U.S. FOOD & DRUG ADMINISTRATION

CENTER FOR DRUG EVALUATION AND RESEARCH

CLINICAL OUTCOME ASSESSMENT (COA) COMPENDIUM

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Table of Contents

Disclaimer

The COA Compendium is a communication tool and, it is intended to serve as a starting point in early drug development. The inclusion of a clinical outcome assessment in the COA Compendium does not equate to an endorsement by FDA and does not represent agency guidance.

Drug sponsors are strongly encouraged to seek advice from the relevant Office of New Drug (OND) review division early in drug development to discuss the selection and implementation of the clinical outcome assessment specific to their program. This is irrespective of whether the disease, condition, indication, claim, or clinical outcome assessment is included in the COA Compendium. See [All Guidances for Drugs] for a repository of guidance documents including disease-specific guidances, which may contain additional information relevant to COA selection.

Limitations of the COA Compendium include, but are not limited to:

- It is not a comprehensive list of COAs and is not intended to replace either existing disease-specific guidance or key interactions with FDA concerning drug development (e.g., during pre-IND meetings)
- Inclusion of a COA in the COA Compendium does not necessarily indicate that the measure is or should be the primary or sole determinant of effectiveness in a clinical trial nor is it indicative of endpoint positioning (e.g., primary or secondary)
- The COA Compendium presents information that was available at the time it was compiled and updated; it may not include newer COAs that could be recommended for a drug development program, or more recent scientific and regulatory thinking
- It does not include Biomarkers with the exception of Biomarkers used in composite endpoints
- It does not include the endpoint definition of labeled COAs
- Some of the COAs listed in the COA Compendium may be protected by proprietary rights and, in some cases, a royalty and fee may be charged by the copyright owners for their authorized use

COA COMPENDIUM DESCRIPTION

This *COA Compendium* is part of FDA's efforts to foster patient-focused drug development. The COA Compendium is intended to facilitate communication and to provide clarity and transparency to drug developers and researchers by collating and summarizing COA information for many different diseases and conditions into a single resource. We suggest using the COA Compendium as a starting point when considering a COA for use in clinical trials.

The COA Compendium is a table that:

- Describes how certain COAs have been used in clinical trials to measure the patient's experience (such as disease-related symptoms) and to support labeling claims.
- Identifies COAs that have been qualified for potential use in multiple drug development programs under CDER's Drug Development Tool (DDT) Qualification Program.

This is the first update to the Compendium since the launch of the pilot in January 2016. The update is an extension of the original document and includes COAs from three major sources:

- Labeling of new molecular entity (NME) drugs and biological license application (BLA) drugs approved from 2015 to June 2017
- Efficacy supplements pertaining to new indication and new population for first and second quarter (January to June) of 2017
- Qualified measures based on CDER's COA DDT Qualification Program

The *COA Compendium* is organized by CDER's OND offices and review divisions. The table alphabetically lists conditions or diseases based on each review division's therapeutic assignment. The shaded rows describe information about a COA DDT qualification project, whereas the unshaded rows describe information about COAs from previous labeling.

COLUMNS	ELEMENTS	DESCRIPTION OF CONTENT
Column 1	Disease/Condition	Lists disease or condition
Column 2	Concept	Describes the concept that the COA assesses
Column 3	COA Tool & Type	Describes the: • COA as listed in labeling or the qualification statement • COA Type (i.e., a patient-reported outcome, observer-reported outcome, clinician-reported outcome, or performance outcome tool)
Column 4	COA Context of Use	Describes circumstance under which the outcomes of interest and the COA have been used (i.e., labeled) or have been qualified (for qualified tools under CDER's DDT Qualification program)
Column 5	Drug Name & Approval Date	List the brand and generic name of approved drugs, date of approval for NME labeling and the most recent approval date for efficacy supplements.

OFFICE OF ANTIMICROBIAL PRODUCTS (OAP)

DIVISION OF ANTI-INFECTIVE PRODUCTS (DAIP)				
Disease/Condition	**Concept**	**COA Tool & Type**	**COA Context of Use**	**Drug Name/Approval Date/ Qualification Link**
Acute bacterial exacerbation of chronic bronchitis in patients with COPD (ABECB-COPD)	Symptoms of ABECB-COPD (breathlessness, cough and sputum, chest symptoms, difficulty bringing up sputum, tired or weak, sleep disturbance, scared or worried)	Exacerbations of Chronic Pulmonary Disease Tool (EXACT): **PRO**	Outpatients with ABECB-COPD	**Qualified COA Tool** Visit "Clinical Outcome Assessment Qualification Program Submissions" Website for additional information
Clostridium difficile Infection (CDI)	No diarrhea for two consecutive days	Clinical cure: **ClinRO**[1]	Adult patients with CDI	1. Zinplava (bezlotoxumab) *October 21, 2016* 2. Dificid (fidaxomicin) *May 27, 2011*
	Sustained clinical response post initial treatment	No recurrence of CDI-interview based: **ClinRO**[1,2]		
Cystic Fibrosis (CF)	Changes in respiratory symptoms (cough, wheezing, sputum production)	CF Questionnaire—Revised (CFQ-R) respiratory domain: **PRO**	Patients with CF age 7 years and above	Cayston (aztreonam) *February 22, 2010*
Impetigo	Absence or improvement of treated lesions and no need for further antimicrobial treatment	**ClinRO**	Adult and pediatric patients with impetigo	Altabax (retapamulin) *April 12, 2007*
Leishmaniasis (cutaneous, mucosal and visceral)	Resolution of edema, erythema, infiltration and erosion and/or epithelialization of lesions	**ClinRO**	Adolescents and adult patients with cutaneous leishmaniasis	Impavido (miltefosine) *March 19, 2014*
	No enlargement of lesions or no appearance of new lesions			
	Clearance of the parasites	Laboratory measure: **Biomarker**		

DIVISION OF ANTI-INFECTIVE PRODUCTS (DAIP) (CONTINUED)				
Disease/Condition	**Concept**	**COA Tool & Type**	**COA Context of Use**	**Drug Name/Approval Date/ Qualification Link**
Travelers' diarrhea	Clinical response based on time to last unformed stool	Patient diary: **PRO** and laboratory measure: **Biomarker**	Patients with travelers' diarrhea caused by noninvasive strains of *Escherichia coli*	Xifaxan (rifaximin) *May 25, 2004*
	Resolution of symptoms			
	Microbiological eradication			

DIVISION OF ANTIVIRAL PRODUCTS (DAVP)				
Disease/Condition	**Concept**	**COA Tool & Type**	**COA Context of Use**	**Drug Name & Approval Date**
Influenza	Symptoms improvement (e.g., cough, sore throat, nasal congestion, headache, feverishness, myalgia and fatigue)	Patient diary: **PRO**	Treatment of acute uncomplicated influenza	Rapivab (peramivir) *December 19, 2014*

DIVISION OF TRANSPLANT AND OPHTHALMOLOGY PRODUCTS (DTOP)				
Disease/Condition	**Concept**	**COA Tool & Type**	**COA Context of Use**	**Drug Name/Approval Date/ Qualification Link**
Allergic conjunctivitis (itching associated with allergic conjunctivitis)	Ocular itching severity	5-point itching severity numerical rating scale with half unit increments: **PRO**	Pediatric and adult patients with itching associated with allergic conjunctivitis	1. Lastacaft (alcaftadine) *July 28, 2010* 2. Bepreve (bepotastine besilate) *September 8, 2009* 3. Elestat (epinastine) *October 16, 2003*

DIVISION OF TRANSPLANT AND OPHTHALMOLOGY PRODUCTS (DTOP) (CONTINUED)				
Disease/Condition	**Concept**	**COA Tool & Type**	**COA Context of Use**	**Drug Name/Approval Date/ Qualification Link**
Bacterial conjunctivitis	Clinical resolution based on absence of all three clinical signs (e.g., ocular discharge, bulbar conjunctival injection, and palpebral conjunctival injection)	**ClinRO**	Pediatric and adult patients with bacterial conjunctivitis along with other key efficacy measures (e.g., microbiology)	Besivance (besifloxacin hydrochloride) *May 28, 2009*
	Microbiological eradication	Laboratory measure: **Biomarker**		
Diabetic retinopathy (DR)	Severity of retinopathy	Early Treatment Diabetic Retinopathy Study Diabetic Retinopathy Severity Scores (ETDRS-DRSS): **ClinRO**	Adults with diabetic retinopathy	Lucentis (ranibizumab) *April 15, 2017*
Dry eye disease (DED)	Symptoms of DED: Extent of eye dryness	Eye Dryness Score (EDS) rated by a Visual Analogue Scale (VAS): **PRO**	Adults with eye dryness	Xiidra (lifitegrast ophthalmic solution) *July 11, 2016*
	Signs of DED	Inferior fluorescein corneal staining score (ICSS): **ClinRO**		
Kidney transplantation (prophylaxis of organ rejection)	Composite • Incidence of biopsy proven acute rejection • Death • Graft loss • Patient loss to follow up	Composite • **ClinRO** • **ClinRO** • **Biomarker** • Patient loss to follow up	Patients with kidney transplant	Nulojix (beletacept) *June 15, 2011*
Myopic choroidal neovascularization (mCNV)	Best Corrected Visual Acuity (BCVA)	BCVA Assessment: **PerfO**	Adults with high myopia and choroidal neovascularization	Lucentis (ranibizumab) *January 5, 2017*
Neovascular (wet) age-related macular degeneration	Best Corrected Visual Acuity (BCVA)	BCVA assessment: **PerfO**	Adults with age-related macular degeneration	1. Eylea (aflibercept) *November 18, 2011* 2. Macugen (pegaptanib sodium) *September 17, 2004* 3. Lucentis (ranibizumab) *June 30, 2006*

DIVISION OF TRANSPLANT AND OPHTHALMOLOGY PRODUCTS (DTOP) (CONTINUED)				
Disease/Condition	**Concept**	**COA Tool & Type**	**COA Context of Use**	**Drug Name/Approval Date/ Qualification Link**
Ocular inflammation and pain associated with ocular surgery	Absence of post-surgical ocular inflammation	Slit lamp evaluation and anterior chamber cell/flare grade score: **ClinRO**	Adults undergoing ocular surgery	1. Durezol (difluprednate) *June 23, 2008* 2. Nevanac (nepafenac) *August 19, 2005*
	Absence of post-surgical ocular pain/ discomfort	Visual Analog Scale (VAS) and/or 6-point numeric pain rating scale: **PRO**		
Ophthalmic surgery aid	Anterior lens capsule staining	Biomicroscopy: **ClinRO**	Patients undergoing ophthalmic surgical procedures	VisionBlue (trypan blue) *December 16, 2004*
Vitreomacular adhesion	Nonsurgical vitreomacular adhesion resolution	Biomicroscopy using 4-point scale: **ClinRO**	Adults with symptomatic vitreomacular adhesion	Jetrea (ocriplasmin) *October 17, 2012*
	Best Corrected Visual Acuity (BCVA)	BCVA assessment: **PerfO**		

OFFICE OF DRUG EVALUATION I (ODEI)

DIVISION OF CARDIOVASCULAR AND RENAL PRODUCTS (DCARP)				
Disease/Condition	**Concept**	**COA Tool &Type**	**COA Context of Use**	**Drug Name/Approval Date/ Qualification Link**
Acute Coronary Syndrome (ACS)	Composite • Incidence of cardiovascular death • Non-fatal myocardial infarction • Non-fatal stroke	Composite: **ClinRO**	Adults with ACS	1. Brilinta (ticagrelor) *July 20, 2011* 2. Effient (prasugrel) *July 10, 2009*
Acute myocardial infarction (MI)	Composite • All-cause mortality • MI • Ischemia-driven revascularization • Stent thrombosis	Composite: **ClinRO**	Adults receiving percutaneous coronary intervention (PCI)	Kengreal (cangrelor) *June 22, 2015*
Atrial fibrillation (AF) / atrial flutter (AFL)	Hospitalization due to cardiovascular cause or death from any cause	**ClinRO**	Adults in sinus rhythm with a history of paroxysmal or persistent AF/AFL	Multaq (dronedarone HCL) *July 1, 2009*
	First symptomatic AF/AFL recurrence	**ClinRO**		
Chronic coronary artery disease	Composite • Incidence of cardiovascular death, myocardial infarction and stroke • Avoidance of hospitalization for unstable angina • Avoidance of coronary revascularization	Composite: **ClinRO(s)**	Adults with a history of atherosclerosis involving the coronary, cerebral, or peripheral vascular systems	Zontivity (vorapaxar) *May 8, 2014*

DIVISION OF CARDIOVASCULAR AND RENAL PRODUCTS (DCARP) (CONTINUED)				
Disease/Condition	**Concept**	**COA Tool & Type**	**COA Context of Use**	**Drug Name/Approval Date/ Qualification Link**
Chronic stable angina	Exercise duration	Modified Bruce Treadmill Exercise test: **PerfO**	Adults with chronic angina	Ranexa (ranolazine) *January 27, 2006*
	Angina attack frequency	Patient diary—measures frequency: **PRO**		
	Nitroglycerin use	Patient diary: **PRO**		
Chronic thromboembolic pulmonary hypertension (CTEPH)	Exercise capacity	6-Minute Walking Distance (6MWD): **PerfO**	Adults with CTEPH	Adempas (riociguat) *October 8, 2013*
	World Health Organization functional class / lack of deterioration	World Health Organization functional assessment: **ClinRO**		
Heart Failure	Composite as first event • Cardiovascular death • Hospitalization due to heart failure	Composite: **ClinRO**	Adults with chronic heart failure	1. Corlanor (ivabradine) *April 15, 2015* 2. Entresto (sacubitril and valsartan) *July 7, 2015*
Neurogenic orthostatic hypotension	Symptom severity (e.g., dizziness, lightheadedness, feeling faint, and "feeling like you might blackout"	Orthostatic Hypotension Questionnaire Item (OHQ) #1: **PRO**	Adults with symptomatic neurogenic orthostatic hypotension	Northera (droxidopa) *February 18, 2014*
Pulmonary Arterial Hypertension (PAH)	Exercise capacity	6-Minute Walking Distance (6MWD): **PerfO**[2,3,4,5]	Adults with PAH	1. Uptravi (selexipag) *December 21, 2015* 2. Opsumit (macitentan) *October 18, 2013* 3. Adempas (riociguat) *October 8, 2013* 4. Letairis (ambrisentan) *June 15, 2007* 5. Ventavis (iloprost) *December 29, 2004*
	Incidence of death or clinical deterioration	**ClinRO**[2,3,4,5]		
	Composite • Incidence of PAH • Worsening of PAH	Composite[1] • Hospitalization for PAH: **ClinRO** • PAH worsening resulting in need for lung transplantation or balloon atrial septostomy: **ClinRO**		

DIVISION OF CARDIOVASCULAR AND RENAL PRODUCTS (DCARP) (CONTINUED)				
Disease/Condition	**Concept**	**COA Tool & Type**	**COA Context of Use**	**Drug Name & Approval Date**
Non-valvular atrial fibrillation (NVAF)	Composite • Stroke • Systemic embolic event	Composite • **ClinRO** • **ClinRO**	Adults with NVAF	1. Savaysa (edoxaban) *January 8, 2015* 2. Eliquis (apixaban) *December 28, 2012* 3. Xarelto (rivaroxaban) *July 1, 2011* 4. Pradaxa (dabigatran) *October 19, 2010*
Patients with a history of atherosclerosis	Composite • Incidence of cardiovascular death, myocardial infarction, and stroke • Avoidance of hospitalization for unstable angina • Avoidance of coronary revascularization	Composite: **ClinRO**	Adult patients with a history of atherosclerosis involving the coronary, cerebral, or peripheral vascular systems	Zontivity (vorapaxar) *May 8, 2014*
Varicose veins	Improvement of varicose veins (symptoms and appearance)	Digital photographs of the treatment area: **ClinRO**	Adult patients with spider or reticular varicose veins	Asclera (polidocanol) *March 30, 2010*
	Patient satisfaction with treatment	5-point verbal rating scale: **PRO**		

DIVISION OF NEUROLOGY PRODUCTS (DNP)				
Disease/Condition	**Concept**	**COA Tool & Type**	**COA Context of Use**	**Drug Name & Approval Date**
Alzheimer's disease (AD)	Day-to-day function	Modified Alzheimer's Disease Cooperative Study—Activities of Daily Living: **ClinRO**	Adult patients with moderate to severe AD	Namenda (memantine hydrochloride) *October 16, 2003*
	Cognitive function	Severe Impairment Battery (SIB): **PerfO**		
	Global impression	Clinical Global Impression (CGI-C): **ClinRO**		

DIVISION OF NEUROLOGY PRODUCTS (DNP) (CONTINUED)				
Disease/Condition	**Concept**	**COA Tool & Type**	**COA Context of Use**	**Drug Name & Approval Date**
Amyotrophic lateral sclerosis (ALS)	Functional disability	ALS Functional Rating Scale—Revised (ALSFRS-R): **ClinRO**	Adults with ALS	Radicava (edaravone injection) *May 5, 2017*
Blepharospasm	Signs and symptoms of blepharospasm	Jankovic Rating Scale (JRS)—severity domain: **ClinRO**	Adults with blepharospasm	Xeomin (incobotulinumtoxinA) *July 30, 2010*
Cervical dystonia	• Severity of dystonia • Disability • Pain	Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) (composite of **ClinRO** and **PRO**)	Adults with cervical dystonia	1. Xeomin (incobotulinumtoxinA) *July 30, 2010* 2. Dysport (abobotulinumtoxinA) *April 29, 2009*
Duchenne muscular dystrophy (DMD)	Muscle strength	Medical Research Council (MRC) 11-point scale: **ClinRO**[1]	Children (5 years and up) and adults with DMD	1. Emflaza (deflazacort) *February 9, 2017* 2. Exondys 51 (eteplirsen) *September 19, 2016*
	Physical function speed	Timed functional tests: **PerfO**[1]		
	Walking distance	6 Minute Walk Test (6MWT): **PerfO**[2]		
Huntington's chorea	Chorea	Total chorea score item of the Unified Huntington's Disease Rating Scale (UHDRS): **ClinRO**	Adults with chorea associated with HD	Austedo (deutetrabenazine) *April 3, 2017*
	Global Impression	Patient-rated Global Impression (PGI): **PRO**		
	Global Impression	Physician-rated Clinical Global Impression (GCI): **ClinRO**		
Huntington's disease (HD)	Chorea	Total chorea score item of the Unified Huntington's Disease Rating Scale (UHDRS): **ClinRO**	Adults with chorea associated with HD	Xenazine (tetrabenazine) *August 15, 2008*
	Global impression	Clinical Global Impression (CGI): **ClinRO**		

DIVISION OF NEUROLOGY PRODUCTS (DNP) (CONTINUED)				
Disease/Condition	**Concept**	**COA Tool & Type**	**COA Context of Use**	**Drug Name & Approval Date**
Migraine headache	Migraine frequency	Patient diary: **PRO**	Adults and adolescents (12 years and up) with migraine headaches	1. Trokendi XR (topiramate) *April 5, 2017* 2. Qudexy XR (topiramate) *March 29, 2017*
Multiple sclerosis (MS)	Physical disability	Expanded Disability Status Scale (EDSS): **ClinRO**	Adults with primary progressive forms of MS	Ocrevus (ocrelizumab) *March 28, 2017*
	Walking speed	Timed 25-foot walk: **PerfO**		
Multiple sclerosis (MS)	Relapse frequency	**ClinRO**	Adults with relapsing forms of MS	1. Ocrevus (ocrelizumab) *March 28, 2017* 2. Zinbryta (daclizumab) *May 27, 2016* 3. Tecfidera (dimethyl fumarate) *March 27, 2013* 4. Aubagio (teriflunomide) *September 12, 2012* 5. Gilenya (fingolimod) *September 21, 2010*
	Physical disability	Expanded Disability Status Scale (EDSS): **ClinRO**		
Multiple sclerosis (MS)	Walking speed	Timed 25-foot walk: **PerfO**	Adults with MS	Ampyra (dalfampridine) *January 22, 2010*
	Ambulatory disability	12-item Multiple Sclerosis Walking Scale: **PRO**		
Non-24-hour sleep-wake disorder	Nighttime sleep time and daytime nap time	Patient diary: **PRO**	Adults with non-24-hour sleep wake disorder	Hetlioz (tasimelteon) *January 31, 2014*
Parkinson's disease (PD)	Signs and symptoms of dyskinesia	Patient diary: **PRO**	Adults with PD experiencing "off" episodes	Xadago (safinamide) *March 21, 2017*
	Motor function	Uniform Parkinson's Disease Rating Scale (UPDRS)—Part III (motor examination): **ClinRO**		

DIVISION OF NEUROLOGY PRODUCTS (DNP) (CONTINUED)				
Disease/Condition	**Concept**	**COA Tool & Type**	**COA Context of Use**	**Drug Name & Approval Date**
Parkinson's Disease (PD) (Early Stage)	Motor findings	Unified Parkinson's Disease Rating Scale (UPDRS)—Part III: **ClinRO**	Adults with PD	1. Neupro (rotigotine) *May 9, 2007* 2. Azilect (rasagiline mesylate) *May 16, 2006*
	Activities of daily living	Unified Parkinson's Disease Rating Scale (UPDRS)—Part II: **ClinRO**		
Parkinson's disease (PD) (Advanced stage)	"Off" time	Patient diary: **PRO**[1,2] Unified Parkinson's Disease	Adults with PD	1. Azilect (rasagiline mesylate) *May 16, 2006* 2. Apokyn (apomorphine HCl) *April 20, 2004*
	Motor findings	Unified Parkinson's Disease Rating Scale (UPDRS)—Part III: **ClinRO**[1,2]		
	Activities of daily living	Unified Parkinson's Disease Rating Scale (UPDRS)—Part II: **ClinRO**[1]		
Restless legs syndrome (RLS)	Sensory and motor symptom severity and impacts on sleep, daytime tiredness or sleepiness, activities of daily living, and mood associated with RLS	International Restless Legs Syndrome (IRLS) Rating Scale: **PRO**	Adults with moderate to severe primary RLS	Horizant (gabapentin enacarbil) *April 6, 2011*
	Global impression—RLS symptoms	Clinical Global Impression (CGI): **ClinRO**		
Seizure disorder	Seizure frequency	Patient/Observer diary: [**PRO and/or ObsRO**] as appropriate	Adults and pediatrics 6 years and up with partial onset or primary generalized tonic-clonic seizures	Trokendi XR (topiramate) *April 5, 2017*
			Adults and pediatrics 16 years and up with partial onset or primary generalized tonic-clonic seizures	Briviact (brivaracetam) *February 18, 2016*

DIVISION OF NEUROLOGY PRODUCTS (DNP) (CONTINUED)				
Disease/Condition	**Concept**	**COA Tool &Type**	**COA Context of Use**	**Drug Name & Approval Date**
Seizure disorder: Infantile spasm	Electroencephalogram (EEG)—cessation of hypsarrhythmia	Video/electroencephalogram (EEG): **ClinRO**	Pediatric (1 month–2 years) patients with infantile spasms	Sabril (vigabatrin) *August 21, 2009*
	Complete cessation of seizures	Observer diary: **ObsRO**		
Seizure disorder: Lennox-Gastaut Syndrome (LGS)	Seizure frequency	Patient/Observer diary: **PRO and/or ObsRO** as appropriate	Pediatric (2 years and up) and adult patients with LGS	1. Onfi (clobazam) *October 21, 2011* 2. Banzel (rufinamide) *November 14, 2008*
Seizure disorder: Refractory Complex Partial Seizures	Seizure frequency	Patient/Observer diary: **PRO** and/or **ObsRO** as appropriate	Pediatric (2 years and up) and adult patients with refractory complex partial seizures	Sabril (vigabatrin) *August 21, 2009*
Spasticity	Muscle tone	Modified Ashworth Scale (MAS): **ClinRO**	Adults with spasticity and pediatric patients (2 years and up) with lower limb spasticity	Dysport (abobotulinumtoxinA) *June 14, 2017*
	Global impression	Physician Global Assessment (PGA): **ClinRO**		
Spinal muscular atrophy (SMA)	Motor development	Section 2 of Hammersmith Infant Neurologic Exam (HINE—motor milestones: **ClinRO**	Adults and pediatric patients with SMA	Spinraza (nusinersen) *December 23, 2016*
	Motor Skills	Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND): **ClinRO**		

DIVISION OF PSYCHIATRY PRODUCTS (DPP)				
Disease/Condition	**Concept**	**COA Tool &Type**	**COA Context of Use**	**Drug Name & Approval Date**
Attention deficit hyperactivity disorder (ADHD)	Severity of ADHD for patients 13 to 55 years old	ADHD Rating Scale (ADHD-RS): **ClinRO**[1,2]	Patients with ADHD	1. Mydayis (mixed salts of a single-entity amphetamine product) *June 20, 2017* 2. Vyvanse (lisdexamfetamine dimesylate) *February 23, 2007*
	Severity of ADHD in pediatric patients (13 to 17 years old)	Connor's Parent Rating Scale: **ObsRO**[2]		
	Attentional symptoms measurement in ADHD	Permanent Product Measure of Performance (PERMP): **PerfO**[1]		
	Deportment (behavior) in ADHD	Swanson, Kotkin, Angler, M-Flynn, and Pelham (SKAMP) Deportment Scores: **ClinRO**[2]		
Bipolar disorder (manic or mixed)	Manic symptoms	Young Mania Rating Scale (YMRS): **ClinRO**[1,2]	Adults with manic or mixed episodes associated with bipolar I disorder	1. Vraylar (cariprazine) *September 17, 2015* 2. Saphris (asenapine) *August 13, 2009*
	Global clinical impression of bipolar disorder severity*	Clinical Global Impression—Bipolar Severity of Illness score (CGI-BP-S): **ClinRO**[1,2]		
Bipolar disorder (depressive)	Depressive symptoms	Montgomery-Åsberg Depression Rating Scale (MADRS) version 10: **ClinRO**	Adults with depressive episodes associated with bipolar I disorder	Latuda (lurasidone hydrochloride) *January 27, 2017*
	Global clinical impression of bipolar disorder severity**	Clinical Global Impression—Bipolar-Severity of Illness Scale (CGI-BP-S): **ClinRO**		
Insomnia	Sleep latency (sleep onset)	Patient diary: **PRO1**[1,2,3]	Adults with insomnia characterized by difficulty with sleep onset and/or maintenance	1. Belsomra (suvorexant) *August 13, 2014* 2. Rozerem (ramelteon) *July 22, 2005* 3. Lunesta (eszopiclone) *December 15, 2004*
	Wake time after sleep onset [WASO] (sleep maintenance)	Polysomnography: **Biomarker**[1,3]		

*Clinical Global Impression-Severity measures were only used as secondary endpoints in approved labeling

**Clinical Global Impression-Severity measures were only used as secondary endpoints in approved labeling

DIVISION OF PSYCHIATRY PRODUCTS (DPP) (CONTINUED)				
Disease/Condition	**Concept**	**COA Tool &Type**	**COA Context of Use**	**Drug Name & Approval Date**
Major depressive disorder (MDD)	Symptoms of MDD	Montgomery-Åsberg Depression Rating Scale (MADRS) version 10: **ClinRO**[1,2,3]	Adults with MDD	1. Rexulti (brexpiprazole) *July 10, 2015* 2. Trintellix (vortioxetine) *September 30, 2013* 3. Viibryd (vilazodone hydrochloride) *January 21, 2011* 4. Pristiq (desvenlafaxine succinate) *February 29, 2008* 5. Cymbalta (duloxetine hydrochloride) *August 3, 2004*
	Symptoms of MDD	Hamilton Depression Rating Scale 24 items or 17 items: **ClinRO**[2,4,5]		
Major depressive disorder (MDD)	Symptoms of MDD	Major Depressive Disorder Scale (SMDDS): **PRO**	Adults with MDD	**COA Qualified Tool** Visit "Clinical Outcome Assessment Qualification Program Submissions" Website for additional information
Parkinson's disease (PD) psychosis	Severity of hallucinations and delusions	PD adapted Scale for the Assessment of Positive Symptoms (SAPS-PD) hallucinations and delusions: **ClinRO**	Adults with hallucinations and delusions associated with PD psychosis	Nuplazid (pimavanserin) *April 29, 2016*

DIVISION OF PSYCHIATRY PRODUCTS (DPP) (CONTINUED)				
Disease/Condition	**Concept**	**COA Tool &Type**	**COA Context of Use**	**Drug Name & Approval Date**
Schizophrenia	Severity of schizophrenia syndrome	Positive and Negative Syndrome Scale (PANSS): **ClinRO**[1,2,3,4,5,6]	Adults with schizophrenia	1. Aristada (aripiprazole lauroxil) *October 5, 2015* 2. Vraylar (cariprazine) *September 17,2015* 3. Latuda (lurasidone hydrochloride) *October 28, 2010 Efficacy Supplement (January 27, 2017)** 4. Saphris (asenapine) *August 13, 2009* 5. Fanapt (iloperidone) *May 6, 2009* 6. Invega (paliperidone) *December 19, 2006*
	Positive symptoms of psychosis**	Brief Psychiatric Rating Scale derived (BPRSd): **ClinRO**[3,5]		
	Global clinical impression of severity***	Clinical Global Impression-Severity (CGI-S): **ClinRO**[2,3]		
	Personal and social functioning	Personal and Social Performance (PSP) scale: **ClinRO**[6]		
Tardive dyskinesia (TD)	Involuntary movements associated with TD	Abnormal Involuntary Movement Scale (AIMS): **ClinRO**	Adults with TD	Ingrezza (valbenazine) *April 11, 2017*

*Latuda (efficacy supplement) is approved for adults and adolescents (13 to 17 years) with schizophrenia

**The BPRSd is derived from the PANSS and focuses on primarily positive symptoms

***Clinical global Impression-Severity measures were only used as secondary endpoints in approved labeling

OFFICE OF DRUG EVALUATION II (ODE II)

DIVISION OF ANESTHESIA, ANALGESIA AND ADDICTION PRODUCTS (DAAAP)				
Disease/Condition	**Concept**	**COA Tool & Type**	**COA Context of Use**	**Drug Name & Approval Date**
Alcoholism	Attaining and maintaining abstinence or low risk drinking (e.g., frequency of alcohol consumption, quantity of alcohol consumed, and laboratory measure)	Composite • Patient diary: **PRO** • Laboratory confirmation: **Biomarker**	Adult patients who are alcohol-dependent	Campral (acamprosate calcium) *July 29, 2004*
Chronic musculoskeletal pain	Pain intensity	Numerical pain rating scale or visual analog scale: **PRO**	Patients with chronic musculo-skeletal pain	Refer to the following draft guidance for industry for specific type of chronic musculoskeletal pain
Pain (acute)	Pain intensity	Numerical pain rating scale or visual analog scale: **PRO**	Patients with acute pain	Nucynta (tapentadol hydrochloride) *November 20, 2008*
Pain (chronic)	Pain intensity	Numerical pain rating scale or visual analog scale: **PRO**	Patients with chronic pain	Prialt (ziconotide acetate intrathecal infusion) *December 28, 2004*
Pain (neuropathic)	Pain intensity	Numerical pain rating scale or visual analog scale: **PRO**	Patients with neuropathic pain	1. Qutenza (capsaicin 8% patch) *November 16, 2009* 2. Lyrica (pregabalin) *December 30, 2004*
Smoking cessation	Abstinence	Composite • Patient-reported abstinence: **PRO** • Laboratory measure: **Biomarker**	Current smokers	Chantix (varenicline tartrate) *May 10, 2006*

DIVISION OF METABOLISM AND ENDOCRINOLOGY PRODUCTS (DMEP)				
Disease/Condition	**Concept**	**COA Tool & Type**	**COA Context of Use**	**Drug Name/Approval Date/ Qualification Link**
Human immunodeficiency virus (HIV)-related lipodystrophy	Body image	Belly appearance distress score: **PRO**	Adult patients with HIV-related lipodystrophy	Egrifta (tesamorelin) *November 10, 2010*

DIVISION OF PULMONARY, ALLERGY, AND RHEUMATOLOGY PRODUCTS (DPARP)				
Disease/Condition	**Concept**	**COA Tool & Type**	**COA Context of Use**	**Drug Name/Approval Date/ Qualification Link**
Allergic rhinitis	Nasal symptoms severity (e.g., runny nose, nasal itching, sneezing, and nasal congestion)	4-point categorical nasal symptom severity scale: **PRO**	Pediatric and adult patients with allergic rhinitis	Omnaris (ciclesonine) *October 20, 2006*
Ankylosing spondylitis	Signs and symptoms of ankylosing spondylitis (e.g., pain, inflammation)	Composite: Assessment in Ankylosing Spondylitis (ASAS): **PROs** • VAS pain scale • Bath Ankylosing Spondylitis Functional Index • Bath Ankylosing Spondylitis Disease Activity Index • Patient global assessment	Adult patients with ankylosing spondylitis	Simponi (golimumab) *April 24, 2009*
Asthma	Signs and symptoms of asthma and adequacy of asthma control	Asthma Control Questionnaire (ACQ-7) • Asthma symptoms: **PRO**	Patients 6 years of age and older for the maintenance treatment of asthma	Spiriva Respimat (tiopropium bromide) *February 15, 2017*
	Health Related Quality of life	Asthma Quality of Life Questionnaire (AQLQ): **PRO**		
	Signs and symptoms of asthma and measure of asthma exacerbation	Composite: Asthma exacerbation • Peak Expiratory Flow (PEF): **Biomarker** • Asthma symptoms: **PRO**		

DIVISION OF PULMONARY, ALLERGY, AND RHEUMATOLOGY PRODUCTS (DPARP) (CONTINUED)				
Disease/Condition	**Concept**	**COA Tool & Type**	**COA Context of Use**	**Drug Name/Approval Date/ Qualification Link**
Asthma	Functional problems related to asthma (physical, emotional and social)	Pediatric Asthma Quality of Life Questionnaire (PAQLQ): **PRO**	Patients with asthma 6 to less than 12 years of age	Symbicort (budesonide/formoterol) *January 27, 2017*
Asthma	Functional problems related to asthma	Asthma Quality of life questionnaire (AQLQ): **PRO**	Adults with severe with an eosinophilic phenotype for add on maintenance treatment	Cinqair (reslizumab) *March 23, 2016*
	Adequacy of and change in asthma control	Asthma Control Questionnaire (ACQ-7): **PRO**		
	Asthma exacerbation	Composite: **ClinRO** • Use or increase in the use of a systemic corticosteroid • Asthma-related emergency treatment or asthma-related hospitalization		
Asthma	Asthma exacerbation	Composite: **ClinRO** • Use of oral/systemic steroids • Hospitalization • Emergency department visits	Patients with severe asthma aged 12 years and older, and with an eosinophilic phenotype as an add-on maintenance treatment	Nucala (mepolizumab) *November 4, 2015*
	Asthma control	Asthma Control Questionnaire-5 (ACQ-5): **PRO**		
	Symptoms frequency and severity, physical activity limitations, and impact on daily life	St. Georges Respiratory Questionnaire (SGRQ): **PRO**		

DIVISION OF PULMONARY, ALLERGY, AND RHEUMATOLOGY PRODUCTS (DPARP) (CONTINUED)				
Disease/Condition	**Concept**	**COA Tool & Type**	**COA Context of Use**	**Drug Name/Approval Date/ Qualification Link**
Asthma	Frequency and severity of asthma exacerbation	Patient diary: **PRO**	Pediatric and adult patients with asthma	Xolair (omalizumab) *June 20, 2003*
	Lung function	FEV1: **Biomarker**		
	Improvement in asthma symptoms severity	Asthma symptoms score: **PRO**		
Chronic obstructive pulmonary disease (COPD)	Respiratory symptoms of stable COPD	Evaluating Respiratory Symptoms in Chronic Obstructive Pulmonary Disease (E-RS: COPD): **PRO**	Adult outpatients with stable COPD	**Qualified COA Tool** Visit "Clinical Outcome Assessment Qualification Program Submissions" Website for additional information
Chronic obstructive pulmonary disease (COPD)	Symptoms frequency and severity, physical activity limitations, and impact on daily life	St. George's Respiratory Questionnaire: **PRO**[2]	Adult patients with COPD	1. Breo Ellipta (fluticasone furoate and vilanterol trifenatate) *May 10, 2013* 2. Arcapta Neohaler (indacaterol maleate) *July 1, 2011* 3. Daliresp (roflumilast) *February 28, 2011*
	Composite • Symptoms of exacerbation • Therapeutic intervention • Hospitalization	Composite of pulmonary exacerbations: **ClinRO**[1,3]		
Cryopyrin-associated periodic syndromes (CAPS)	Signs and symptoms severity (e.g., rash, fatigue, joint pain, feeling of fever/chills, eye redness/pain)	Severity rating of each symptom on a 0-10-point scale with half point increments on the Daily Health Assessment Form: **PRO**[2]	Pediatric and adult patients with CAPS	1. Ilaris (canakinumab) *June 17, 2009* 2. Arcalyst (rilonacept) *February 27, 2008*
	Physician global assessment of disease activity and skin disease assessment	Physician's global rating using a categorical rating scale: **ClinRO**[1]		
Cystic fibrosis	Respiratory symptoms (cough, sputum production, difficulty breathing)	Cystic Fibrosis Questionnaire—Revised (CFQ-R) Respiratory Domain: **PRO**	Patients age 12 years and older with cystic fibrosis (CF)	Orkambi (lumacaftor/ivacaftor) *July 2, 2015*
	Sino-pulmonary signs and symptoms of exacerbation	Pulmonary exacerbation: **ClinRO**		

DIVISION OF PULMONARY, ALLERGY, AND RHEUMATOLOGY PRODUCTS (DPARP) (CONTINUED)				
Disease/Condition	**Concept**	**COA Tool & Type**	**COA Context of Use**	**Drug Name/Approval Date/ Qualification Link**
Cystic fibrosis	Respiratory symptoms severity	Cystic Fibrosis Questionnaire—Revised respiratory domain (CFQ-R): **PRO**	Pediatric and adult patients with cystic fibrosis	Kalydeco (ivacaftor) *January 31, 2012* *Efficacy supplement (May 17, 2017)*
	Sino-pulmonary signs and symptoms of exacerbation	Pulmonary exacerbation: **ClinRO**		
Hereditary angioedema (HAE)	Signs and symptoms severity (e.g., skin swelling, skin pain, abdominal pain)	100mm visual analog scale or evaluating each sign/ symptom severity: **PRO**[1]	Pediatric and adult patients with HAE	1. Firazyr (icatibant acetate) *August 25, 2011* 2. Kalbitor (ecallantide) *December 1, 2009*
		4-point categorical scale (Mean Symptom Complex Severity score): **PRO**[2]		
	Improvement of each anatomic site of attack	Categorical scale evaluating treatment improvement (Treatment Outcome Score): **PRO**[2]		
Idiopathic pulmonary fibrosis (IPF)	IPF exacerbation (defined as worsening or development of dyspnea and imaging abnormalities)	Composite • **ClinRO** and **Biomarker**	Adult patients with idiopathic pulmonary fibrosis	Ofev (nintedanib) *October 15, 2014*

DIVISION OF PULMONARY, ALLERGY, AND RHEUMATOLOGY PRODUCTS (DPARP) (CONTINUED)				
Disease/Condition	**Concept**	**COA Tool & Type**	**COA Context of Use**	**Drug Name/Approval Date/ Qualification Link**
Psoriatic Arthritis	• Improvement in number of tender and swollen joints • Pain intensity • Patient's global assessment of disease activity • Physician's global assessment of disease activity • Disability • Physical functioning • Laboratory measure (Biomarker(s)) (e.g., sedimentation rate)	American College of Rheumatology (ACR) core set of outcome measures: [**ClinRO**, **PRO** and **Biomarker**][1,2,3]	Adults with active Psoriatic Arthritis (PsA)	1. Orencia (abatacept) *June 30, 2017* 2. Otezla (apremilast) *March 21, 2014* 3. Simponi (golimumab) *April 24, 2009*
	Physical function	Health Assessment Questionnaire Disability Index (HAQ-DI): **PRO1**[1,2,3]		
Respiratory distress syndrome (RDS)	Prevention of RDS in premature infants at high risk for RDS	Incidence of RDS and RDS related mortality: **ClinRO**	Premature infants at high risk for RDS	*Surfaxin (lucinactant) *March 6, 2012*

*Surfaxin is no longer marketed but the clinical outcome assessment is still considered acceptable

DIVISION OF PULMONARY, ALLERGY, AND RHEUMATOLOGY PRODUCTS (DPARP) (CONTINUED)				
Disease/Condition	**Concept**	**COA Tool & Type**	**COA Context of Use**	**Drug Name/Approval Date/ Qualification Link**
Rheumatoid arthritis (RA)	Composite • Improvement in number of tender and swollen joints • Pain intensity • Patient's global assessment of disease activity • Physician's global assessment of disease activity • Disability • Physical functioning • Laboratory measure (Biomarker(s)) (e.g., sedimentation rate)	Composite • American College of Rheumatology (ACR) core set of outcome measures: [**ClinRO**, **PRO**, and **Biomarker(s)**][1,2,3,4,5]	Adult patients with RA	1. Kevzara (sarilumab) *May 22, 2017* 2. Simponi Aria (golimumab) *July 18, 2013* 3. Xeljanz (tofacitinib) *November 6, 2012* 4. Actemra (tocilizumab) *January 8, 2010* 5. Orencia (abatacept) *December 23, 2005*
	Physical function	Health Assessment Questionnaire Disability Index (HAQ-DI): **PRO**[1,2,3,4,5]		
	General health status	Short Form (SF-36): **PRO**[1,5]		
Systemic lupus erythematosus	Signs and symptoms and disease activity severity Global impression	Composite • Systemic Lupus Erythematosus Disease Activity Index: **ClinRO** • British Isles Lupus Activity Group: **ClinRO** • Clinician's Global Assessment: **ClinRO**	Patients with systemic lupus erythematosus	Benlysta (belimumab) *March 9, 2011*

OFFICE OF DRUG EVALUATION III (ODE III)

DIVISION OF DERMATOLOGY AND DENTAL PRODUCTS (DDDP)				
Disease/Condition	**Concept**	**COA Tool & Type**	**COA Context of Use**	**Drug Name/Approval Date/ Qualification Link**
Actinic keratosis (topical therapy)	Clearance of actinic keratosis lesions	**ClinRO**	Adult patients with actinic keratosis	Picato (ingenol mebutate) *January 23, 2012*
Atopic Dermatitis	Global assessment of the overall severity of the disease (e.g., erythema and papulation/infiltration	Investigator's Global Assessment Scale (IGA): **ClinRO**	Adults with moderate-to-severe atopic dermatitis	Dupixent (dupilumab) *March 28, 2017*
	Extent and severity of the disease (e.g., thickness, scratching and lichenification)	Eczema Area and Severity Index (EASI-75): **ClinRO**		
	Itching intensity	Pruritus Numeric Rating Scale (NRS): **PRO**		
Atopic Dermatitis	Global assessment of the overall severity of the disease (e.g., clear or almost clear)	Investigator's Static Global Assessment (ISGA): **ClinRO**	Patients 2 years of age and older with mild to moderate atopic dermatitis	Eucrisa (crisaborole) *December* 14, 2016
External genital and perianal warts (topical therapy)	Clearance of external genital and perianal warts	**ClinRO**	Adult patients with external genital and perianal warts	Veregen (kunecatechins) *October 31, 2006*
Head lice infestations (topical therapy)	Absence of live lice	**ClinRO**	Pediatric and adult patients with head lice infestations	1. Natroba (spinosad) *January 18, 2011* 2. Ulesfia 5% Lotion (benzyl alcohol) *April 9, 2009*

DIVISION OF DERMATOLOGY AND DENTAL PRODUCTS (DDDP) (CONTINUED)				
Disease/Condition	**Concept**	**COA Tool & Type**	**COA Context of Use**	**Drug Name/Approval Date/ Qualification Link**
Interdigital tinea pedis, tinea cruris, tinea corporis (topical therapy)	Composite • Clearance of signs and symptoms (e.g., erythema, scaling, and pruritus) • Mycological cure (fungal culture and potassium hydroxide (KOH) tests)	Composite[1] • **ClinRO** & **PRO** • Laboratory measure: **Biomarker(s)** Note: pruritus symptoms are assessed based on patient-reported outcome	Pediatric and/or adult patients with interdigital tinea pedis, tinea cruris, and/or tinea corporis	1. Luzu cream 1% (luliconazole) *November 14, 2013* 2. Ertaczo (sertaconazole nitratecream 2%) *December 10, 2003*
	Clearance of signs and symptoms (e.g., erythema, scaling, and pruritus)	**PRO**[2] & **ClinRO**[2]		
Onychomycosis (topical therapy)	Composite • Clinical evidence of the disease (absence of signs/symptoms) • Mycological cure (fungal culture and potassium hydroxide (KOH) tests)	Composite • **ClinRO** • Laboratory measures: **Biomarker(s)**	Adults patients with onychomycosis	1. Kerydin (Tavaborole) *July 7, 2014* 2. Jublia (efinaconazole) *June 6, 2014*
Plaque Psoriasis	Extent and severity of affected body surface area (e.g., induration, erythema, and scaling)	Psoriasis Area and Severity Index (PASI 75): **ClinRO**[1,2,3,4]	Adults with moderate-to-severe plaque psoriasis	1. Siliq (brodalumab) *February 15, 2017* 2. Taltz (ixekizumab) *March 22, 2016* 3. Cosentyx (secukinumab) *January 21, 2015* 4. Stelara (ustekinumab) *September 25, 2009*
	Global assessment of the overall severity of the disease (e.g., plaque thickness/ induration, erythema, and scaling)	Physician's Global Assessment (PGA): **ClinRO**[1,2,3,4]		
	Symptoms of plaque psoriasis	Psoriasis Symptom Inventory (PSI): **PRO**[1]		
	Itching severity	Itch numeric Rating Scale: **PRO**[2]		
	Patient reported symptoms	Psoriasis Symptom Diary: **PRO**[3]		

DIVISION OF DERMATOLOGY AND DENTAL PRODUCTS (DDDP) (CONTINUED)				
Disease/Condition	**Concept**	**COA Tool & Type**	**COA Context of Use**	**Drug Name/Approval Date/ Qualification Link**
Submental Fat	Improvement in submental convexity or fullness	Composite • Clinician Reported Submental Fat Rating Scale (CR-SMFRS): **ClinRO** • Patient Reported Submental Fat Rating Scale (PR-SMFRS): **PRO**	Adults with moderate to severe convexity or fullness associated with submental fat	Kybella (deoxycholic acid) *April 29, 2015*
	Visual and emotional impact of submental fat	6 questions survey: **PRO**		

DIVISION OF GASTROENTEROLOGY AND INBORN ERROR PRODUCTS (DGIEP)				
Disease/Condition	**Concept**	**COA Tool & Type**	**COA Context of Use**	**Drug Name/Approval Date/ Qualification link**
Carcinoid syndrome diarrhea	Bowel movement	Patient diary: **PRO**	Adults with carcinoid syndrome diarrhea	Xermelo (telotristat ethyl) *February 28, 2017*
	Abdominal pain			
	Flushing			
Chronic idiopathic constipation	Frequency of complete spontaneous bowel movements (CSBM)	Patient diary: **PRO**[1,2]	Adults with chronic idiopathic constipation	1. Trulance (plecanatide) *January 19, 2017* 2. Linzess (linaclotide) *August 30, 2012* 3. Amitiza (lubiprostone) *January 31, 2006*
	Frequency of spontaneous bowel movements (SBM)	Patient diary: **PRO**[1,2,3]		
	Straining—amount of time pushing or physical effort to pass stool	Patient diary: **PRO**[1]		
	Stool consistency	Bristol Stool Form Scale (BSFS): **PRO**[1,2]		
	Signs and symptoms related to constipation (e.g., abdominal pain, stool consistency, severity of straining)	Numeric rating scale assessing signs and symptoms: **PRO**[2,3]		

DIVISION OF GASTROENTEROLOGY AND INBORN ERROR PRODUCTS (DGIEP) (CONTINUED)				
Disease/Condition	**Concept**	**COA Tool & Type**	**COA Context of Use**	**Drug Name/Approval Date/ Qualification link**
Crohn's disease (CD)	Composite • Signs and symptoms of the disease • Disease activity	Composite • **PRO** & **ClinRO** • **Biomarkers**	Adults with CD	1. Cimzia (certolizumab pegol *April 22, 2008* 2. Entyvio (vedolizumab) *May 20, 2014*
Irritable bowel syndrome with constipation (IBS-C)	Frequency of complete spontaneous bowel movement	Patient diary: **PRO**	Adults with IBS-C	Linzess (linaclotide) *August 30, 2012*
	Abdominal pain intensity	11-point abdominal pain numeric rating scale: **PRO**		
Irritable bowel syndrome with diarrhea (IBS-D)	Abdominal pain intensity and stool consistency	Composite • Patient Diary: **PRO** • Bristol Stool Scale (BSS): **PRO**	Adults with IBS-D with diarrhea	Viberzi (eluxadoline) *May 27, 2015*
		11-point abdominal pain numeric rating scale: **PRO**		
Hypophosphatasia (HPP)	Assessment of gait	Modified Performance Oriented Mobility Assessment—Gait (MPOMA-G): **PerfO**	Patients with perinatal/ infantile and juvenile-onset HPP	Strensiq (asfotase alfa) *October 23, 2015*
	Walking distance	6 Minute Walk Test (6MWT): **PerfO**		
	Assess skeletal burden in HPP	Radiographic Global Impression of Change (RGI-C): **ClinRO**		
Mucopolysaccharidosis I (MPS I) (Hurler and Hurler-Scheie forms of MPS I)	Walking distance	6-Minute Walk Test: **PerfO**	Pediatric and/or adult patients with MPS I	Aldurazyme (laronidase) *April 30, 2003*
Mucopolysaccharidosis II (MPS II) (Hunter syndrome)	Walking distance	6-Minute Walk Test: **PerfO**	Pediatric and/or adult patients with MPS II	Elaprase (idursulfase) *July 24, 2006*

DIVISION OF GASTROENTEROLOGY AND INBORN ERROR PRODUCTS (DGIEP) (CONTINUED)				
Disease/Condition	**Concept**	**COA Tool & Type**	**COA Context of Use**	**Drug Name/Approval Date/ Qualification link**
Mucopolysaccharidosis IVA (MPS IVA) (Morquio A syndrome)	Walking distance	6-Minute Walk Test: **PerfO** 3-Minute Stair Climb Test: **PerfO**	Pediatric and/or adult patients with MPS IVA	Vimizim (elosulfase) *February 14, 2014*
Mucopolysaccharidosis VI (MPS VI) (MaroteauxLamy syndrome)	Walking distance	12-Minute Walk Test: **PerfO**	Pediatric and/or adult patients with MPS VI	Naglazyme (galsulfase) *May 31, 2005*
	Stair-climbing capacity	3-Minute Stair Climb Test: **PerfO**		
N/A*	Successful excellent bowel prep (visualization of mucosa and minimal need for additional washing)	**ClinRO**	Adults scheduled for elective colonoscopy	Prepopik (citric acid; magnesium oxide; sodium picosulfate) *July 16, 2012*
Nausea and vomiting associated with chemotherapy	Absence of vomiting, retching or nausea and no use of rescue medication[2]	Patient Diary: **PRO**[1,2]	Adults with delayed nausea and vomiting associated with emetogenic chemotherapy[2]	1. Aloxi (palonosetron hydrochloride) *July 25, 2003* 2. Varubi (rolapitant) *September 1, 2015*
	Absence of emetic episodes and no use of rescue medication[1]		Adults at risk for nausea and vomiting associated with emetogenic chemotherapy[1]	
Neuronal ceroid lipofuscinosis type 2 (CLN2)	Measure of motor related functioning/mobility	CLN2 Clinical Rating Scale (motor domain): **ClinRO**	Symptomatic pediatric patients 3 years of age and older with late infantile (CLN2)	Brineura (cerliponase alfa) *April 27, 2017*
Non-infectious diarrhea	Stool consistency	Bristol Stool Form Scale: **PRO**	Adults with noninfectious diarrhea, HIV related	Mytesi (crofelemer) *December 31, 2012*
	Frequency of the watery bowel movement	Patient diary: **PRO**		
Opioid induced constipation	Frequency of spontaneous bowel movements without laxative use	Patient diary: **PRO**[1,2]	Adults with opioid induced constipation	1. Amitiza (lubiprostone) *January 31, 2006* 2. Symproic (naldemedine) *March 23, 2017*
	Frequency of complete spontaneous bowel movement	Patient diary: **PRO**[2]		

*Cleansing of the colon as a preparation for colonoscopy

DIVISION OF GASTROENTEROLOGY AND INBORN ERROR PRODUCTS (DGIEP) (CONTINUED)				
Disease/Condition	**Concept**	**COA Tool & Type**	**COA Context of Use**	**Drug Name/Approval Date/ Qualification link**
Opioid induced ileus, postoperative	Resolution of opioid induced ileus, both the upper and lower gastrointestinal tract (i.e., toleration of solid food and first bowel movement)	Patient diary: **PRO**	Adults with opioid induced ileus, postoperative	Entereg (alvimopan) *May 20, 2008*
Pancreas divisum undergoing endoscopic retrograde cholangiopancreatography (ERCP)	Cannulation of the minor duct of the pancreas	**ClinRO**	Adults with pancreas divisum undergoing ERCP	Chirhostim (secretin synthetic human) *April 9, 2004*
Pompe disease, late-onset	Walking distance	6-Minute Walk Test: **PerfO**	Patients with Pompe disease, late-onset	Lumizyme (alglucosidase alfa) *May 24, 2010*
Ulcerative colitis (UC)	Disease activity and severity	Endoscopy: **ClinRO**	Adults with UC	Entyvio (vedolizumab) *May 20, 2014*
	Signs and symptoms of UC (blood and stool frequency)	Patient diary: **PRO**		
Urea Cycle Disorder (UCD)	Composite • Signs and symptoms of hyperammonemia • Venous ammonia value	Composite • Hyperammonemia: **PRO** • Laboratory measure: **Biomarker**	Patients 2 months to less than 2 years with UCD	Ravicti (glycerol phenybutyrate) *April 28, 2017*

DIVISION OF BONE, REPRODUCTIVE AND UROLOGY PRODUCTS (DBRUP)				
Disease/Condition	**Concept**	**COA Tool & Type**	**COA Context of Use**	**Drug Name/Approval Date/ Qualification Link**
Benign prostatic hyperplasia (BPH)	BPH symptoms severity (irritative and obstructive symptoms)	International prostate symptom score (IPSS): **PRO**	Adults with BPH	1. Rapaflo (silodocin) *October 8, 2008* 2. Uroxatral (alfuzosin hydrochloride) *June 12, 2003*

DIVISION OF BONE, REPRODUCTIVE AND UROLOGY PRODUCTS (DBRUP) (CONTINUED)				
Disease/Condition	**Concept**	**COA Tool & Type**	**COA Context of Use**	**Drug Name/Approval Date/ Qualification link**
Erectile dysfunction	Erectile function	Erectile function domain of the International Index of Erectile Function (IIEF): **PRO**	Adult men diagnosed with erectile dysfunction	1. Stendra (avanafil) *April 27, 2012* 2. Cialis (tadalafil) *November 21, 2003* 3. Levitra (vardenafil hydrochloride) *August 19, 2003*
	Attainment and maintenance of erection	Sexual Encounter Profile (SEP) patient diary: **PRO**		
Hypoactive sexual desire disorder	Sexual satisfaction	Satisfying sexual events (SSEs): **PRO**	Adult premenopausal women with acquired, generalized hypoactive sexual desire disorder	Addyi (flibanserin) *August 18, 2015*
	Sexual desire	Sexual desire from e-Diary: **PRO**		
	Sexual desire	Female Sexual Function Index (FSFI): **PRO**		
	Sexually-related distress	Female Sexual Distress Scale—Revised (FSDS-R): **PRO**		
Nocturia	Improvement of nocturia episodes	Nocturic episodes: **PRO**	Adults with nocturnal polyuria who waken at least 2 times per night to void	Noctiva (desmopressin acetate) *March 3, 2017*
	Nighttime urination bother	Impact of Nighttime Urination (INTU) questionnaire: **PRO**		
Overactive bladder	Incontinence episodes, urinary frequency and urinary void volume	Patient voiding diary: **PRO**	Patients with overactive bladder with symptoms of urge urinary incontinence, urgency, and urinary frequency	1. Myrbetriq (mirabegron) *June 28, 2012* 2. Toviaz (fesoterodine) *October 31, 2008* 3. Enablex (darifenacin hydrobromide) *December 22, 2004* 4. Vesicare (solifenacin succinate) *November 19, 2004*

DIVISION OF BONE, REPRODUCTIVE AND UROLOGY PRODUCTS (DBRUP) (CONTINUED)				
Disease/Condition	**Concept**	**COA Tool & Type**	**COA Context of Use**	**Drug Name/Approval Date/ Qualification link**
Vasomotor symptoms (VMS)	Frequency of VMS (hot flashes/flushes)	Patient diary: **PRO**	Postmenopausal women with moderate to severe VMS due to menopause	Duavee (conjugated estrogens/bazedoxifene) *October 3, 2013*
	Severity of VMS (hot flashes/ flushes)	Daily severity score: **PRO**		
Vulvar and vaginal atrophy (VVA)	Symptoms of vulvar and vaginal atrophy (e.g., vaginal dryness, dyspareunia, vaginal irritation/itching)	Patient diary: **PRO**	Postmenopausal women with moderate to severe symptoms of VVA due to menopause	Osphena (ospemifene) *February 26, 2013*

OFFICE OF HEMATOLOGY AND ONCOLOGY PRODUCTS (OHOP)

DIVISION OF HEMATOLOGY PRODUCTS (DHP)				
Disease/Condition	**Concept**	**COA Tool & Type**	**COA Context of Use**	**Drug Name & Approval Date**
Chronic lymphocytic leukemia (CLL)	Composite • Incidence of palpable hepatosplenomegaly. Size of lymph nodes; incidence of lymph nodes with nodularity • B symptoms evaluation (night sweats, fever, unexplained weight loss) • Laboratory measures (lymphocytes, neutrophils, platelets, histology)	Composite • **ClinRO** • **ClinRO** • Laboratory measures: **Biomarker(s)**	Adult patients with CLL	Treanda (bendamustine hydrochloride) *March 20, 2008*
Cutaneous T-cell lymphoma (CTCL)	Skin involvement	Severity Weighted Assessment Tool (SWAT) in addition to other outcomes (e.g., response duration, time to progression, time to objective response): **ClinRO**	Adult patients with CTCL	Zolinza (vorinostat) *October 6, 2006*
	Physician's global assessing improvement or worsening in overall disease	7-Point Physician's Global Assessment (PGA) scale: **ClinRO**		
Mucositis	Incidence and severity of oral mucositis (e.g., soreness/erythema, ulcers, oral intake tolerability)	World Health Organization Oral Mucositis Scale: **PRO**	Adult patients with hematologic malignancies receiving myelotoxic therapy requiring hematopoietic stem cell support	Kepivance (palifermin) *December 15, 2004*
Myelofibrosis (MF)	Myelofibrosis symptom severity (e.g., tiredness, night sweats, itchiness, abdominal discomfort, pain under the ribs, feeling of fullness, bone or muscle pain)	Composite • Myelofibrosis Symptoms Assessment Form (MFSAF) diary*: **PRO**	Patients with intermediate or high risk MF, post polycythemia-vera MF and post essential thrombocythemia MF who are symptomatic	Jakafi (ruxolitinib) *November 16, 2011*

*MFSAF v4.0 is the currently recommended version instead of v2.0

DIVISION OF HEMATOLOGY PRODUCTS (DHP) (CONTINUED)				
Disease/Condition	**Concept**	**COA Tool & Type**	**COA Context of Use**	**Drug Name/Approval Date/ Qualification link**
Paroxysmal Nocturnal Hemaglobinuria (PNH)	Disease related fatigue	Functional Assessment of Chronic Illness Therapy—Fatigue (FACIT-F): **PRO**	Adult patients with PNH and hemolysis requiring transfusion	Soliris (eculizumab) *March 16, 2007*
Systemic Mastocytosis	Assessment of complete remission (CR) response	2013 International Working Group—Myeloproliferative Neoplasms Research and Treatment—European Competence Network on Mastocytosis (IWG-MRT-ECNM): **ClinRO**	Adult patients with systemic mastocytosis associated with hematological neoplasm	Rydapt (midostaurin) *April 28, 2017*
Venous thromboembolism (VTE)	DVT/PE related symptomatic events • Asymptomatic proximal Deep Vein Thrombosis (DVT) (detected by ultrasound) • Symptomatic proximal or distal DVT • Non-fatal Pulmonary Embolism (PE), or • VTE-related death	Composite[1] • **Biomarker(s)** • **ClinRO** • **ClinRO** • **ClinRO**	Prophylaxis of venous thromboembolism (VTE) in adult patients	1. Bevyxxa (betrixaban) *June 23, 2017* 2. Savaysa (edoxaban) *January 8, 2015* 3. Xarelto (rivaroxaban) *July 1, 2011*
	DVT/PE related symptomatic events • Recurrent DVT • New non-fatal symptomatic PE • Fatal PE	Composite: **ClinRO**[2]		
	DVT/PE related symptomatic events: • Recurrent DVT • Non-fatal • Fatal PE	Composite: **ClinRO**[3]		

DIVISION OF ONCOLOGY PRODUCTS (DOP1)				
Disease/Condition	**Concept**	**COA Tool & Type**	**COA Context of Use**	**Drug Name & Approval Date**
Prostate cancer (metastatic castration-resistant)	Pain intensity	Brief Pain Inventory Item #3—Short Form: **PRO**	Adult patients with metastatic castration-resistant prostate cancer along with other key oncology endpoints (e.g., overall survival)	Zytiga (abiraterone acetate) *April 28, 2011*

DIVISION OF ONCOLOGY PRODUCTS (DOP2)				
Disease/Condition	**Outcome of Interest**	**COA Tool & Type**	**COA Context of Use**	**Drug Name & Approval Date**
Non-small cell lung cancer (NSCLC)	Overall severity of the following NSCLC symptoms: cough, pain, dyspnea, fatigue, and appetite	Non-Small Cell Lung Cancer Symptom Assessment Questionnaire (NSCLC-SAQ): **PRO**	Adults with stage IIIB or IV NSCLC	Visit "Clinical Outcome Assessment Qualification Program Submissions" Website for additional information
Metastatic non-small cell lung cancer (NSCLC)	Delay in time to development or worsening of shortness of breath	European Organization for Research and Treatment of Cancer, Quality of Life Questionnaire (EORTC QLQ C-30 / LC13): **PRO**	Adults with NSCLC whose tumors are anaplastic lymphoma kinase (ALK)-positive	Zykadia (ceritinib) *May 26, 2017*

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