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Centers for Medicare & Medicaid Services
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200 Independence Avenue SW
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Subject: **Creation of the 2018 Benefit Year HHS-Operated Risk Adjustment Adult Models Draft Prescription Drug (RXCUIs) to HHS Drug Classes (RXCs) Crosswalk**

The 2018 benefit year HHS-operated risk adjustment adult models include twelve drug classes, or RXCs, in addition to age-sex, enrollment duration, and diagnostic categories or hierarchical condition categories (HCCs).[1] This memo describes the criteria used to create the RXCs finalized in the 2018 benefit year Payment Notice final rule, including how CMS determined the inclusion criteria for the underlying drugs.[2] This memo accompanies a draft crosswalk for classifying drugs into RXCs for 2018 benefit year risk adjustment for which the underlying drugs will be updated for 2018 benefit year risk adjustment operations based on more current data. CMS developed the RXCs in contract with RTI International.

Drug Classification for the 2018 Final RXC Drug Classes

In developing the final 2018 benefit year drug classes, we adhered to the principles we described in the 2016 risk adjustment conference white paper on creating and incorporating RXCs into the risk adjustment model.[3,4]

There are several levels of classification to map National Drug Codes (NDCs) up to RXCs. CMS is providing a draft RxNorm concept unique identifiers (RXCUIs) to RXC crosswalk, but in operations, CMS will map NDCs submitted on the EDGE server to final RXCs for risk adjustment risk score calculation. The final 2018 RXCs were created based on drugs listed in CMS's Medicare Part D Formulary Reference File (FRF) as classified by the United States Pharmacopeial Convention (USP) Medicare Model Guidelines (MMGs). The below schematic demonstrates the various summary levels necessary to develop the crosswalk from NDCs to the final RXCs:

NDC → RxNorm → RXCUI → MMG/FRF Alignment File → USP class → Modifications → 2018 final RXC drug classes

1.0 USP Medicare Model Guidelines (MMGs)

To create RXC drug classes, we began with the USP MMGs, which are a set of drug categories and classes developed for use in managing the Medicare Part D benefit. USP is a publicly available and transparent classification, and therefore, we determined that USP would be preferable to the

[1] Final risk adjustment model coefficients for the 2018 benefit year were published on April 18, 2017 and are available at: https://www.cms.gov/CCIIO/Programs-and-Initiatives/Premium-Stabilization-Programs/index.html.
[2] https://www.gpo.gov/fdsys/pkg/FR-2016-12-22/pdf/2016-30433.pdf
[3] https://www.regtap.info/uploads/library/RA_March_31_White_Paper_033116_V1_5CR_032416.pdf
[4] https://www.regtap.info/uploads/library/RA_ConferenceSlides_033116_5CR_040516.pdf

initial proposal to use the American Hospital Formulary Service (AHFS) Pharmacologic-Therapeutic Classification©.[5] The USP classification is periodically updated to reflect changes in therapeutic uses of covered Part D drugs and the additions of new covered Part D drugs. The USP classification system itself is updated every three years.

We created the list of candidate drugs for inclusion in the RXCs based on USP MMGs V6 and V7.[6] All underlying drugs in the two latest USP versions were evaluated because (i) the 2018 HHS risk adjustment models will be used to determine 2018 risk adjustment transfers, so the most recent USP classification at the time of model finalization is best suited for implementation and (ii) the 2018 HHS risk adjustment models are recalibrated using 2013-2015 MarketScan data, so for recalibration, the RXCs should include drugs utilized in 2013-2015. Thus, the combination of V6 and V7 best captured drugs available in 2013-2018 at the time of rulemaking.

2.0 Crosswalk of NDCs to RXCUIs to USP Classes

A crosswalk between the NDCs and the USP classes is a useful starting point for identifying and mapping drugs in EDGE claims data to the HHS risk adjustment RXCs. This not only operationalizes the drugs that will contribute to enrollees' risk scores in the 2018 adult risk adjustment models, but also it assists stakeholders in identifying the specific drugs that will contribute to enrollees' risk score calculations. The NDC is present in the MarketScan claims data used to calibrate the HHS risk adjustment models, and is collected as part of the EDGE server claims data submission.

CMS utilized the RxNorm tool developed by the U.S. National Library of Medicine to aggregate the NDCs to a broader set of RxNorm concept unique identifiers (RXCUIs) which differ by chemical (drug ingredient), strength, and dose form, but not by manufacturer or package size, to aggregate NDCs up to a uniquely identifiable but less granular classification level. Each NDC is associated with only a single RXCUI through this process, though a single RXCUI can consist of many NDCs.[7]

The USP MMG-FRF Alignment File maps the USP MMGs to the CMS Formulary Reference File (FRF), a list of potentially eligible Part D drugs identified by RXCUI published by CMS.[8] Each RXCUI can be assigned to up to three USP classes, without priority (i.e., there is no ranking of assignments into "primary," "secondary," and "tertiary"). Some RXCUIs in the Alignment File are labeled "No USP Class," including certain "combination products," since RXCUIs can include more than one drug ingredient. Although these RXCUIs are assigned a USP category, the RXCs are generally defined in terms of USP classes. Thus, RXCUIs on the Alignment File without a

[5] We have further described our reasoning for using the USP classification in the Notice for Benefit and Payment Parameters for 2018 benefit year, proposed (81 FR 61455) and final (81 FR 94058) rules.

[6] The latest USP classification system update, version 7, was released in February 2017 and the previous version, version 6, was released in February 2014.

[7] For our calibration of the 2018 HHS risk adjustment adult models on 2013-2015 MarketScan data, we used the January 4, 2016 version of RxNorm.

[8] "RXCUIs are generally included on the FRF if, based on information available at that time, at least one NDC associated to that RXCUI may satisfy the definition of a Part D drug." *Formulary Reference File Frequently Asked Questions*, April 8, 2014, available at: https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/RxContracting_FormularyGuidance.html

USP class required separate attention in order to determine whether they should be assigned to an RXC.

3.0 Modification of USP Classes to Obtain RXCs

CMS translated the preliminary RXC categories, based on the originally used AHFS classification, to the USP MMG classification. An RXC may be broader or narrower in scope than the corresponding preliminary AHFS RXC, and the specific drugs included in each could also differ.

The preliminary, single RXC for Insulins and Anti-Diabetics was split into two RXCs for the final 2018 adult risk adjustment models: RXC 6 Insulin and RXC 7 Anti-Diabetic Agents Except Insulin and Metformin Only. Insulin was separated from other anti-diabetic drugs because insulin is typically used in more advanced (and often more expensive) cases of diabetes. For this reason, a hierarchy was established such that enrollees with RXC 6 Insulin are excluded from also having RXC 7 Anti-Diabetic Agents Except Insulin and Metformin Only, resulting in enrollees prescribed both insulin and other anti-diabetic agents receiving only RXC 6 in risk score calculation. Metformin was excluded from RXC 7, as metformin is often prescribed prophylactically and does not necessarily identify individuals with diabetes.

3.1 Association of RXCs with HCCs

The major purposes for including prescription drugs in the adult risk adjustment models were to impute missing diagnoses and/or to determine the level of severity associated with a particular condition, and therefore, HCCs (diagnosis code categories) were associated with the final HHS RXCs. The twelve 2018 benefit year RXCs and their associated USP classes and HCCs are listed in Table 1. The RXCs are often primarily associated with one of the HCCs, for example, the RXC Anti-Hepatitis C Agents with HCC 37-1 Chronic Viral Hepatitis C. Due to the hierarchical nature of the HCCs, we also associate HCCs hierarchically above the HCC primarily associated with the drug category. That is, because HCC 36 Cirrhosis of Liver takes precedence over HCC 37-1 Chronic Viral Hepatitis C in the HCC diagnostic liver hierarchy, an enrollee could have cirrhosis of the liver caused by chronic hepatitis C, but only have HCC 36 Cirrhosis of the Liver. By associating the RXC with all HCCs above HCC 37-1 in the liver hierarchy, we are able to identify enrollees who are prescribed hepatitis C antivirals and have cirrhosis of the liver caused by chronic hepatitis C. Empirically, this means that HCC 37-1 and all liver hierarchy HCCs above HCC 37-1 are included in the interaction of the HCC diagnostic categories associated with the RXC Anti-Hepatitis C Agents in the HHS risk adjustment adult models recalibration.

3.2 Modifications of USP Classes for RXCs

Starting with the RXCUIs included in the USP classes associated with the RXCs, CMS conducted a clinical and empirical review to determine the final set of RXCUIs to include in each RXC. Since an RXCUI can be mapped to as many as 3 USP classes, with no priority attached to any one among multiple classes as noted above, we associated an RXCUI with an RXC if the RXCUI was mapped to a USP class associated with an RXC in any of the 3 positions. Although RXCUIs can be mapped to multiple USP classes, no RXCUI is mapped to more than one final 2018 HHS RXC. RXCUIs were included or excluded from the RXCs, as described below. The reasons for exclusion discussed below were not independent; multiple sources of information were often used to make a determination for a specific RXCUI. RXC development was an iterative process that included exploratory data analysis as well as recurring consultations with a panel of clinicians.

Reasons for Exclusion of RXCUIs from RXCs:

1) Clinical research and expert clinician input determined that the RXCUI was not specifically linked with the HCC(s) associated with the RXC or was commonly indicated for conditions other than the associated HCC(s).

For example, a major use of some drugs in the USP class Immune Suppressants is prevention of rejection in organ transplant recipients. Since we did not associate the organ transplant HCCs with RXC 9, we excluded these drugs from RXC 9. Clinical research included examining the indications in the official FDA-approved label for drugs, as well as other research on the conditions drugs are used for (on or off label). In addition, a group of clinical consultants comprised of two physicians, who have experience in health services research, and a pharmacist examined and approved or rejected each exclusion of RXCUIs from RXCs.

2) Empirical/statistical analysis of the 2014 MarketScan data revealed a weak association of the RXCUI with the HCC(s) associated with an RXC.

CMS assessed each RXCUI in each selected USP class empirically based on its "positive predictive value" (PPV).[9] The PPV is a conditional proportion of patients who are diagnosed with an HCC of patients that are prescribed a drug in a certain RXCUI. A PPV of 100% means that all enrollees taking a drug within a RXCUI had the associated HCC, and a PPV of 0% means that none of the enrollees taking a drug within a RXCUI had the associated HCC.

3) In some instances, USP classes contained a mix of newer, more expensive drug treatments, and older, often generic, lower-cost drug treatments. In some classes, the lower-cost treatments, which are less likely to be the focus of risk-selection behavior by health plans, were excluded from the RXC.

For example, the combined USP classes Immune Suppressants and Immunomodulators encompass a wide range of drugs. They include expensive biologics costing several thousands of dollars each month and drugs like generic methotrexate, a month's supply of which can cost less than one hundred dollars. Clinician review determined that many of the drugs in this class are substitutable and the general prescribing process would be to first prescribe a cheaper drug, and if the patient does not respond to that then move to a more expensive biologic. However, because concern over patient access and health plan selection behavior (reflected in formulary design) centers around the expensive biologics, the cheaper non-biologics were removed from RXC 9.

4) Some drugs are primarily used for prophylaxis—not treatment—and may not reliably indicate the presence of the related condition (HCC). These were excluded from the RXCs.

For example, the USP class Anti-HIV Agents includes the brand name drug Truvada, which is used prophylactically to avoid infection with HIV and many who take Truvada do not have HIV.

[9] The "PPV" we calculate is not a true PPV because we lack a "gold standard" for the presence of the diagnosis, such as a medical record (the HCCs are based on diagnoses recorded on claims). Nevertheless, the conditional probability we calculate is analogous to the PPV and provides useful information in our context.

Because Truvada does not reliably indicate an actual HIV/AIDS diagnosis, it was removed from RXC 1. Similarly, as discussed above, metformin can be prescribed for pre-diabetes, so an enrollee with a prescription for only metformin may not have diabetes. Therefore, a prescription for metformin was excluded from RXC 7, as it would not reliably indicate an actual diabetes diagnosis.

5) Manufacturer-discontinued drugs.

CMS did not undertake a systematic review to exclude discontinued drugs from the RXCs. But, in its review of (direct acting) anti-hepatitis C drugs, CMS found that the RXCUIs for the brand name drugs Victrelis (boceprevir) and Incivek (telaprevir) were still included in USP MMGs V7. These drugs were discontinued in the U.S. by the manufacturer (Vertex Pharmaceuticals) in 2015 and 2014, respectively. CMS removed these two RXCUIs from RXC 2. These two drugs are older anti-hepatitis C drugs that have been supplanted in clinical practice by newer drugs such as Sovaldi and Harvoni.

6) RXCUIs not classified by USP.

As noted above, USP does not assign a USP class to all RXCUIs included in the MMG/FRF Alignment File. These unassigned drugs appear to largely or entirely consist of certain "combination products" (pharmaceuticals combining several drug ingredients), Part B drugs, and older RXCUIs.[10] CMS analyzed these "unclassified" RXCUIs using our PPV empirical method described above and our clinical review. If an RXCUI met clinical and empirical criteria, CMS included it in an RXC. All of the unassigned RXCUIs included in the MMG/FRF Alignment File that met the evaluation criteria and were added to RXCs are combination products.

The final results of the RXC drug selection process are summarized in Table 2. For each RXC included in the model, we show the number of RXCUIs that constitute the RXC and counts showing the relationship between the RXCs and the USP classes they are based on. For example, column 1 indicates that 104 RXCUIs are included in RXC 1, Anti-HIV Agents. Column 2 shows that this RXC began with the 112 RXCUIs in the five USP classes that contain Anti-HIV agents (see Table 1). Of those 112 RXCUIs, nine were excluded from the RXC for the reasons described above. One combination drug, unassigned to a USP class, was added to the RXC based on our clinical and empirical evaluation criteria. The number of RXCUIs in this RXC is thus equal to $112 - 9 + 1 = 104$.

Only two of the RXCs exactly replicate the USP classes they are based on: RXC 4 (Phosphate Binders) and RXC 10 (Cystic Fibrosis Agents). All the other RXCs were altered from the preliminary USP classes by adding and/or removing some drugs.

4.0 Constraints on RXC Coefficients to Limit Incentives for Inappropriate Prescribing

CMS remains cognizant of the incentives for health plans to encourage inappropriate prescribing of drugs if a course of treatment (prescriptions) for an inexpensive drug can trigger a large increase in an enrollee's risk score. This can occur when an inexpensive drug treats a medically expensive

[10] USP assigns a USP category to all of the RXCUIs on the Alignment File. But in many cases, a USP category is not sufficient to assign an RXCUI to an RXC; a USP class is necessary to do that.

condition. To examine incentives, CMS tabulated the average annual per capita cost of each RXC among enrollees in the 2014 MarketScan adult calibration sample.

Based on the average annual per capita cost of each RXC, CMS decided to impose *a priori* constraints on the coefficients of certain RXCs in the calibration of the 2018 benefit year risk adjustment adult models. To understand the constraints, it is important to remember that for RXCs 1 through 10, the HHS adult model includes terms for the RXC only and for the RXC interacted with its associated HCC(s). For RXCs 11 and 12 (the "severity only" RXCs), the HHS adult model includes only a term for the RXC interacted with its associated HCC(s).

CMS imposed the following constraints in calibrating the 2018 benefit year HHS-operated risk adjustment adult models:

1. For
   - RXC 3 Antiarrhythmics
   - RXC 4 Phosphate Binders

i) the coefficients of their RXC terms were constrained to be equal to the average annual (per capita) cost of the RXC in each of the three MarketScan calibration years (2013, 2014, 2015);
ii) the coefficients of their interaction term (RXC*HCC) with their associated HCC(s) were constrained to be zero for each of the three calibration years.

2. For
   - RXC 11 Ammonia Detoxicants
   - RXC 12 Diuretics, Loop and Select Potassium-Sparing

i) the coefficients of their interaction term (RXC*HCC) with their associated HCC(s) were constrained to be equal to the average annual (per capita) cost of the RXC in each of the three MarketScan calibration years (2013, 2014, 2015).

The effect of the constraints on the RXC 3 and RXC 4 terms is as follows. An enrollee can have either the RXC only, the associated HCC(s) only, or both. If the enrollee has RXC 3 or RXC 4 only, the increment to predicted expenditures (and hence to the risk score) is constrained equal to the average annual cost of the drugs in the RXC. If the enrollee also has the associated HCC(s), the increment to predicted expenditures is the coefficient of the RXC plus the coefficient of the HCC plus the coefficient of the RXC*HCC interaction. The constraints on the RXC 3 and 4 coefficients constrain this sum to equal the average annual cost of the RXC (the constrained RXC coefficient) plus the coefficient of the HCC, since the coefficient of the RXC*HCC interaction is constrained to equal zero. The increment to the risk score or predicted expenditures from an RXC always equals the average annual cost of the RXC, whether the associated HCC(s) are present or not. This limits the incentive for inappropriate prescribing, because the gain in predicted expenditures (the risk score) from prescribing is always offset by the cost of prescribing the RXC.[11]

The constraints on the RXC 11 and RXC 12 RXC*HCC interaction coefficients limit the increment to predicted expenditures (i.e., the risk score) from prescribing a drug in RXC 11 or in RXC 12 to the average annual cost of RXC 11 or RXC 12. This should reduce the incentives for inappropriate

[11] This is true on average for the drugs in the RXC; it may not be true for any particular drug in the RXC.

prescribing of drugs in RXC 11 or RXC 12 because the gain in predicted expenditures/risk score is offset by the cost of prescribing the drug.

No other *a priori* constraints were imposed on any of the RXC coefficients. Note, however, that additional constraints on the RXC coefficients can be imposed during the model calibration process on empirical grounds. For example, this could occur if the preliminary model estimates would result in a lower enrollee risk score when both a diagnosis (HCC) and related drug utilization (RXC) are reported than if the diagnosis alone or the drug utilization alone is reported. The purpose of any constraints imposed in this case would be to ensure that health plans are incentivized to report both the diagnosis and the associated drug utilization.

5.0 Updating the RXC Crosswalk

CMS has defined the 2018 benefit year RXCs using crosswalks available as of spring 2017. The accompanying RXCUI to RXC crosswalk serves as a draft crosswalk as of the most recent data included in the final 2018 risk adjustment adult models. The USP MMGs and corresponding MMG/FRF Alignment File were recently updated in February 2017 and are not scheduled to be revised again until 2020. Updated NDCs and RXCUIs are available on a monthly basis from RxNorm, but new RXCUIs need to be mapped to USP classes and then to the HHS RXCs. Therefore, CMS will provide a final NDC to RXC crosswalk for calculation of the 2018 benefit year risk scores. Because the 2018 benefit year HCCs, including the RXCs, will be implemented in the 2018 calendar year, new drugs will be introduced—and existing drugs will be discontinued—between now and the end of 2018.

USP is also developing a new drug classification ("USP Drug Classification" or "USP DC") extending to all outpatient drugs commonly available in the U.S. market, as the current classification focuses on Medicare Part D drugs. The initial version of the USP DC is expected in January 2018. The USP DC will also be mapped annually to RxNorm (RXCUIs). The USP DC could potentially be used in updating the NDC to RXC crosswalk, in early 2018 and, depending on operational feasibility, again in early 2019. CMS's initial review of the preliminary USP DC classification, which has since been removed from USP's website while it is being revised in response to public comments, showed very few differences from the V7 USP MMGs.

CMS notes that more recent MarketScan and enrollee-level EDGE data will also become available every calendar year and these data will contain new drug utilization patterns and indications. CMS intends to analyze PPVs by RXCUI every year when the next year of data become available. These empirical results could be combined with clinical input to classify new drugs into the RXCs, or to remove drugs based on more recent data.

Table 1: USP Classes and HCCs Associated with 2018 Benefit Year HHS RXCs

V6 and V7 USP Classes Associated with the RXC	RXCs	RxC Label	Associated HCCs	HCC Label
Anti-HIV Agents, Non-nucleoside Reverse Transcriptase Inhibitors (NNRTI)	RXC 1	Anti-HIV Agents	HCC 1	HIV/AIDS
Anti-HIV Agents, Integrase Inhibitors (INSTI)	RXC 1	Anti-HIV Agents	HCC 1	HIV/AIDS
Anti-HIV Agents, Nucleoside and Nucleotide Reverse Transcriptase Inhibitors (NRTI)	RXC 1	Anti-HIV Agents	HCC 1	HIV/AIDS
Anti-HIV Agents, Protease Inhibitors	RXC 1	Anti-HIV Agents	HCC 1	HIV/AIDS
Anti-HIV Agents, Other	RXC 1	Anti-HIV Agents	HCC 1	HIV/AIDS
Anti-hepatitis C (HCV) Agents, Direct Acting*	RXC 2	Anti-Hepatitis C (HCV) Agents	HCC 34	Liver Transplant Status/Complications
			HCC 35	End-Stage Liver Disease
			HCC 36	Cirrhosis of Liver
			HCC 37.1	Chronic Viral Hepatitis C
Anti-hepatitis C (HCV) Agents, Other*	RXC 2	Anti-Hepatitis C (HCV) Agents	HCC 34	Liver Transplant Status/Complications
			HCC 35	End-Stage Liver Disease
			HCC 36	Cirrhosis of Liver
			HCC 37.1	Chronic Viral Hepatitis C
Antiarrhythmics	RXC 3	Antiarrhythmics	HCC 142	Specified Heart Arrhythmias
Phosphate Binders	RXC 4	Phosphate Binders	HCC 183	Kidney Transplant Status
			HCC 184	End Stage Renal Disease
			HCC 187	Chronic Kidney Disease, Stage 5
			HCC 188	Chronic Kidney Disease, Severe (Stage 4)
Glucocorticoids**	RXC 5	Inflammatory Bowel Disease Agents	HCC 41	Intestine Transplant Status/Complications
			HCC 48	Inflammatory Bowel Disease

V6 and V7 USP Classes Associated with the RXC	RXCs	RxC Label	Associated HCCs	HCC Label
Sulfonamides**	RXC 5	Inflammatory Bowel Disease Agents	HCC 41	Intestine Transplant Status/Complications
			HCC 48	Inflammatory Bowel Disease
Aminosalicylates**	RXC 5	Inflammatory Bowel Disease Agents	HCC 41	Intestine Transplant Status/Complications
			HCC 48	Inflammatory Bowel Disease
Insulins	RXC 6	Insulin	HCC 18	Pancreas Transplant Status/Complications
			HCCs 19-21	Diabetes
Antidiabetic Agents	RXC 7	Anti-Diabetic Agents, Except Insulin and Metformin Only	HCC 18	Pancreas Transplant Status/Complications
			HCCs 19-21	Diabetes
Glycemic Agents	RXC 7	Anti-Diabetic Agents, Except Insulin and Metformin Only	HCC 18	Pancreas Transplant Status/Complications
			HCCs 19-21	Diabetes
Multiple Sclerosis Agents	RXC 8	Multiple Sclerosis Agents	HCC 118	Multiple Sclerosis
Immune Suppressants	RXC 9	Immune Suppressants and Immunomodulators	HCC 56	Rheumatoid Arthritis and Specified Autoimmune Disorders
			HCC 57	Systemic Lupus Erythematosus and Other Autoimmune Disorders
			HCC 41	Intestine Transplant Status/Complications
			HCC 48	Inflammatory Bowel Disease
Immunomodulators	RXC 9	Immune Suppressants and Immunomodulators	HCC 56	Rheumatoid Arthritis and Specified Autoimmune Disorders
			HCC 57	Systemic Lupus Erythematosus and Other Autoimmune Disorders
			HCC 41	Intestine Transplant Status/Complications
			HCC 48	Inflammatory Bowel Disease

V6 and V7 USP Classes Associated with the RXC	RXCs	RxC Label	Associated HCCs	HCC Label
Cystic Fibrosis Agents	RXC 10	Cystic Fibrosis Agents	HCC 158	Lung Transplant Status/Complications
			HCC 159	Cystic Fibrosis
Laxatives	RXC 11	Ammonia Detoxicants	HCC 34	Liver Transplant Status/Complications
			HCC 35	End-Stage Liver Disease
			HCC 36	Cirrhosis of Liver
Diuretics, Loop	RXC 12	Diuretics, Loop and Select Potassium-Sparing	HCC 128	Heart Assistive Device/Artificial Heart
			HCC 129	Heart Transplant
			HCC 130	Congestive Heart Failure
Diuretics, Potassium-sparing	RXC 12	Diuretics, Loop and Select Potassium-Sparing	HCC 128	Heart Assistive Device/Artificial Heart
			HCC 129	Heart Transplant
			HCC 130	Congestive Heart Failure
No USP Class***	Various RXCs 1-12		As indicated above.	

*V6 USP has a single anti-hepatitis C agents class, which is split into direct acting versus other agents in V7. Originally CMS considered drugs (RXCUIs) in the single V6 class for RXC 2. But the final RXC 2 includes only drugs in the "direct acting" USP class.

**USP classes included in the USP Category "Inflammatory Bowel Disease Agents".

***USP does not place some combination products and other drugs (RXCUIs) in a USP class in the MMG/FRF Alignment File. CMS placed some of these drugs in RXCs based on empirical association with HCCs (calculated "positive predictive values" or "PPVs") and clinical research and expert opinion.

Source: 2017 USP Medicare Model Guidelines V7.0, 2014 USP Medicare Model Guidelines V6.0

USP: United States Pharmacopeial Convention. RxNorm: U.S. National Library of Medicine.

Table 2. Relationship of Number of Drugs (RXCUIs) in the 2018 Benefit Year HHS RXCs to Number of Drugs in the Associated USP MMGs

		(1) =	(2)	- (3)	+ (4)
RXC	**RXC Label**	**Total # of RXCUIs in the RXC**	**Total # of RXCUIs in the USP Classes Associated w/ RXC**	**Total # of RXCUIs from associated USP classes excluded from the RXC**	**# of RXCUIs added to the RXC**
Total		**465**	**680**	**226**	**11**
RXC 1	Anti-HIV Agents	104	112	9	1
RXC 2	Anti-Hepatitis C (HCV) Agents	11	13	2	0
RXC 3	Antiarrhythmics	61	62	1	0
RXC 4	Phosphate Binders	15	15	0	0
RXC 5	Inflammatory Bowel Disease Agents	21	110	89	0
RXC 6	Insulin	36	34	0	2
RXC 7	Anti-Diabetic Agents, Except Insulin and Metformin Only	104	117	21	8
RXC 8	Multiple Sclerosis Agents	18	20	2	0
RXC 9	Immune Suppressants and Immunomodulators	39	136	97	0
RXC 10	Cystic Fibrosis Agents	13	13	0	0
RXC 11	Ammonia Detoxicants	8	9	1	0
RXC 12	Diuretics, Loop and Select Potassium-Sparing	35	39	4	0

Notes:

The RXCUIs added to RXCs include RXCUIs with the USP Class designation "No USP Class (Combination Product)."