

Supplemental Materials for Comparing manufacturer submitted and pCODR reanalysed ICERs for novel oncology drugs

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Supplementary Table 1. Characteristics of the included submissions

Drug	pCODR #	Route	Indication	Date of pCODR Final Recommendation	pERC Recommendation
2012					
Sunitinib malate	10004	Oral	Pancreatic neuroendocrine tumours	3-May-12	Pos. conditional
Everolimus	10007	Oral	Pancreatic neuroendocrine tumours	30-Aug-12	Pos. conditional
Pazopanib Hydrochloride	10009	Oral	Soft Tissue Sarcoma (STS)	29-Nov-12	Negative
2013					
Ruxolitinib	10012	Oral	Myelofibrosis	14-Jan-13	Pos. conditional
Bortezomib	10016	IV	Multiple Myeloma	25-Mar-13	Pos. unconditional
Crizotinib	10008	Oral	Advanced Non-Small Cell Lung Cancer	2-May-13	Pos. Conditional
Pertuzumab	10018	IV	Metastatic Breast Cancer	1-Aug-13	Pos. Conditional
Abiraterone acetate	10028	Oral	Metastatic castration resistant prostate cancer	22-Oct-13	Pos. Conditional
Lenalidomide	10029	Oral	Multiple Myeloma	22-Oct-13	Pos. Conditional
Trametinib	10030	Oral	Metastatic Melanoma	22-Oct-13	Pos. Conditional
Pemetrexed	10027	IV	Advanced Non-Squamous Non Small Cell Lung Cancer	19-Nov-13	Pos. Conditional
Dabrafenib	10025	Oral	Metastatic Melanoma	5-Dec-13	Pos. Conditional
2014					
Cetuximab	10031	IV	Metastatic Colorectal Cancer	10-Jan-14	Negative
Arsenic Trioxide	10033	IV	Acute Promyelocytic Leukemia	18-Feb-14	Pos. Unconditional
Regorafenib	10034	Oral	Gastrointestinal Stromal Tumours	2-May-14	Pos. conditional
Afatinib	10032	Oral	Advanced Non Small Cell Lung Cancer	2-May-14	Pos. Conditional
Pomalidomide	10036	Oral	Multiple Myeloma	31-Jul-14	Pos. Conditional
Nab-paclitaxel	10037	IV	Metastatic Pancreatic Cancer	23-Sep-14	Pos. Conditional
Ipilimumab	10042	IV	First Line Advanced Melanoma	22-Dec-14	Pos. Conditional
2015					
Obinutuzumab	10041	IV	Chronic Lymphocytic Leukemia	27-Jan-15	Pos. Unconditional
Ofatumumab	10038	IV	Chronic Lymphocytic Leukemia	29-Jan-15	Negative
Ibrutinib	10043	Oral	Chronic Lymphocytic Leukemia/ Small Lymphocytic Lymphoma (previously treated)	5-Mar-15	Pos. Conditional
Bevacizumab	10045	IV	Cervical Cancer	23-Mar-15	Pos. Conditional
Bosutinib	10039	Oral	Chronic Myeloid Leukemia	21-Apr-15	Pos. Conditional
Romidepsin	10048	IV	Peripheral T-Cell Lymphoma	19-May-15	Pos. Conditional
Bevacizumab	10047	IV	Ovarian Cancer	4-Jun-15	Pos. Conditional
Enzalutamide	10044	Oral	First Line Metastatic Castration-Resistant Prostate Cancer	22-Jun-15	Pos. conditional
Siltuximab	10052	IV	Multicentric Castleman's Disease (MCD)	22-Jun-15	Pos. Conditional
Pertuzumab	10050	IV	Neoadjuvant Breast Cancer	16-Jul-15	Negative
Sorafenib	10049	Oral	Metastatic Progressive Differentiated Thyroid Carcinoma (DTC)	16-Jul-15	Negative
Bevacizumab	10055	IV	Metastatic Colorectal Cancer	21-Jul-15	Pos. Conditional
Crizotinib	10054	Oral	First Line ALK Positive Advanced NSCLC	21-Jul-15	Pos. conditional
Dabrafenib & Trametinib combo	10053	Oral	Metastatic Melanoma	21-Jul-15	Pos. Conditional

Ponatinib	10056	Oral	Chronic Myeloid Leukemia/ Acute Lymphoblastic Leukemia	1-Oct-15	Pos. Conditional
Ramucirumab	10059	IV	Metastatic Gastric Cancer or Gastro-Esophageal Junction Adenocarcinoma	29-Oct-15	Pos. Conditional
Pembrolizumab	10058	IV	Metastatic Melanoma	16-Nov-15	Pos. Conditional
Lenalidomide	10061	Oral	Multiple Myeloma (newly diagnosed)	3-Dec-15	Pos. Conditional
2016					
Ruxolitinib	10065	Oral	Polycythemia vera	3-Mar-16	Pos. Conditional
Nivolumab	10063	IV	Metastatic Melanoma	1-Apr-16	Pos. Conditional
Nivolumab	10069	IV	Non-Small Cell Lung Cancer	3-Jun-16	Pos. Conditional
Carfilzomib (with lenalidomide)	10067	IV	Multiple Myeloma	21-Jun-16	Pos. Conditional
Cobimetinib	10070	Oral	Metastatic Melanoma	30-Jun-16	Pos. Conditional
Trabectedin	10071	IV	Metastatic Liposarcoma or Leiomyosarcoma	5-Aug-16	Negative
Nivolumab	10074	IV	Metastatic Renal Cell Carcinoma	1-Sep-16	Pos. Conditional
Pembrolizumab	10077	IV	Non-Small Cell Lung Cancer (Second Line or Beyond)	3-Nov-16	Pos. conditional
Ibrutinib	10085	Oral	Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (previously untreated)	3-Nov-16	Pos. Conditional
Palbociclib (Resubmission)	10093	Oral	Advanced Breast Cancer	21-Nov-16	Pos. Conditional
2017					
Ceritinib (Resubmission)	10094	Oral	Non-Small Cell Lung Cancer	21-Mar-17	Pos. Conditional
Carfilzomib	10084	IV	Multiple Myeloma (relapsed)	30-Mar-17	Pos. conditional
Vandetanib	10090	Oral	Medullary Thyroid Cancer	30-Mar-17	Pos. Conditional
Alectinib	10092	Oral	Non-Small Cell Lung Cancer (with CNS metastases)	4-May-17	Negative
Ixazomib	10088	Oral	Multiple Myeloma	29-Jun-17	Negative
Pembrolizumab	10101	IV	Non-Small Cell Lung Carcinoma (First Line)	23-Aug-17	Pos. Conditional
Blinatumomab	10099	IV	Pediatric Acute Lymphoblastic Leukemia (ALL)	23-Aug-17	Pos. Conditional
Rituximab	10102	IV	Acute Lymphoblastic Leukemia	31-Aug-17	Negative
Nivolumab	10095	IV	Squamous Cell Carcinoma of the Head and Neck (SCCHN)	31-Aug-17	Pos. Conditional
Blinatumomab (Resubmission)	10097	IV	Adult Acute Lymphoblastic Leukemia (ALL)	31-Aug-17	Pos. Conditional
Olaparib (Resubmission)	10103	Oral	Ovarian Cancer	20-Sep-17	Pos. Conditional
Daratumumab	10104	IV	Multiple Myeloma (second-line or beyond)	5-Oct-17	Pos. Conditional
Nivolumab & Ipilimumab in combo	10098	IV	Metastatic Melanoma	30-Nov-17	Pos. Conditional
2018					
Irinotecan Liposome	10107	IV	Metastatic Pancreatic Cancer	5-Jan-18	Pos. Conditional
Fulvestrant	10110	IV	Locally Advanced or Metastatic Breast Cancer	1-Feb-18	Pos. Conditional
Brentuximab Vedotin	10116	IV	Hodgkin's Lymphoma at high risk of relapse or progression post-ASCT	21-Feb-18	Pos. Conditional
Venetoclax	10105	Oral	Chronic Lymphocytic Leukemia	2-Mar-18	Pos. Conditional
Pembrolizumab	10117	IV	Metastatic Urothelial Carcinoma	2-Mar-18	Pos. Conditional
Avelumab	10124	IV	Metastatic Merkel Cell Carcinoma	21-Mar-18	Pos. Conditional
Panitumumab	10118	IV	Left Sided Metastatic Colorectal Cancer	29-Mar-18	Negative
Alectinib	10114	Oral	Locally advanced or metastatic non-small cell lung cancer (second line)	29-Mar-18	Pos. Conditional

Regorafenib	10119	Oral	Unresectable Hepatocellular Carcinoma (HCC)	18-Apr-18	Pos. conditional
Olaratumab	10111	IV	Advanced Soft Tissue Sarcoma (STS)	18-Apr-18	Pos. conditional
Ribociclib	10112	Oral	Advanced or Metastatic Breast Cancer	18-Apr-18	Pos. conditional
Trifluridine and Tipiracil	10122	Oral	Metastatic Colorectal Cancer	6-Jul-18	Negative
Inotuzumab Ozogamicin	10121	IV	Acute Lymphoblastic Leukemia (ALL)	6-Jul-18	Pos. conditional

Data organized based on year of pCODR final recommendation. pCODR, pan-Canadian Oncology Drug Review; Final Rec, final recommendation; pERC, pCODR Expert Review Committee; Pos. Conditional, positive conditional – pERC recommends funding conditional on certain metrics (i.e. cost-effectiveness) being improved to an acceptable level.

Supplementary Table 2. Economic values of the included submissions

pCODR #	Drug		Manufacturer submitted values			EGP reanalyzed values					
	Experimental	Comparator	ICER (\$/QALY)	ΔC (\$)	ΔE (QALY)	LL ICER (\$/QALY)	LL ΔC (\$)	LL ΔE (QALY)	UL ICER (\$/QALY)	UL ΔC (\$)	UL ΔE (QALY)
2012											
10004	Sunitinib malate	Placebo + BSC	79,765	55,806	0.70	204,559	46,601	0.23	268,055	45,598	0.17
10007	Everolimus	Placebo + BSC	111,805	90,247	0.81	165,129	78,696	0.48	273,781	69,538	0.25
10009	Pazopanib Hydrochloride	Placebo	143,778	25,635	0.18	146,950	25,555	0.17	167,782	29,178	0.17
2013											
10012	Ruxolitinib	BAT	101,207	83,246	0.82	276,191	20,360	0.070	383,686	21,620	0.060
10016	Bortezomib	SOC	131,100	50,500	0.37	130,874	47,843	0.37	271,642	99,303	0.37
N/A	Crizotinib	SOC	124,472	180,973	1.45	124,472	180,973	1.45	246,117	118,764	0.48
10018	Pertuzumab	Trastuzumab + Docetaxel	238,014	120,287	0.51	262,263	117,932	0.45	303,726	100,699	0.33
10028	Abiraterone acetate	Prednisone	128,197	44,844	0.35	128,197	44,844	0.35	258,428	44,642	0.17
10029	Lenalidomide	Placebo	158,129	279,657	1.77	171,702	279,032	1.77	183,366	279,657	1.53
10030	Trametinib	Vemurafenib	Dominant	-27,956	0.12	104,663	27,677	0.26	391,708	27,321	0.071
10027	Pemetrexed	SOC	143,261	36,396	0.25	170,272	37,460	0.21	173,864	38,250	0.22
10025	Dabrafenib	Dacarbazine	245,245	74,452	0.30	245,245	74,471	0.30	264,156	74,452	0.28
2014											
10031	Cetuximab	Bevacizumab+ FOLFOX	28,546	5,868	0.21	76,591	8,631	0.11	233,500	10,909	0.047
10033	Arsenic Trioxide	All-trans retinoic + chemotherapy	20,443	38,188	1.87	13,338	32,148	2.41	80,263	35,809	0.45
10034	Regorafenib	BSC	104,660	61,286	0.59	143,317	56,592	0.41	205,299	64,197	0.31
10032	Afatinib	Gefitinib	72,153	15,153	0.21	39,060	574	0.015	211,189	540	0.0026
10036	Pomalidomide	BSC + HDex	84,476	44,858	0.53	132,217	70,208	0.53	173,430	67,397	0.39
10037	Nab-paclitaxel	Gemcitabine	155,549	20,030	0.13	182,714	22,900	0.13	192,995	22,900	0.12
10042	Ipilimumab	Dacarbazine	151,014	111,419	0.74	165,389	108,880	0.53	197,382	110,343	0.67
2015											
10041	Obinutuzumab	Chlorambucil	30,844	30,065	0.98	32,369	29,958	0.93	49,823	29,240	0.59
10038	Ofatumumab	Chlorambucil	68,647	27,866	0.41	106,012	26,246	0.25	162,897	32,500	0.20
10043	Ibrutinib	SOC	124,954	148,364	1.19	80,941	185,089	1.94	382,134	117,601	0.31
10045	Bevacizumab	Chemotherapy	145,957	44,228	0.30	157,829	43,872	0.28	245,452	47,107	0.19
10039	Bosutinib	Interferon	45,955	101,954	2.22	44,198	60,013	0.42	146,587	62,047	1.56
10048	Romidepsin	SOC	186,253	102,266	0.55	217,588	105,224	0.48	387,056	144,434	0.32
10047	Bevacizumab	Carboplatin + Paclitaxel	96,261	36,021	0.37	87,033	36,943	0.42	113,473	35,158	0.32
10044	Enzalutamide	BSC + docetaxel	109,397	72,807	0.67	125,424	60,433	0.27	224,266	65,108	0.52
10052	Siltuximab	Placebo + BSC	204,332	294,782	1.44	232,663	294,782	1.27	648,163	195,047	0.30

10050	Pertuzumab	Trastuzumab + Docetaxel	25,388	7,879	0.31	17,103	6,585	0.39	27,550	8,550	0.31
10049	Sorafenib	BSC	142,843	74,527	0.52	189,647	79,609	0.42	206,945	80,148	0.38
10055	Bevacizumab	Chemotherapy	212,938	54,007	0.25	212,938	54,007	0.25	309,763	53,036	0.17
10054	Crizotinib	SOC	153,597	37,366	0.24	173,570	36,548	0.21	285,299	37,387	0.13
10053	Dabrafenib & Trametinib combo	Vemurafenib	332,129	114,493	0.35	323,454	46,052	0.14	446,238	153,830	0.37
10056	Ponatinib	Hydroxyurea	68,454	248,656	3.63	94,518	241,446	2.41	100,065	375,860	3.98
10059	Ramucirumab	Placebo + Paclitaxel	332,628	29,812	0.09	432,159	38,732	0.09	490,437	43,955	0.09
10058	Pembrolizumab	Ipilimumab	52,829	39,099	0.74	114,389	63,060	0.55	151,369	56,320	0.37
10061	Lenalidomide	Bortezomib	100,784	102,826	1.02	Dominated	146,793	0	Dominated	150,304	0
2016											
10065	Ruxolitinib	BAT	156,250	211,240	1.35	282,785	169,575	0.60	284,555	170,274	0.60
10063	Nivolumab	Ipilimumab	94,176	80,234	0.85	120,851	104,067	0.89	198,776	145,608	0.52
10069	Nivolumab	Docetaxel	133,520	84,918	0.64	183,386	80,014	0.44	236,851	80,014	0.34
10067	Carfilzomib (with lenalidomide)	Lenalidomide + Dexamethasone	201,216	152,034	0.76	270,652	155,134	0.57	347,640	174,431	0.50
10070	Cobimetinib	Vemurafenib	317,648	157,117	0.50	314,268	157,117	0.50	426,815	156,853	0.37
10071	Trabectedin	Dacarbazine	167,863	25,019	0.15	318,519	28,626	0.090	583,041	52,458	0.09
10074	Nivolumab	Everolimus	131,349	63,185	0.48	186,312	89,625	0.48	242,521	89,625	0.37
10077	Pembrolizumab	Docetaxel	143,730	76,742	0.53	149,342	71,649	0.48	254,945	68,441	0.27
10085	Ibrutinib	Chlorambucil	101,405	291,214	2.87	141,616	249,509	1.76	233,945	178,941	0.77
10093	Palbociclib (Resubmission)	Letrozole	310,007	198,623	0.64	295,925	174,484	0.65	745,785	227,517	0.26
2017											
10094	Ceritinib (Resubmission)	Pemtrexed or Docetaxel or BSC or historical controls	118,676	70,293	0.59	159,750	75,766	0.47	208,377	98,829	0.47
10084	Carfilzomib	Bortezomib + Dexamethasone	192,997	147,701	0.77	261,648	157,554	0.60	294,931	163,029	0.55
10090	Vandetanib	BSC	285,627	128,566	0.45	314,801	131,250	0.42	434,852	128,963	0.30
10092	Alectinib	SOC	108,958	156,501	1.44	67,993	127,124	1.96	417,128	185,878	0.42
10088	Ixazomib	Lenalidomide + Dexamethasone	378,299	350,680	0.93	464,746	348,272	0.75	1,751,236	345,495	0.20
10101	Pembrolizumab	SOC	99,392	98,298	0.99	111,769	107,632	0.96	154,273	103,406	0.67
10099	Blinatumomab	Chemotherapy	15,940	67,913	4.26	6,577	48,572	7.38	100,948	112,363	1.11
10102	Rituximab	Chemotherapy	39,181	45,259	1.16	46,894	32,299	0.69	4,193,972	44,372	0.01
10095	Nivolumab	Docetaxel	67,616	30,816	0.46	109,743	37,682	0.34	145,855	33,802	0.23
10097	Blinatumomab (Resubmission)	Chemotherapy	72,488	158,183	2.18	223,060	158,224	0.71	971,327	158,270	0.16
10103	Olaparib (Resubmission)	Watchful waiting	243,249	258,015	1.06	195,112	251,171	1.29	421,637	257,020	0.61

10104	Daratumumab	Lenalidomide + Dexamethasone	181,212	539,113	2.97	165,496	622,746	3.76	594,144	422,874	0.71
10098	Nivolumab & Ipilimumab in combo	Ipilimumab	66,750	149,556	2.24	86,758	125,019	1.44	116,541	145,958	1.25
2018											
10107	Irinotecan Liposome	5-FU/LV	182,719	23,871	0.13	326,774	43,039	0.15	335,528	44,496	0.13
10110	Fulvestrant	Anastrozole	32,361	41,405	1.28	33,476	52,416	1.24	185,631	35,095	0.19
10116	Brentuximab Vedotin	SOC	26,303	113,900	4.33	105,383	125,510	1.19	139,286	123,999	0.89
10105	Venetoclax	SOC	124,050	184,319	1.49	139,074	359,461	2.59	1,474,649	69,893	0.047
10117	Pembrolizumab	Paclitaxel/Docetaxel	126,150	94,317	0.75	217,954	89,225	0.41	285,514	84,631	0.30
10124	Avelumab	Chemotherapy	57,051	111,214	1.95	84,155	97,282	1.16	97,962	126,533	1.13
10118	Panitumumab	Bevacizumab + FOLFOX	110,414	36,118	0.33	126,389	40,686	0.32	275,255	18,594	0.068
10114	Alectinib	Chemotherapy	84,444	123,767	1.47	87,357	120,560	1.38	159,544	152,170	0.95
10119	Regorafenib	BSC	138,322	34,194	0.25	152,657	34,084	0.25	175,700	40,411	0.23
10111	Olaratumab	Doxorubicin	175,001	127,075	0.73	224,817	128,682	0.57	263,340	124,109	0.47
10112	Ribociclib	Letrozole	136,140	231,283	1.70	175,827	231,283	1.32	204,805	164,261	0.84
10122	Trifluridine and Tipiracil	BSC	96,971	16,688	0.17	123,849	18,141	0.15	130,314	19,088	0.15
10121	Inotuzumab Ozogamicin	Chemotherapy	91,841	120,883	1.32	178,801	109,370	0.75	335,752	140,560	0.67

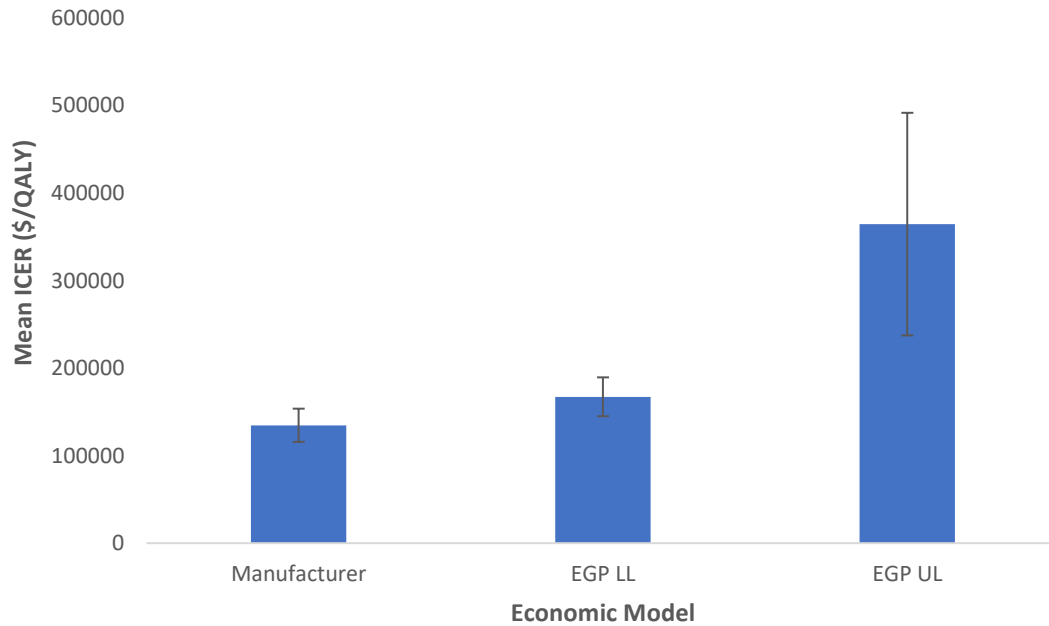
Data organized based on year of pCODR final recommendation. All costs are in Canadian dollars. pCODR, pan-Canadian Oncology Drug Review; ICER, incremental cost-effectiveness ratio; ΔC, incremental cost; ΔE, incremental effectiveness; LL, lower limit; UL, upper limit; QALY, quality-adjusted life year, BSC, best supportive care; SOC, Standard of care; BAT, Best available therapy; EGP, Economic guidance panel.

Supplementary Table 3. Summary Statistics for Manufacturer submitted and EGP-reanalyzed ICERs (\$/QALY)

	Mean	Std Dev.	Median	Min	Max
Manufacturer Submitted	134,241	79,803.45	124,713	15,940	378,299
EGP Lower Limit Estimates	166,382	93,545.76	155,243	65,77	464,746
EGP Upper Limit Estimates	365,018	533,382	245,784.50	27,550	4,193,972

ICER, Incremental Cost-Effectiveness Ratio; EGP, Economic Guidance Panel.

Supplementary Figure 1. Average ICERs generated by the manufacturer-submitted and EGP-re-analyzed economic models.



Note: Excluded ICERs for all three economic models if 1 economic model deemed the drug as dominant (1) or dominated (1) and did not provide a numerical ICER value. Whiskers represent 95% confidence intervals. ICER, incremental cost-effectiveness ratio; EGP, Economic Guidance Panel; LL, lower limit; UL, upper limit

Supplementary Figure 2. Change in manufacturer-submitted and EGP-reanalysed ICERs over time. Cost is presented in CAD.

