

Supplemental Table 1. List of approved and publicly available Value-Based Contracts (VBC) in USA, Europe, and UK (2015-2021)

USA ⁽¹⁻³⁾						
Brand name	Drug	Manufacturer	Payer(s)	Disease area	Outcome metric and terms	Year
Stiolto®	tiotropium bromide/ olodaterol	Boehringer Ingelheim	Highmark	COPD	Reduces the total cost for both in-patient and out-patient COPD care for members vs. other available drugs	2019
Enbrel®	etanercept	Amgen	Abarca	Rheumatoid arthritis	Rebates to Abarca's clients for eligible members who discontinue the use of the drug after three months of treatment.	2019
Givlaari®	givosiran	Alnylam Pharmaceuticals	HPHC	Neurology Acute hepatic porphyria	Payers will pay the full value for GIVLAARI only when it delivers patient outcomes in the real-world setting similar to results demonstrated in clinical trials.	2019
Tecfidera®	dimethyl fumarate	Biogen	UPMC Health Plan	Multiple Sclerosis	Reimbursement by the drug manufacturer will be linked to reported measures of disability progression in a real-world population.	2019
Avonex®	interferon beta-1a	Biogen	UPMC Health Plan	Multiple Sclerosis	Reimbursement by the drug manufacturer will be linked to reported measures of disability progression in a real-world population.	2019
Luxturna®	voretigene neparovecrzyl	Spark Therapeutics	Cigna	Retinal Dystrophy	Reduces net-cost to payer and determines payment amount based on selected clinical outcomes. If a Luxturna treatment fails (based on beneficiary light sensitivity), the payer would receive a rebate from Spark Therapeutics.	2019
Zolgensma®	onasemnogene abeparvovec-xioi	Novartis (Avexis)	Cigna; HPHC	Spinal muscular atrophy	Refunds will take place if drug is not effective over 5 years	2019
Mavyret®	glecaprevir/pibrentas vir	AbbVie	WSHCA	Hepatitis C	-	2019
Brilinta®	ticagrelor	AstraZeneca	UPMC Health Plan	Acute Coronary Events	Reimbursement linked to CV outcomes following a recent hospitalization for heart attack or unstable angina	2019
Invega Trinza®	paliperidone palmitate 2018	Janssen	Oklahoma Health Care Authority	Schizophrenia	Expenses for medical services	2018
Fycompa®	perampanel	Eisai	-	Epilepsy	Patients' outcomes and healthcare utilization and costs, including costs related to hospitalizations	2018
Stelara®	ustekinumab 2018 Immunology	Janssen	Prime Therapeutics	Psoriasis	Pharmacy and medical claims data to determine the duration of benefit from therapy	2018
Jardiance®	empagliflozin	Boehringer Ingelheim	UPMC Health Plan	Diabetes	Reimbursement linked to costs associated with clinical outcomes in the real-world population	2018
Orbativ®	oritavancin	Melinta Therapeutics	Oklahoma Health Care Authority	Acute Bacterial Skin Infections	Refunds if oritavancin results in a net increase in costs. Outcome based on reduction in hospitalizations when compared with conventional therapies	2018
Aristada®	aripiprazole lauroxil	Alkermes	Oklahoma Health Care Authority	Schizophrenia	Patients' adherence and improved outcomes	2018
Vivitrol®	naltrexone	Alkermes	UPMC Health	Opioid Dependence	Positive clinical outcomes; Reduction in the risk of relapse; Increase in adherence	2018
Cosentyx®	secukinumab	Novartis	Prime Therapeutics	Psoriasis	Medication persistence/costs	2018
Onpattro®	patisiran	Alnylam Pharmaceuticals	HPHC	hATTR Amyloidosis	Payment based on the ability to deliver outcomes in the real- world setting vs. performed clinical trials	2018
Jardiance®	empagliflozin	Boehringer Ingelheim	Highmark	Diabetes	analysis of the total cost of care for adults with type 2 diabetes and established cardiovascular disease	2018
Symbicort®	budesonide/formoter ol	AstraZeneca	HPHC	Asthma	Harvard Pilgrim to be charged a lower amount if asthma exacerbations/worsening of symptoms requiring medical intervention in real-world settings exceed thresholds determined in clinical trials.	2018

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Symbicort®	budesonide/formoterol	AstraZeneca	Highmark	Asthma, COPD	If Symbicort doesn't perform as expected (based on outcomes published clinical trials), AstraZeneca will provide a corresponding rebate to Highmark.	2018
Victoza®	liraglutide	Novo Nordisk	SelectHealth	Diabetes	Effectiveness of Victoza to determine reimbursement to commercial clients if certain measures not achieved.	2018
Repatha®	evolocumab	Amgen	Abarca	Hypercholesterolemia	Amgen provides additional discounts if LDL cholesterol reductions not in line with clinical trial results.	2018
Jardiance®	empagliflozin	Boehringer Ingelheim	Prime Therapeutics	Diabetes	Medical and pharmacy claims data to evaluate and manage total cost of care	2018
Luxturna®	voretigene neparvovecrzyl	Spark Therapeutics	HPHC; Express Scripts	Retinal Dystrophy	If the therapy fails to perform as agreed, the payer will receive a rebate from Spark Therapeutics.	2018
Aimovig®	erenumab-aooe	Amgen / Novartis	Express Scripts	Migraine	Money-back guaranteed for plan sponsors when a patient discontinues therapy in the first 90 days.	2018
Victoza®	liraglutide	Novo Nordisk	Prime Therapeutics	Diabetes	Overall costs; effectiveness	2017
Xtampza ER®	oxycodone	Collegium	Cigna	Pain management	Collegium will reduce the cost of the medication if prescriptions exceed a specific daily dose threshold	2017
MS Portfolio	Multiple	Biogen	HPHC; Moda Care; Select Care	Multiple Sclerosis	Outcomes-based measures that tie pricing terms to an annualized relapse rate for their populations	2017
MS Portfolio	Multiple	Biogen	Prime Therapeutics	Multiple Sclerosis	Patients' adherence; Biogen provides an incremental discount based on patients who discontinue our therapies within the initial weeks of treatment.	2017
MS Portfolio	Multiple	Biogen	Abarca	Multiple Sclerosis	Biogen provides a rebate for discontinued treatment	2017
Brilinta®	ticagrelor	AstraZeneca	HPHC	Acute Coronary Events	Outcome based on the reduction in hospitalizations for acute coronary events in Brilinta-treated patients vs. other oral antiplatelets.	2017
Bydureon®	exenatide	AstraZeneca	HPHC	Diabetes	HbA1c levels and adherence get to a predetermined HbA1c goal	2017
Repatha®	evolocumab	Amgen	HPHC	Hypercholesterolemia	Full refund for the drug if a patient is hospitalized for MI or stroke after ≥6-month treatment with Repatha while adhering to the drug	2017
Enbrel®	etanercept	Amgen	HPHC	Rheumatoid arthritis	Two-year contract based on an effectiveness algorithm in real life. If patient scores are below a specified level while adhering to the drug, Harvard Pilgrim will pay less for Enbrel.	2017
Forteo®	teriparaside	Eli Lilly	HPHC	Osteoporosis	Rewards improvement in adherence compared to baseline; if meaningful improvements are found, Lilly reduces the cost of the drug for Harvard Pilgrim	2017
Victoza®	liraglutide	Novo Nordisk	Humana	Diabetes	-	2017
Trulicity®	dulaglutide	Eli Lilly	HPHC	Diabetes	Price rebates tied to how well Trulicity performs vs. other GLP-1 agonists.	2016
Entresto ®	sacubitril/valsartan	Novartis	HPHC; Aetna; Cigna	Chronic heart failure	Novartis accepts lower net price if hospitalization reduction rates do not replicate clinical trials.	2016
Effient®	prasugrel	Eli Lilly	Humana	Acute coronary events	Links reimbursement to reductions in hospitalization rates	2016
Iressa®	geitinib	Astra zeneca	Express Scripts	Lung cancer	Number of patients who fill the medicine three times	2016
Repatha®	evolocumab	Amgen	Cigna	Hypercholesterolemia	Amgen provides additional discounts if LDL cholesterol reductions not in line with clinical trial results.	2016
Brilinta®	ticagrelor	AstraZeneca	UPMC Health Plan	Acute Coronary Events	Measures the reduction in hospitalizations for repeat acute coronary events for patients on Brilinta against competitors	2016
Janumet®/Januvia®	Metformin/sitagliptin	Merk	Aetna	Diabetes	Merck will pay larger rebates if patients need to use additional therapy to reach HbA1C goals	2016
Repatha®	evolocumab	Amgen	HPHC	Hypercholesterolemia	Amgen provides additional discounts if LDL cholesterol reductions not in line with clinical trial results. Harvard Pilgrim can receive a full rebate if a patient experiences a MI or stroke while on the drug	2015
Repatha®	evolocumab	Amgen	CVS Health	Hypercholesterolemia	Net price linked to cholesterol reduction, appropriate patient use in return for preferred formulary status.	2015
Repatha®	evolocumab	Amgen	Prime Therapeutics	Hypercholesterolemia	Amgen provides additional discounts if LDL cholesterol reductions not in line with clinical trial results.	

Harvoni®	sofosbuvir/ledipasvir	Gilead	Cigna	Hepatitis C	Net price discount, linked to outcomes, in return for preferred formulary status.	2015
Praluent®	alirocumab	Sanofi, Regeneron	Cigna	Hypercholesterolemia	Extra price discounts if results are not in line with clinical trial results	2015
Avastin®	bevacizumab	Genentech	Priority Health	Lung Cancer	The shorter the PFS in a given patient, the greater the rebate to Priority Health. If a patient remained PFS on bevacizumab >6 months, Priority Health would not receive a rebate.	2015
Tarceva®	erlotinib	Genentech	Express Scripts	Pancreatic/Lung cancer	Specific details are not spelled, but price could depend on OS in different diseases (indication-based pricing)	2015
EU-Italy^(2, 4)						
Brand name	Drug	Manufacturer	Payer(s)	Disease area	Outcome metric and terms	Year
Zolgensma®	Onasemnogene abeparvovec	Novartis	SSN	SMA	Reimbursement in patients up to 13.5 kg in weight with a) clinical diagnosis and onset of symptoms in the first 6 months of life or b) genetic diagnosis. Reimbursement deal with checkpoints at 12, 24, 36, and 48 months	2021
Rubraca®	rucaparib	Clovis Oncology	SSN	Ovarian Cancer	Reimbursement in women with relapsed platinum-sensitive ovarian cancer	2019
Yescarta®	axicabtagene ciloleucel	Gilead Sciences	SSN	diffuse large B-cell lymphoma (DLBCL)	Payments in three installments at 180, 270, and 365 days post-treatment, subject to outcomes being achieved and sustained. Specifics not disclosed	2019
Kymriah®	tisagenlecleucel	Novartis	SSN	B-cell acute lymphoblastic leukaemia (ALL)	Payments in three installments: the first at time of treatment, the subsequent two at 6 and 12 months post. Specifics not disclosed	2019
Kymriah	tisagenlecleucel	Novartis	SSN	diffuse large B-cell lymphoma (DLBCL)	Payments in three installments: the first at time of treatment, the subsequent two at 6 and 12 months post. Specifics not disclosed	2019
Holoclar®	ex vivo expanded autologous human corneal epithelial cells containing stem cells	Holostem Terapie Avanzate	SSN	Limbal stem cell deficiency (LSCD)	-	2017
Vargatef®	nintedanib	Boehringer Ingelheim	SSN	Non-small cell lung carcinoma	-	2017
Strimvelis®	autologous CD34+ enriched cell fraction	GSK	SSN	Severe combined immunodeficiency due to adenosine deaminase deficiency (ADA-SCID)	Pay-back in case of treatment failure	2016
Zelboraf®	vemurafenib	Roche	SSN	Melanoma	-	2015
Sustent®	Sunitinib	Pzifer	SSN	Pancreatic neuroendocrine tumors	-	2015
Abraxane®	paclitaxel-albumina	Bristol Myers Squibb	SSN	Pancreatic tumor	Effectiveness of the two agents in the enhancement of anti-tumor response vs. either agent alone	2015
EU-SPAIN⁽⁵⁾						
Brand name	Drug	Manufacturer	Payer(s)	Disease area	Outcome metric and terms	Year
Crysvita®	Burosumab	Kyowa Kirin	NHS	X-Linked hypophosphatemic rickets	Normalization of phosphate levels, resolving skeletal abnormalities and derived symptoms (pain). Follow up on the possible appearance of complications	2021
Dupixent®	Dupilumab	Sanofi-Aventis	NHS	Refractory atopic dermatitis	Reduction of symptoms (pruritus and dermatitis, prevention of exacerbations and minimization the risk of immunosuppressive treatment	2020
Veklury®	Remdesivir	Gilead Sciences	NHS	COVID-19	Prevention of the progression of the severity of the disease, promotion of clinical recovery and reduction of the length of hospital stay, and HCRU	2020

Kymriah®	tisagenlecleucel	Novartis	NHS	ALL; DLBCL	Complete response with negative MRD for over 18 months	2019
UK ⁽⁶⁾						
Brand name/Trial	Drug	Manufacturer	Payer(s)	Disease area	Outcome metric and terms	Year
SPR1NT trial [NCT03505099]	Onasemnogene abeparvovec	Novartis	NICE/NHS	SMA	Clinical and cost-effectiveness	2021
DESTINY-Breast02 trial [NCT03523585]	Trastuzumab deruxtecan	Daiichi Sankyo	NICE/NHS	Unresectable or metastatic breast cancer	Relative effectiveness vs. other conventional therapies. PFS and OS data	2021
SOLO-2 trial	Olaparib	AstraZeneca	NICE/NHS	Advanced ovarian, fallopian tube or primary peritoneal cancer	PFS and OS data	2021
ZUMA-2 trial [NCT02601313]	Autologous anti- CD19-transduced CD3+ cells	Gilead	NICE/NHS	refractory mantle cell lymphoma	PFS, PPFS, and OS data and quality of life in long-term survivors	2021
ENGOT-OV16/NOVA trial	Niraparib	Glaxo Smith Kline	NICE/NHS	Advanced ovarian, fallopian tube and peritoneal cancer	OS and time to second progression; long-term PFS	2021
CLL13 trial (MO29596) NCT02950051]	Venetoclax/obinutuzu mab	AbbVie	NICE/NHS	Chronic lymphocytic leukaemia	OS; Relative effectiveness vs. other conventional treatments	2020
ICARIA-MM trial [NCT02990338]	Isatuximab / pomalidomide / dexamethasone	Sanofi	NICE/NHS	relapsed and refractory multiple myeloma	PFS and OS data; estimation of time-on-treatment; Proportion of patients who progress onto 4 th line therapy	2020
JAVELIN Renal 101 [NCT02684006]	Avelumab / axitinib	Merk / Pfizer	NICE/NHS	Untreated advanced or metastatic renal cell carcinoma	OS data; effectiveness for non-clear-cell disease; cost/benefits	2020
STARTRK-2 and STARTRK-NG trial	Entrectinib	Roche	-	Solid tumors	Prevalence and characterization of NTRK gene fusions and tumor type; long- term efficacy and safety; comparative effectiveness	2020
NAVIGATE [NCT02576431], SCOUT [NCT02637687] and LOXO-TRK-14001trial [NCT02122913]	Larotrectinib	Bayer	-	Solid tumors	Prevalence and characterization of NTRK gene fusions and tumor type; Prognostic importance of NTRK gene fusions; Management of patients; Long- term survival; Post-progression health utility state	2020
ENGOT-OV16/NOVA trial	Niraparib	Glaxo Smith Kline	NICE/NHS	Ovarian cancer	PFS and OS data	2019
Not specified	Cerliponase alfa	BioMarin	NICE/NHS	CLN2 Disease	Long-term disease stabilization; Improvements in motor language score starting distribution	2019
ARIEL3 trial	Rucaparib	Clovis oncology	NICE/NHS	Relapsed ovarian, fallopian tube or primary peritoneal cancer	OS data	2019
KEYNOTE-407 trial [NCT02775435]	Pembrolizumab / carboplatin / paclitaxel or nab- paclitaxel	Merk	NICE/NHS	metastatic squamous non-small-cell lung cancer	OS vs. standard care	2019
SOLO-1 trial	Olaparib	AstraZeneca	NICE/NHS	Advanced ovarian, fallopian tube or primary peritoneal cancer	Long-term OS; Proportion of patients who have residual disease at 2 years	2019
CheckMate 214 trial [NCT02231749]	Nivolumab / ipilimumab	Bristol-Myers Squibb	NICE/NHS	Advanced renal cell carcinoma	Long-term benefit in OS; Treatment duration; Subsequent therapies used in clinical practice; Proportion of patients with poor-risk or intermediate-risk renal cell carcinoma in clinical practice	2019

MONARCH 2 trial	Abemaciclib / fulvestrant	Eli Lilly	NICE/NHS	Breast cancer	Long-term survival data; Estimation of time-on-treatment	2019
PACIFIC trial	Durvalumab	Astra Zeneca	NICE/NHS	Unresectable non-small cell lung cancer	Long-term PFS and OS benefit following discontinuation	2019
JULIET trial	Tisagenlecleucel	Novartis	NICE/NHS	relapsed or refractory diffuse large B-cell lymphoma	OS data; proportion of people who need treatment for B-cell aplasia with Ig and duration of treatment	2019
ZUMA-1 trial [NCT02348216]	Axicabtagene ciloleucel	Gilead Sciences	NICE/NHS	diffuse large B-cell lymphoma and primary mediastinal B-cell lymphoma	OS at 5-year follow-up; convergence of PFS and OS curves at 5-years follow-up; intravenous Ig use	2019
EMPOWER-CSCC 1 trial	Cemiplimab	Sanofi	NICE/NHS	cutaneous squamous cell carcinoma	Baseline characteristics of the target population Long-term benefit Comparative effectiveness with standard treatments in clinical practice	2019
CASTOR trial	Daratumumab / bortezomib / dexamethasone	Janssen	NICE/NHS	multiple myeloma	OS at 6 years	2019
KEYNOTE-087 trial	Pembrolizumab	Merck	NICE/NHS	refractory classical Hodgkin lymphoma	The time at which allogeneic stem cell transplant occurs. proportion of patients who receive an allogeneic stem cell transplant	2018
Not specified	Daratumumab	Janssen	NICE/NHS	multiple myeloma	OS Subsequent treatment following daratumumab	2018
PROFILE 1001 trial	Crizotinib	Pfizer	NICE/NHS	ROS1-positive advanced non-small-cell lung cancer	Effectiveness comparison with standard care Post-progression and overall survival estimates	2018
IMvigor 130 trial	Atezolizumab	Roche	NICE/NHS	Untreated metastatic urothelial cancer	OS and PFS compared with standard care HRQoL for patients with SD and PD receiving atezolizumab and standard care	2018
ELIANA, ENSIGN and B2101J trials	Tisagenlecleucel	Novartis	NICE/NHS	relapsed or refractory B-cell acute lymphoblastic leukaemia	Curative nature of tisagenlecleucel Subsequent stem cell transplant Number of people who need treatment for B-cell aplasia with intravenous Ig, and duration of the treatment	2018
KEYNOTE-054 trial [NCT02362594]	Pembrolizumab	Merk Sharp Dohme	NICE/NHS	melanoma	Distant metastases free survival and OS benefit vs, standard therapy	2018
TOURMALINE MM-1 trial	Ixazomib / lenalidomide / dexamethasone	Takeda	NICE/NHS	relapsed or refractory multiple myeloma	OS; Duration of treatment; Quality of life (EQ 5D)	2018
Study 1118E and the phase 3 Study 1127 [iNNOVATE]	Ibrutinib	Janssen	NICE/NHS	Waldenstrom's macroglobulinaemia	Pre-progression mortality and treatment duration	2017
CheckMate 141	Nivolumab	Bristol-Myers Squibb	NICE/NHS	Recurrent or metastatic squamous-cell carcinoma of the head and neck	Effectiveness according to PD-L1 expression	2017
Not specified	Venetoclax	AbbVie	NICE/NHS	chronic lymphocytic leukaemia	OS; PPS	2017

HPHC = Havard Pilgrim Health Care; OS = Overall survival; PFS = Progression-free survival; PPFS = Post-progression-free survival; SSN = National Health System (Italy); UPMC = University of Pittsburgh Medical Center; WSHCA = Washington State Healthcare Authority.

SUPPLEMENTAL REFERENCES

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