Evaluation of Potential Criteria for Use of Multiple Hypoglycemic Agents

BACKGROUND

The Division of Medicaid (DOM) has been exploring development of prior authorization (PA) criteria regarding the use of multiple diabetic agents. The 2015 ADA guidelines for secondary agents are very vague. Older guidelines from the ADA & European Association for the Study of Diabetes are a little more specific, but still do not list a clear roadmap. Gould Health Services (GHS), DOM's rebate and PDL management vendor, proposed the following recommendations based on guidelines published by Up To Date:

- Patients can use up to 3 preferred agents for diabetes (metformin, sulfonylurea, TZD, DPP-4 Inhibitor, Meglitinide, GLP-1 Agonist or insulin) in any combination.
- Metformin should be included in every regimen unless contraindicated.
- The following combinations should not be permitted without PA:
    - Sulfonylureas + insulin
    - Sulfononylureas + meglitinides
    - DPP-4 Inhibitors + GLP-1 Agonist
- Use of combination products count as two agents (i.e. Janumet contains sitagliptin and metfomrin….this counts as two of the three preferred agents).
- Prior to use of a 4th agent, a PA would be required with an explanation as to why insulin would be contraindicated. If insulin is part of the original 3 drug regimen, an explanation as to why the dose cannot be tapered up would be required prior to adding a 4th agent.
- Use of a GLP-1 Agonist would be considered if weight loss is needed and the patient is close to A1C goals (≤ 1mg/dL).
- Use of an SGLT-2 Inhibitor would be considered if the patient could not take insulin.
- Approved PAs for a 4th agent would require a re-evaluation every 6 months with updated A1C values for proof that the regimen of 4 agents is yielding positive outcomes/results

MS-DUR was asked to analyze current use patterns of diabetic agents In order to assist DOM in evaluating the potential impact of the proposed multiple agent PA criteria.

METHODS

A retrospective analysis was conducted using all Mississippi Medicaid (fee-for-service and coordinated care) pharmacy claims data for the period July 1, 2014 to February 28, 2015. All antidiabetic product claims were extracted for analysis.

Identification of multiple agent regiments was performed using the following criteria:

- Patients were considered to be "covered" by a product between the time of the first prescription fill identified and the date of the last prescription fill plus the number of days therapy of the last fill.
- Medication possession gaps of less than 60 days were considered to be compliance gaps and the patient was considered to still be covered by the product during these compliance gaps.
- For each day during the observation period, coverage arrays were computed for each drug product being taken by the patient. Combination products were recorded as coverage for both therapeutic classes included in the product.
- For each patient, a regimen was computed for each day that included all of the therapeutic classes for which the patient had coverage.
- When coverage of a discontinued therapeutic category resulted in an overlap of less than 30 days from the initiation of new therapeutic category, the overlap period for the discontinued category was eliminated under the assumption that the overlap only occurred due to residual possession of the drug after a patient's regimen was changed.
- Any therapy combinations that had continuous coverage of < 30 days were eliminated as titration or incidental occurrences.

The antidiabetic therapeutic classes used to classify regimens are listed in Table 1.

TABLE 1: Antidibetic Therapy Classes Used to Determine Regimen Combinations

Antidiabetic Agent Classes	
Abbreviation in Regimens	**Description**
Sulf	Sulfonylureas
Metf	Metformin
TZD	Thiazolidinediones
Megl	Meglitinides
DPP4	Dipeptidyl peptidase 4 inhibitors
GLP1	Glucagon-like peptide-1 receptor agonists
Insu	Insulin
SGLT	Sodium-glucose transporter-2 inhibitors
Amyl	Amylin analogs
AlGl	Alpha-glucosidase inhibitors

RESULTS

TABLE 2: Number of Different Regiments Used During Observation Period

Number of Regimens*	N	%
0	2,025	12.2%
1	4,788	28.9%
2	3,943	23.8%
3	3,028	18.3%
4	1,888	11.4%
5	747	4.5%
6	145	0.9%
7	10	0.1%

** Regimens were identified as therapeutic combinations with > 30 days consecutive coverage.*

A total of 16,574 beneficiaries were identified as taking antidiabetic agents during the observation period. As shown in Table 2, 2,025 of these beneficiaries did not take a steady regimen for 30 days or more. These may have been newly diagnosed patients that did not reach a stable therapy during the observation period or one-time users of an antidiabetic agents.

The results in Table 2 also illustrate the instability of diabetic treatment over time. Only 29% of the diabetic patients treated during the observation period remained on the same regimen for the complete 242 days observed. Almost one-fourth made only 1 change in regimen. However, almost two-thirds of patients made 2 or more regimen changes during the observation period.

Table 3 shows the different regimens being used for > 30 days during the observation period. Overall there were 33,985 patient/regimen combinations during the observation period. The frequency cells for cases using regimens with more than 3 agents are highlighted in dark orange.

TABLE 3: Regimens Used to Treat Beneficiaries During Observation Period

Regimen	N	Average # Days	Maximum # Days	Regimen	N	Average # Days	Maximum # Days
Sulf	3,366	38.9	232	Megl	9	33.3	60
Sulf	127	32.9	90	DPP4	762	41.6	175
Sulf / AlGl	4	46.3	95	DPP4 / GLP1	5	48.0	90
Sulf / DPP4	155	36.1	110	GLP1	117	35.3	90
Sulf / DPP4 / SGLT	4	41.0	59	SGLT	27	36.0	90
Sulf / GLP1	10	40.1	90	Insu	10,575	40.0	237
Sulf / Metf	2,760	38.7	217	Insu / AlGl	6	48.2	60
Sulf / Metf / AlGl	7	55.7	120	Insu / DPP4	140	38.1	120
Sulf / Metf / DPP4	300	39.6	179	Insu / GLP1	18	43.2	119
Sulf / Metf / GLP1	7	37.3	56	Insu / Megl	3	66.7	109
Sulf / Metf / SGLT	3	30.3	31	Insu / Megl / DPP4	2	47.5	65
Sulf / Metf / TZD	65	38.3	148	Insu / Metf	1,240	38.2	180
Sulf / Metf / TZD / DPP4	6	34.5	52	Insu / Metf / DPP4	50	38.7	127
Sulf / Metf / TZD / DPP4	3	80.0	180	Insu / Metf / DPP4	26	39.6	120
Sulf / Metf / TZD / GLP1	2	30.0	30	Insu / Metf / DPP4 / SGLT	1	30.0	30
Sulf / SGLT	3	30.0	30	Insu / Metf / GLP1	1	30.0	30
Sulf / TZD	52	38.7	94	Insu / Metf / TZD	10	43.8	89
Sulf / TZD / DPP4	5	41.4	60	Insu / Metf / TZD / DPP4	1	30.0	30
Metf	11,965	38.5	228	Insu / SGLT	6	39.5	60
Metf / AlGl	1	30.0	30	Insu / Sulf	369	38.5	180
Metf / DPP4	452	39.4	233	Insu / Sulf / DPP4	15	37.3	59
Metf / DPP4	400	42.7	180	Insu / Sulf / Metf	294	37.3	127
Metf / DPP4 / GLP1	38	44.1	120	Insu / Sulf / Metf / DPP4	21	37.8	60
Metf / DPP4 / SGLT	2	30.0	30	Insu / Sulf / Metf / SGLT	1	30.0	30
Metf / GLP1	17	40.6	81	Insu / Sulf / Metf / TZD	6	49.5	82
Metf / Megl	1	30.0	30	Insu / Sulf / Metf / TZD /DPP4 / AlGl	3	49.7	60
Metf / SGLT	6	40.0	90	Insu / Sulf / TZD	6	42.8	77
Metf / TZD	175	42.8	226	Insu / TZD	36	39.3	99
Metf / TZD / DPP4	14	48.4	115	Insu / TZD / DPP4	7	38.3	60
TZD	264	42.7	150				
TZD / DPP4	14	35.4	60				

** Regimens were identified as therapeutic combinations with > 30 days consecutive coverage.*

NOTE: List includes all regimens appearing during observation period. Beneficiaries are included for each regimen used during observation period.

Requiring a manual PA for regimens using more than 3 agents would not produce a heavy burden for the manual PA process if these could be identified without having to manually screen all diabetic agent prescriptions. Only 44 cases occurred during the observation period where patients were treated with more than 3 agents for more than 30 days.

Requiring Metformin to be part of every regimen except when contraindicated might be more challenging. Of the 33,985 patient/regimen combinations occurring, only 17,878 (52.6%) included Metformin. Although Metformin might be contraindicated in some of the other regimen combinations present, there may be a large number of cases that would have to be reviewed for possible Metformin inclusion. Detecting this prospectively or even retrospectively will be complicated by the fact that Metformin is on most $4 prescription lists and many patients may be paying cash if they are at the prescription limit in Medicaid.

Of the contraindicated regimens identified in the recommendations, concomitant use of Sufonylureas and Insulin would produce the greatest number of PA reviews (715). Only 43 cases were identified with concomitant use of a GLP-1 and a DPP-4 and no cases were identified with concomitant use of Sulfonylureas and Meglitinides.

CONCLUSIONS

Implementation of diabetic agent prior authorization criteria will not be cost effective if electronic PA is not used. Even using electronic PA will be problematic due to:

- the large number of changes in regimen that occur,
- the difficulty of identifying concomitant coverage of multiple drugs, and
- the need to break down combination products into their corresponding individual agents.

Contraindicated regimens are occurring infrequently.

- Concomitant use of Sulfonylureas and Insulin only occurred 715 times.
- Concomitant use of GLP-1 and DPP-4 only occurred 43 times.
- Concomitant use of Sulfonylureas and Meglitinides did not occur at all.

Current treatment patterns among DOM beneficiaries with diabetes are fairly well in compliance with the recommended criteria with the exception of including Metformin in almost all regimens. Accurately determining whether Metformin is being used will be difficult since this product is included in almost all “$4” prescription plans and prescriptions paid for in cash are not included in the data for analysis.

Recommendations:

Electronic PA should be used to the extent possible to assure compliance with guidelines.

Retrospective DUR educational programs should be utilized to address cases that do not comply with the approved guidelines.

- Use of regimens with more than 3 agents should be identified through retrospective DUR with intervention through educational feedback to providers.
- Use of contraindicated regimens should be addressed through retrospective DUR exceptions monitoring with appropriate educational interventions.

Action Needed:

- DUR Board input on appropriateness of proposed guidelines.

- DUR Board support for educational intervention programs.