

## CYTOKINE AND CAM ANTAGONIST UTILIZATION IN MISSISSIPPI MEDICAID

CARRIED OVER FROM JULY 2017 DUR BOARD MEETING WITH UPDATES

### BACKGROUND

Cytokine and cell-adhesion molecule (CAM) antagonists have a major role in the treatment of chronic inflammatory diseases such as rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, plaque psoriasis and inflammatory bowel disease. Utilization of this class of medications continues to increase. Pharmacy payers across the United States are tasked with the responsibility of ensuring these medications are appropriately prescribed.

Mississippi Division of Medicaid's (DOM) current Universal Preferred Drug List (UPDL) for this class of medications is shown below. Presently, Cosentyx®, Enbrel®, Humira® and generic methotrexate are preferred products.

#### DOM Universal Preferred Drug List – Effective 7-1-2017

CYTOKINE & CAM ANTAGONISTS			
COSENTYX (secukinumab) <sup>SmartPA</sup> ENBREL (etanercept) HUMIRA (adalimumab) methotrexate	ACTEMRA (tocilizumab) CIMZIA (certolizumab) ENTYVIO (vedolizumab) ILARIS (canakinumab) INFLECTRA (infliximab) KINERET (anakinra) ORENCIA (abatcept) OTEZLA (apremilast) OTREXUP (methotrexate) RASUVO (methotrexate) REMICADE (infliximab) RHEUMATREX (methotrexate) SILIQ (brodalumab) <sup>NR</sup> SIMPONI (golimumab) STELARA (ustekinumab) TALTZ (ixekizumab) TREXALL (methotrexate) XELJANZ (tofacitinib) XELJANZ XR (tofacitinib)	Orencia IV Infusion, Remicade IV Infusion and Stelara (first dose) are for administration in hospital or clinic setting. PA will not be issued at Point of Sale without justification.	<p style="color: red;"><b>Cosentyx</b></p> <ul style="list-style-type: none"> <li>• &gt; 18 years = Minimum Age</li> <li>• Documented diagnosis of plaque psoriasis, psoriatic arthritis or ankylosing spondylitis in the past 2 years <b>AND</b></li> <li>• 90 consecutive days of Humira in the past year</li> </ul>

MS-DUR reviewed prior authorization (PA) criteria for cytokine and CAM antagonists across Medicaid programs and health plans in several states. Many of these programs require a prior authorization process for these medications. All PA forms examined included requirements for approved diagnoses according to the FDA labeling and for other conditions, required prior failure with other products (step-therapy). Step therapy examples included the following: 1) for Crohn's and ulcerative colitis- failure on corticosteroids, aminosalicylates, or immunomodulators; 2) for rheumatoid arthritis- failure on methotrexate and/or disease-modifying antirheumatic drugs (DMARDs).

Due to increasing utilization for this category, MS-DUR examined cytokine and CAM antagonist utilization to determine if additional criteria might be needed to appropriately manage this class of medications.

## METHODS

A retrospective analysis was conducted using Mississippi Medicaid medical and pharmacy claims for the period January 2016 – May 2017. The analysis included data from the fee-for-service (FFS) program and the coordinated care organizations (CCOs). Pharmacy and office-administered medical claims for all drugs listed in the Cytokine & CAM Antagonists class in the UPDL were extracted. Utilization and program payments were examined monthly. Since there is not a current diagnosis check, beneficiaries with paid claims for Enbrel® and Humira® were evaluated for the presence of an approved diagnosis in the medical claims during the time period examined.

## RESULTS

### *Type of Claims*

Table 1 provides the number of claims from this class with the majority accounted for in the pharmacy point-of-sale (POS) system. Remicade® was almost exclusively office-administered. Simponi®, Orenzia® and methotrexate had both medical and pharmacy claims. Enbrel® and Humira® are almost always paid through the POS system and can be easily managed through an electronic or manual PA.

TABLE 1: Number of Claims by Type and Drug (January 2016 - May 2017)						
Drug	FFS		UHC		MAG	
	Type of Claim		Type of Claim		Type of Claim	
	Medical	Pharmacy	Medical	Pharmacy	Medical	Pharmacy
TOTAL for class	263	2,441	124	3,668	523	4,725
Actemra (tocilizumab)	9	3	22	26	50	4
Cimzia (certolizumab)	0	6	0	15	16	30
Cosentyx (secukinumab)	0	5	0	22	0	79
Enbrel (etanercept)	0	308	0	494	0	682
Entyvio (cwsoliumV)	3	2	8	0	13	0
Humira (adalimumab)	1	504	0	1,086	0	1,081
Ilaris (canakinumab)	0	7	0	6	0	0
Kineret (anakinra)	0	19	0	4	0	4
Orenzia (abatacept)	23	28	17	18	24	34
Otezla (apremilast)	0	35	0	59	0	75
Otrexup/Rrasuvo/Trexall/ Rheumatrex (methotrexate)	0	2	0	26	0	15
Remicade (infliximab)	90	0	53	3	245	0
Simponi (golimumab)	20	12	0	21	4	23
Stelara (ustekinumab)	5	3	0	4	3	23
Taltz (ixekizumab)	0	0	0	1	0	8
Xeljanz/Xeljanz XR (tofacitinib)	0	50	0	97	0	70
methotrexate	112	1,457	24	1,796	169	2,597

## Utilization and Payment Trends

Table 2 shows the total number of claims for each drug in this class by month. From January 2016 to May 2017 there has been a 37% increase in total claims for this class. This has been primarily driven by a 54% increase in claims for Humira® and a 43% increase in claims for Enbrel®.

TABLE 2: Number of Prescriptions and Office-Administered Claims by Drug and Month																	
<i>(Includes FFS and CCOs)</i>																	
Drug	Month Filled / Administered																
	Jan-16	Feb-16	Mar-16	Apr-16	May-16	Jun-16	Jul-16	Aug-16	Sep-16	Oct-16	Nov-16	Dec-16	Jan-17	Feb-17	Mar-17	Apr-17	May-17
TOTAL for class	571	633	644	589	649	682	668	735	702	769	697	699	728	702	791	742	742
methotrexate	315	362	357	324	370	384	371	388	359	404	360	339	365	354	382	361	360
Humira (adalimumab)	123	136	137	129	141	143	136	158	156	183	157	176	176	172	193	173	183
Enbrel (etanercept)	72	65	81	82	75	78	85	94	94	93	93	82	89	81	117	98	105
Remicade (infliximab)	19	24	26	17	15	24	17	23	26	25	22	24	30	27	25	27	20
Orencia (abatacept)	8	8	7	5	2	7	7	12	6	4	6	11	8	7	9	14	13
Xeljanz/Xeljanz XR (tofacitinib)	11	6	10	8	13	11	15	15	14	16	15	17	9	15	16	15	11
Otezla (apremilast)	3	7	6	6	10	8	9	11	15	13	14	12	11	10	10	12	12
Cosentyx (secukinumab)	2	2	2	5	8	8	10	9	8	5	7	4	5	5	6	11	9
Stelara (ustekinumab)	0	2	0	0	1	2	2	1	3	2	1	5	2	4	5	2	6
Simponi (golimumab)	6	7	4	4	6	4	2	4	4	4	5	5	4	6	4	4	7
Actemra (tocilizumab)	4	5	8	3	1	5	4	9	5	10	7	12	10	9	9	10	6
Cimzia (certolizumab)	4	6	3	4	2	3	4	5	6	3	3	4	4	4	3	2	3
Otrexup/Rrasuvo/Trexall/Rheumatrex (methotrexate)	0	0	0	0	1	2	2	4	2	5	3	4	5	3	4	5	3
Kineret (anakinra)	2	2	1	1	2	2	2	1	1	1	2	1	2	1	1	3	2
Entyvio (vedolizumab)	0	0	0	1	0	0	0	0	2	0	2	2	5	3	6	4	1
Taltz (ixekizumab)	0	0	0	0	0	0	0	1	1	1	0	1	2	0	1	1	1
Ilaris (canakinumab)	2	1	2	0	2	1	2	0	0	0	0	0	1	1	0	0	0

Table 3 provides details regarding the total monthly payment for each drug in this class. From January 2016 to May 2017 there has been a 97% increase in the total amount paid for drugs in this class. Increased utilization shown in Table 2 accounts for some of the increase. However, increases in the average cost per prescription and the introduction of newer more costly medications have been responsible for most of the increase in the total paid. The cost per prescription for Humira® increased 16.6% from \$4,743 to \$5,528 and Enbrel had a 16.1% increase from \$3,885 to \$4,512 per prescription. Although Stelara® is currently used by only a few beneficiaries, at an average prescription cost of \$15,000 to \$18,000, its use has contributed significantly to the total amount paid in this category.

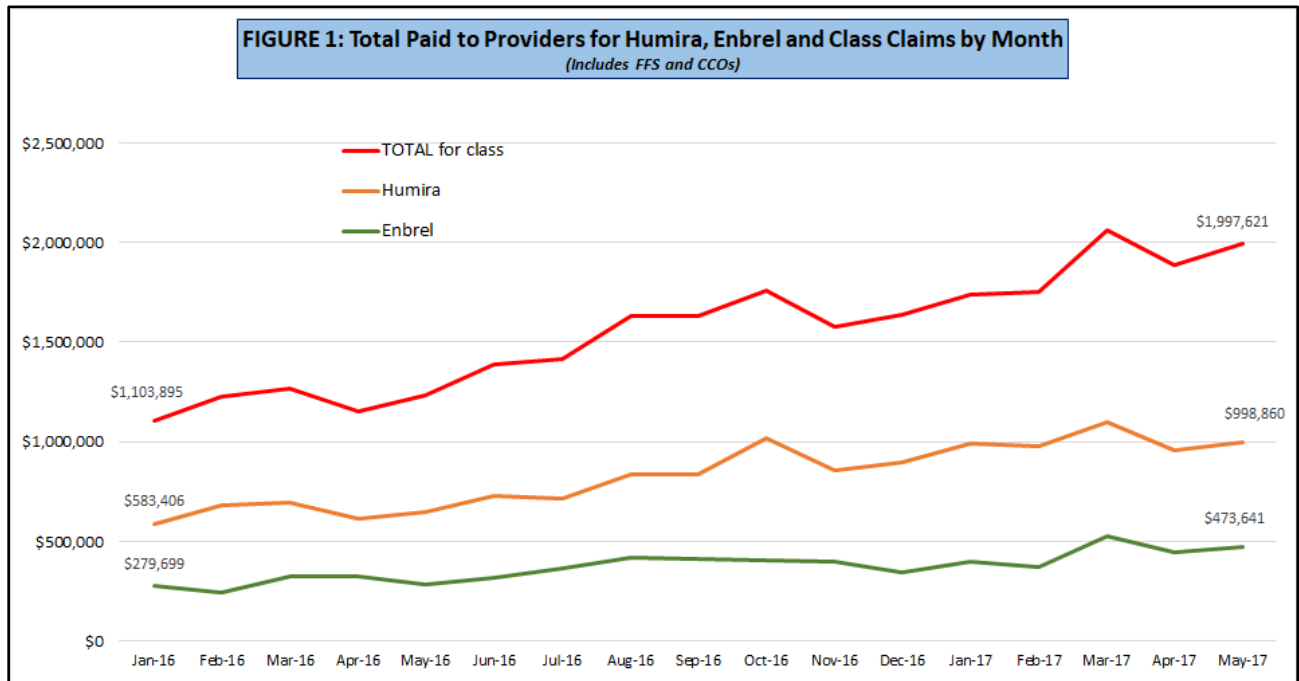
**TABLE 3: Total Paid to Providers for Prescriptions and Office-Administered Claims by Drug and Month**

*(Includes FFS and CCOs)*

Drug	Month Filled / Administered																
	Jan-16	Feb-16	Mar-16	Apr-16	May-16	Jun-16	Jul-16	Aug-16	Sep-16	Oct-16	Nov-16	Dec-16	Jan-17	Feb-17	Mar-17	Apr-17	May-17
TOTAL for class	\$1,103,895	\$1,225,921	\$1,270,043	\$1,154,342	\$1,231,575	\$1,386,378	\$1,417,200	\$1,631,434	\$1,633,154	\$1,758,197	\$1,574,970	\$1,636,473	\$1,738,241	\$1,749,602	\$2,064,574	\$1,890,590	\$1,997,621
methotrexate	\$9,926	\$11,059	\$11,465	\$10,578	\$13,562	\$13,624	\$11,646	\$12,284	\$11,028	\$11,998	\$10,399	\$9,773	\$10,716	\$10,391	\$11,205	\$10,203	\$10,367
Humira (adalimumab)	\$583,406	\$680,532	\$693,888	\$612,169	\$649,784	\$725,964	\$713,295	\$839,060	\$834,714	\$1,020,817	\$855,316	\$899,491	\$990,264	\$980,189	\$1,099,057	\$956,773	\$998,860
Enbrel (etanercept)	\$279,699	\$244,931	\$322,765	\$324,299	\$285,225	\$316,942	\$366,097	\$417,458	\$411,134	\$404,676	\$398,082	\$346,133	\$401,116	\$370,515	\$527,315	\$446,367	\$473,641
Remicade (infliximab)	\$68,903	\$92,466	\$89,509	\$59,559	\$54,931	\$78,179	\$64,855	\$85,231	\$109,045	\$92,689	\$100,149	\$91,291	\$109,167	\$101,771	\$106,977	\$174,583	\$149,280
Orencia (abatacept)	\$27,515	\$27,513	\$22,466	\$17,349	\$3,356	\$19,632	\$21,252	\$41,436	\$22,308	\$13,039	\$20,959	\$36,156	\$27,408	\$24,781	\$31,778	\$43,922	\$49,437
Xeljanz/Xeljanz XR (tofacitinib)	\$33,636	\$20,085	\$33,476	\$26,781	\$43,519	\$40,299	\$54,953	\$54,953	\$51,289	\$58,616	\$54,953	\$62,280	\$36,083	\$60,139	\$64,148	\$60,139	\$44,102
Otezla (apremilast)	\$7,600	\$17,732	\$15,199	\$15,597	\$27,320	\$21,856	\$24,588	\$30,051	\$40,979	\$35,515	\$38,247	\$32,783	\$30,811	\$29,218	\$29,218	\$37,091	\$37,497
Cosentyx (secukinumab)	\$7,723	\$8,256	\$8,256	\$45,403	\$70,168	\$61,914	\$54,487	\$51,514	\$34,345	\$34,342	\$30,052	\$17,172	\$21,465	\$38,634	\$31,081	\$49,375	\$53,922
Stelara (ustekinumab)	\$0	\$26,699	\$0	\$0	\$9,336	\$25,657	\$28,008	\$15,241	\$43,248	\$16,572	\$9,336	\$71,256	\$10,616	\$63,395	\$77,275	\$30,220	\$105,900
Simponi (golimumab)	\$22,695	\$29,539	\$12,513	\$16,166	\$24,968	\$16,917	\$8,051	\$25,312	\$19,088	\$17,743	\$19,137	\$21,661	\$19,383	\$18,339	\$20,118	\$15,582	\$30,508
Actemra (tocilizumab)	\$7,170	\$4,301	\$11,946	\$3,611	\$119	\$12,301	\$12,442	\$22,815	\$12,237	\$26,154	\$13,463	\$18,582	\$15,250	\$16,390	\$13,380	\$14,811	\$9,695
Cimzia (certolizumab)	\$13,813	\$21,197	\$10,598	\$14,131	\$7,066	\$10,598	\$14,831	\$16,771	\$20,479	\$10,239	\$10,239	\$13,947	\$14,613	\$14,613	\$10,726	\$6,823	\$10,710
Otrexup/Rrasuvo/Trexall/Rheumatrex (methotrexate)	\$0	\$0	\$0	\$0	\$412	\$886	\$886	\$2,456	\$1,035	\$3,079	\$1,982	\$2,132	\$2,992	\$1,721	\$2,447	\$3,188	\$1,500
Kineret (anakinra)	\$7,699	\$7,699	\$3,849	\$3,849	\$7,699	\$7,699	\$7,699	\$3,849	\$3,849	\$3,849	\$7,699	\$3,849	\$7,814	\$3,907	\$3,907	\$15,625	\$11,717
Entyvio (vedolizumab)	\$0	\$0	\$0	\$4,851	\$0	\$0	\$0	\$0	\$9,707	\$0	\$4,957	\$5,246	\$26,184	\$15,402	\$31,224	\$21,171	\$5,439
Taltz (ixekizumab)	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$13,001	\$8,668	\$8,668	\$0	\$4,720	\$14,160	\$0	\$4,720	\$4,720	\$5,046
Ilaris (canakinumab)	\$34,112	\$33,912	\$34,112	\$0	\$34,112	\$33,912	\$34,112	\$0	\$0	\$200	\$0	\$0	\$200	\$200	\$0	\$0	\$0

NOTE: Total paid are reimbursement amounts paid to providers and are not representative of final Medicaid costs after rebates.

Figure 1 provides a graphical presentation of the increases in the total amount paid for this category of drugs from Jan 2016 through May 2017.



**Presence of Diagnoses to Support Use of Enbrel® and Humira®**

Table 4 summarizes the various FDA approved indications for Enbrel® and Humira®. Medical claims for beneficiaries taking these two products were examined to determine whether diagnoses were present that supported use for an approved indication. Of note, medical diagnoses searches can only be reviewed for the previous two years within the current electronic PA system. Consequently, only diagnoses that appeared in the last two years and occurred during the observation period were examined for the utilization of these products.

Indication	Enbrel	Humira
Rheumatoid arthritis	X	X
Juvenile idiopathic arthritis	X	X
Psoriatic arthritis	X	X
Plaque psoriasis	X	X
Alkylosing spondylitis	X	X
Adult Crohn's disease		X
Pediatric Crohn's disease		X
Ulcerative colitis		X
Hidradenitis suppurativa		X
Uveitis		X

**(Updated)** As shown in Table 5, both Humira® and Enbrel® claims were broken down by the number of vials and diagnosis associated with each claim. A typical Humira maintenance dose should be 2 vials which corresponds to the majority of its use. With Humira®, loading doses of 4 or 6 vials is standard in the initiation of therapy in Crohn’s disease, plaque psoriasis, hidradenitis suppurativa, ulcerative colitis, and uveitis. Maintenance doses can go up to 4 vials monthly in

rheumatoid arthritis and hidradenitis suppurativa and up to 8 vials for Crohn’s disease exacerbations. Enbrel® dosing is typically 4 vials monthly. There are no approved loading doses for Enbrel®. The only approved dose above 4 vials monthly is for severe plaque psoriasis where the dose can go up to 8 vials monthly for 3 months. Highlighted in the table are the only instances noted where dosing may have been outside of accepted quantities.

**(Updated table)**

<b>Table 5. Number of Vials Per Claim by Drug and Diagnosis*</b> (January 2016 - July 2017 -- FFS and CCOs)						
<b>Drug</b>	<b>Diagnosis</b>	<b>Number of Vials Per Claim</b>				
		1 vial	2 vials	4 vials	6 vials	8 vials
Humira (adalimumab)	Crohn's Disease	0	596	62	47	0
	Plaque Psoriasis	0	368	116	5	0
	Rheumatoid Arthritis	0	962	80	3	0
	Hidradenitis Suppurativa	0	31	163	26	1
	Juvenile Idiopathic Arthritis	0	72	35	0	0
	Psoriatic Arthritis	0	35	2	0	0
	Ankylosing Spondylitis	0	41	0	0	0
	Ulcerative Colitis	0	128	10	11	0
	Uveitis	0	6	1	0	0
	Unknown	0	187	27	7	0
Enbrel (etanercept)	Crohn's Disease*	0	0	9	0	0
	Plaque Psoriasis	11	0	268	0	95
	Rheumatoid Arthritis	19	24	1048	0	0
	Hidradenitis Suppurativa*	2	0	17	0	0
	Juvenile Idiopathic Arthritis	15	0	97	0	0
	Psoriatic Arthritis	0	0	2	0	0
	Ankylosing Spondylitis	0	0	1	0	0
	Unknown	14	0	49	0	4

\* Diagnosis was found in medical claims prior to prescription fill.

\*\* Diagnoses for which Enbrel does not have FDA approval.

## **CONCLUSIONS AND RECOMMENDATIONS (Updated)**

The Cytokine & CAM class experienced a 37% increase in utilization and a 97% increase in total amount paid for claims for the observation period. The increase in total paid can be attributed to an increase in utilization, price increases for the leading products, and the introduction of newer and more expensive medications. With the introduction of new medications and a focused effort from pharmaceutical manufacturers on product marketing, this trend will continue. As an initial focus for management of these products, MS-DUR suggests the following recommendations to the DUR Board.

### **Recommendations: (Updated)**

1. MS-DUR should continue to monitor this category of drugs to ensure providers continue following recommended prescribing in regards to diagnosis and dose.