Protected Classes Review Panel

Objective:

To identify therapeutic classes that meet proposed protected classes criteria.

Background of Clinical Classes of Concern:

Section 3307 of the Affordable Care Act (ACA) revised §1860D-4(b)(3)(G) of the Social Security Act (originally added by the Medicare Improvement for Patients and Providers Act of 2008 (MIPPA)) and directs CMS to identify categories and classes of Part D drugs that require inclusion of all Part D drugs on formularies based on criteria established by CMS through notice and comment rulemaking and subject to exceptions established by CMS through notice and comment rulemaking. Beginning for 2006, CMS established a policy that required all Part D sponsors to include “all or substantially all” Part D drugs within the following 6 categories/classes: antineoplastics, anticonvulsants, antiretrovirals, antidepressants, antipsychotics and immunosuppressants used to prevent transplant rejection. While CMS intended the policy to be temporary for the first year or two, MIPPA established criteria for CMS to use to permanently codify protected categories and classes. However, prior to implementation of MIPPA criteria, the ACA revised §1860D-4(b)(3)(G) and now directs CMS to identify categories and classes of Part D drugs for which all Part D drugs must be on the formulary using criteria established by CMS through notice and comment rulemaking.

Unlike in 2006, we now have significant experience overseeing and ensuring formularies are clinically robust, as well as ensuring transition and exceptions/appeals processes are being implemented correctly. As a direct result of our transition requirements, we firmly believe that the determination to identify a category or class under this requirement should be based solely on initiation of therapy and not a concern with interruption of existing drug therapy.

Consensus Panel Review Process:

CMS convened a consensus panel of CMS pharmacists and the Chief Medical Officer for the Center for Medicare to identify which drug categories or classes met the following proposed criteria to qualify as a protected class:

A PDP Sponsor shall include all covered Part D drugs in the categories and classes such that, for individuals who have a disease or disorder treated by drugs in a category or class:

1) A delay in access, within the period of time allowed when a request for an expedited reconsideration is received and granted consistent with §423.600(d)\(^1\), to any drug in such category or class will likely result in hospitalization, or persistent or significant disability or incapacity, or death; and

2) Access to all drugs in such category or class is necessary because differences between individual drugs in the category or class uniquely determine specific drug therapy; and

3) Access to such drugs in the category or class is not adequately protected by existing formulary protections.\(^2\)

\(^1\) The consensus panel considered this period of time to be 7 days.

\(^2\) The panel began the review process utilizing the third criteria. However after reviewing several classes the panel determined that the criterion was not providing additional clinical utility beyond what was provided by criteria two and thus considered it as part of the second criterion. Existing formulary protections refers to requirements other than the existing protected class review.
The panel was supported by contractors that performed background research and provided specific information on Part D utilization\(^3\) and analyses of widely-accepted treatment guidelines\(^4\) for each drug category or class, when available. The panel reviewed all Part D drugs that were included on the CY 2013 CMS formulary reference file and that had utilization in CY 2012, using the American Hospital Formulary Service (AHFS)-6 classification system. We chose the AHFS-6 classification system as a framework because it allows for the grouping of drugs based on similar pharmacologic, therapeutic, and/or chemical characteristics and therefore provided CMS with a tool to logically, and in stepwise fashion, apply the criteria to all Part D drugs.

As the panel reviewed therapeutic classes, the criteria were applied in order. Generally, with the exception of a few classes, if the panel determined that a class did not meet the first criterion, the determination of whether the class met the other criteria was unnecessary. Only if the panel concluded that a therapeutic class met all defined criteria, then the class was deemed as a protected class.

During the panel’s review, additional consideration was given to CMS’ current formulary review checks (e.g. treatment guidelines review) which are intended to ensure beneficiary access to medically necessary Part D drugs. The panel considered whether a more specific CMS formulary requirement than requiring all drugs in a class was already implemented or could be implemented to ensure appropriate access to classes of drugs.

Results:

A total of 214 AHFS-6 classes were reviewed (Appendix 1). The review panel determined that 86 AHFS-6 classes met the first criteria relating to urgency of access. These 86 classes largely consisted of anti-infective, cardiovascular, and central nervous system agents. When the additional criteria relating to whether non-interchangeability/existing protections are not adequate were applied to these 86 classes, six were deemed as meeting the proposed criteria (Table 1), representing three of the currently protected categories and classes (four AHFS-6 classes were from the anticonvulsants category). Thus, the panel concluded that antineoplastics, anticonvulsants, and antiretrovirals should remain protected, while formulary access to antidepressants, antipsychotics and immunosuppressants would be assured through other formulary review processes.

Table 1. AHFS-6 Classes Meeting Protected Classes Review Criteria.

<table>
<thead>
<tr>
<th>AHFS-6</th>
<th>AHFS Tier 1</th>
<th>AHFS Tier 2</th>
<th>AHFS Tier 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>081808</td>
<td>Anti-infective Agents</td>
<td>Antivirals</td>
<td>Antiretrovirals</td>
</tr>
<tr>
<td>100000</td>
<td>Antineoplastic Agents</td>
<td>Antineoplastic Agents</td>
<td>Antineoplastic Agents</td>
</tr>
<tr>
<td>281208</td>
<td>Central Nervous System Agents</td>
<td>Anticonvulsants</td>
<td>Benzodiazepines</td>
</tr>
<tr>
<td>281212</td>
<td>Central Nervous System Agents</td>
<td>Anticonvulsants</td>
<td>Hydantoins</td>
</tr>
<tr>
<td>281220</td>
<td>Central Nervous System Agents</td>
<td>Anticonvulsants</td>
<td>Succinimides</td>
</tr>
<tr>
<td>281292</td>
<td>Central Nervous System Agents</td>
<td>Anticonvulsants</td>
<td>Anticonvulsants, Miscellaneous</td>
</tr>
</tbody>
</table>

\(^3\) Fu Associates, Ltd analyzed CY2012 prescription drug event (PDE) data to provide the following data elements: 1) the number of beneficiaries utilizing a drug within each AHFS-6; 2) the number of beneficiaries utilizing more than one drug within an AHFS-6 at the same time; and 3) the percentage of beneficiaries that utilized more than one drug at the same time.

\(^4\) Strategic Health Solutions (SHS) analyzed widely accepted treatment guidelines for the disease states treated by the AHFS-6 classes from which beneficiaries most commonly took multiple drugs. For each guideline, SHS determined whether the guideline supported concurrent use of multiple drugs within the class. If multiple drugs were supported, SHS then determined whether failure to obtain access to a drug within the class would result in major or life threatening clinical consequences.
Discussion:

The consensus panel determined that of the current six drug categories or classes of clinical concern, three (anticonvulsants, antineoplastics, and antiretrovirals) met the proposed criteria, and three did not (antidepressants, antipsychotics, immunosuppressants). The panel also determined that while other drug categories and classes met one of the criteria, no other drug categories or classes met all criteria.

Anticonvulsants:

Drugs within the anticonvulsant class met both the criteria relating to criticality and non-interchangeability\(^5\), according to the consensus panel. Guidelines from organizations within the United States tend to make recommendations based on specific drug lists as opposed to recommendations at a subclass level. The American Academy of Neurology, in its 2004 publication on the Efficacy and Tolerability of the New Antiepileptic Drugs, recommends the use of specific agents for the treatment of new onset epilepsy such as carbamazepine, phenytoin, phenobarbital rather than recommending a class of drugs such as benzodiazepines or hydantoin. Further, as noted in the National Institute for Health and Clinical Excellence (NICE) clinical guidelines of 2012, access to optimal treatment maximizes health outcomes and minimizes the often detrimental impacts to individual’s social and employment activities. For example, most states have laws that regulate seizure-free periods for operation of a motor vehicle. The recommended therapies are highly dependent upon seizure type, epilepsy syndrome, concurrent medications and comorbidities. While the goal is to manage the seizure disorder with monotherapy, it is recognized that often multiple medications are required to achieve adequate seizure control. In addition, there is a great deal of diversity among the agents within the AHFS-6 class Anticonvulsants, Miscellaneous that would not lend to within-class interchangeability. It is also recommended that, when possible, a consistency of a drug preparation be maintained as different preparations of some antiepileptic drugs (AEDs) may vary in bioavailability or pharmacokinetic profiles and care needs to be taken to avoid reduced effect or excessive side effects. The panel determined that there was not a more effective way to ensure timely and necessary access other than a requirement of all drug entities on the formulary.

Antineoplastics:

The panel concluded that antineoplastics required prompt initiation of therapy and thus met the criticality criterion. The panel also recognized antineoplastics as meeting the other criteria, non-interchangeability. Antineoplastic drugs are part of dynamic treatment protocols, and are often dependent upon specific genetic variations and other patient-related variables. A cancer patient whose clinical picture is rapidly changing must be able to immediately initiate very specific changes in antineoplastic therapy when the new disease target is identified.

Antiretrovirals:

With respect to antiretrovirals the panel determined that this class of drugs met the criticality criterion. The risk associated with the failure to immediately initiate recommended concurrent antiretroviral therapies could significantly increase the risk of developing drug resistance and the potential for re-exacerbation of the disease. The panel also determined that antiretrovirals met the non-interchangeability criteria. The number of multiple drug combinations and adjunctive therapies involved, frequency with which recommended drug protocols

\(^{5}\) The panel considered therapeutic interchangeability in the context of whether drugs within the class could generally be substituted for one another.
change and the role that changing drug resistance plays in determining the selection of different antiretroviral drugs support this conclusion. The need to adjust specific combination antiretroviral therapy in real time is complex and must consider, among other things, viral sensitivity to the drugs, drug interactions, pregnancy status (if applicable), and potentially the patient's pharmacogenomic profile of the cytochrome P450 system.

Antidepressants:

For antidepressants, the panel concluded that a 7-day delay in initiation of therapy would generally not put the individual at risk of hospitalization, incapacity, disability or death, and thus did not meet the criticality criterion. The panel also concluded that antidepressants did not meet the non-interchangeability criteria. This determination was based upon the similarities of drugs within sub-classes and the lack of unique effects for distinguishing individual drug products when initiating drug therapy for an individual in a Part D setting. The American Psychiatric Association (APA) developed practice guidelines for the treatment of depression in 2010. This is an extensive guideline and provides numerous considerations in the selection of an agent for depression, including side effect profile, relative efficacy, potential for drug interactions, and cost. This guideline addresses each subclass of antidepressants and illustrates the many options within them. This guideline recommends selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), mirtazapine, and buproprion for most patients. Occasionally, different subclasses of antidepressants are used in combination with each other for increased efficacy, or to take advantage of a different pharmacological effect (for example, concurrent therapy of one agent that causes drowsiness with another agent that promotes wakefulness). The panel did not determine that additional protections were necessary for antidepressants based on the current protections afforded by our treatment guideline formulary check.

Antipsychotics:

With respect to antipsychotics, many of these take weeks to reach their full effect (steady state). In addition, with regard to the Medicare population, particularly in long term care settings, current treatment guidelines indicate that the use of antipsychotics in the elderly is, in many cases, unwarranted and in others, possibly dangerous. However, due to the potential that, untreated, a beneficiary with active psychotic symptoms may be dangerous to themselves or others, the panel concluded that a 7-day delay in initiation of therapy met the threshold to put the typical individual with a diagnosis of schizophrenia at risk of hospitalization, incapacity, disability or death, and thus met the criticality criterion. The panel concluded, however, that antipsychotics did not meet the non-interchangeability criteria. The APA developed practice guidelines for the treatment of schizophrenia in 2004 and 2009 that discuss initial selection of these agents in broad terms such as “first” and “second” generation antipsychotics. These guidelines do not recommend specific products over one another, and the 2009 updated guidelines note that the distinction between first and second generation antipsychotics appears to have limited clinical utility. These drugs are normally not used in combination with each other for an additive effect, but they are used in combination with other psychiatric medications to treat symptoms such as depression or anxiety, or in combination with non-pharmacological psychosocial treatments. In addition, there is a high discontinuation rate with all of these medications, which would lead one to conclude that there are multiple options for initiation of pharmacological therapy in these patients. The Part D program allows beneficiaries and clinicians options to obtain formulary exceptions if one particular agent seems to work better than others for a given patient. As a therapeutic class, antipsychotic agents are noted to cause an increased risk of death in patients who have dementia-related psychosis leading to a black box warning in the FDA-approved labeling for these agents. Unfortunately, CMS’ analyses suggest that these agents continue to be prescribed within long term care facilities at an alarming rate. The panel did not determine that additional protections were necessary for antipsychotics based on current protections afforded by our treatment guideline check as well as the nature of the recommendations within the treatment guidelines.
**Immunosuppressants:**

Regarding immunosuppressants for transplant rejection prophylaxis, the panel concluded that timely access to the class of drugs within the specified timeframes was critical. However, in light of how the treatment guidelines recommend subclasses of drugs rather than specific individual drugs, the panel determined that not every drug product should be required on every formulary. For example, the American Society of Transplantation and the American Society of Transplant Surgeons jointly published the 2009 treatment guidelines for the Long-Term Treatment of the Liver Transplant Patient. Within these guidelines, the authors recommend the strategy of using multiple immunosuppressive medications from the following classes: Calcineurin inhibitors, Antimetabolites, Corticosteroids and Sirolimus/rapamycin. The authors do not however recommend specific drugs within each of the classes over any other in the same class. Given that our current formulary review requirements based on treatment guidelines would capture these classes of immunosuppressants, the panel determined that current beneficiary protections were deemed appropriate for this class.