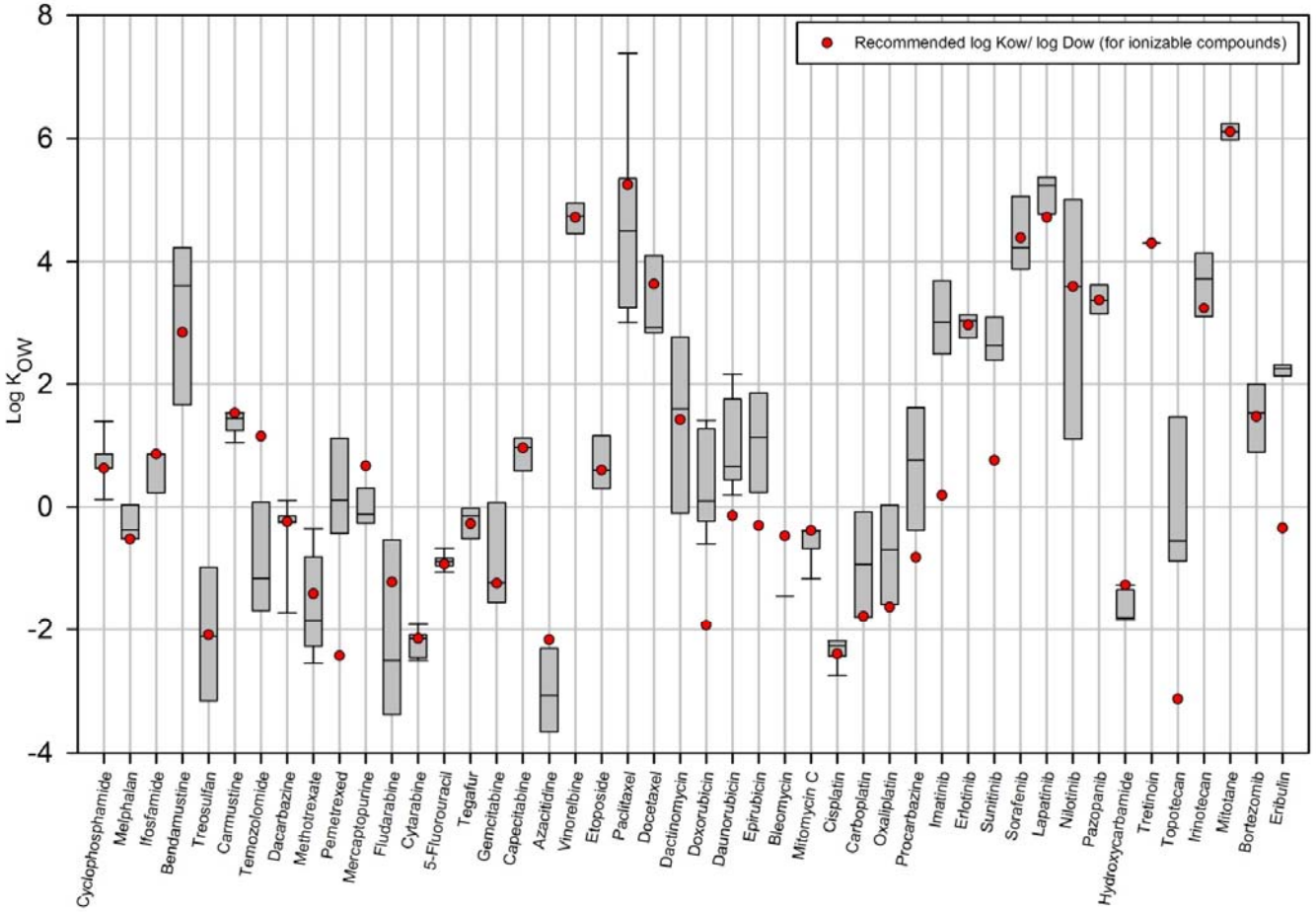
[4] Estimated from EPISUITE biowin model or from biodegradation data table 4. Predictions based on literature values are shown with an asterisk. Where no EPISUITE prediction or literature value could be obtained it was presumed that 100% of the drug remained intact.

[5] 200L/head dilution expected in STP [12]

[6] Further 10-fold dilution in the river [12]

[7] Communication with Blackpool Victoria hospital confirmed that treatments are more likely to commence during outpatients clinics (Mon-Fri), however, predominantly consumed by oral ingestion within the patients' own home)
[8] Used in another ATC class
* Predicted from EPISUITE
** No rate available
*** Priority chemical in surface water
**** Priority chemical in soil

Figure S1: Box and whisker plot of log K_{ow} values for a wide number of anticancer drugs. For each chemical the K_{ow} values were obtained from the literature (i.e. empirically observed) or calculated (*n*=1-22)



Recommended log K_{ow} based on the most reliable data sources with consideration of D_{ow} for ionisable compounds

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