The Iowa Medicaid Pharmaceutical & Therapeutics (P&T) Committee met on April 21, 2016, and as part of the agenda reviewed the Antiretroviral (ARV) class of medications. The P&T Committee became aware of legislative questions related to the costs and benefits of using single tablet regiments (STR) rather than multiple tablet regimens (MTR) in certain circumstances.

2016 Iowa House File (H.F.) 2460, sec. 10 (amending 2015 Iowa Acts, chapter 137, sec. 132(29)), signed into law on May 27, 2016, stated "The department of human services shall review the fiscal impact and potential benefit to Medicaid recipients of including single-tablet regimens or long-acting alternatives for the treatment of HIV or acquired immune deficiency syndrome on the preferred drug list, as an alternative to multi-tablet regimens. The department shall identify opportunities to align the cost of single-tablet regimens for the treatment of HIV or acquired immune deficiency syndrome with the corresponding multi-tablet regimens, and shall pursue manufacturer supplemental rebate offers through the sovereign states drug consortium supplemental rebate negotiation process to determine if any supplemental rebate opportunities are available for calendar year 2018. If such opportunities are available, the department shall implement any such supplemental rebate offer opportunities beginning in calendar year 2018".

Based on the questions and request for review as stated above, the P&T Committee would like to provide an explanation of the review process utilized for recommending preferred or non-preferred status on the PDL for ARV medications, as well as the process utilized for supplemental drug rebate solicitation. The P&T Committee does oppose any requirement that is not supported by current peer reviewed medical literature.

The P&T Committee currently meets three times per year to review newly released drug products, including new generic drugs, for placement on the PDL. A complete PDL review is completed annually. Drugs are reviewed based on safety, efficacy and cost effectiveness as related to agents in the same or similar therapeutic category.

The recommendations from the P&T Committee regarding ARV drug status on the PDL, for human immunodeficiency virus (HIV) and acquired immune deficiency syndrome (AIDS), incorporate two key principles based on the unique needs of this therapeutic class:

1.) Grandfathering: Due to the risk of inducing viral resistance, existing users should not have to change medications if the PDL status of the drugs they currently use changes. Therefore if an ARV drug changes status on the PDL, the existing users are grandfathered (the patient continues on their current medication); and

2.) Prior Authorization (PA) Requirements: Unlike other PDL categories, again due to the risk of inducing viral resistance, failure of preferred products is not a requirement in the consideration of a PA request for a non-preferred product; patients are not asked to fail a particular chemical entity before getting access to another. Rather, prescribers are asked to provide the medical rationale as to why the use of a more expensive, non-preferred product with identical or highly similar ingredients is required to meet the medical need. Prescriptions for ARVs are not generally urgent (since genotype testing typically takes about a week to

obtain); therefore, allowing time to evaluate a PA would not be expected to significantly delay therapy. Additionally PAs are required to be processed within twenty-four hours of receipt of a complete PA request.

There are three guiding factors behind all preferred/non-preferred recommendations for ARVs, clinical considerations, such as efficacy and toxicity, pill burden, and cost.

In considering the clinical aspects of the ARV drugs, the P&T references the Health and Human Services (HHS) Guidelines for the treatment of HIV, which do not state a preference amongst their recommended first line treatment options. Achieving viral suppression currently requires the use of combination ARV regimens that generally include three active drugs from two or more drug classes. According to these guidelines, five integrase strand transfer inhibitor-based combinations and one protease inhibitor-based combination are recommended as preferred initial therapy for antiretroviral-naïve patients. Of these six HHS Guideline recommended options, the Iowa Medicaid PDL has four of the five equally recommended integrase strand transfer inhibitor combinations listed as preferred as well having the one recommended protease inhibitor combination also listed as preferred. The guidelines state that these recommended combinations of three drugs are preferred but specifically state that the regimen is preferred and not necessarily any specific drug. For example, in the case of Triumeq (non-preferred on the PDL), which is a single once daily tablet regimen, the identical active ingredients are available as two tablets once-a-day (using the preferred agents Epzicom and Tivicay each given as one tablet daily). For Stribild (non-preferred on the PDL), another single tablet preferred regimen, Genvoya, is a newer improved formulation with the same active ingredients. Genvoya was recommended for preferred status at the April 2016 meeting. Complera (non-preferred on the PDL), yet another single tablet regimen, the identical active ingredients are available as the preferred drugs, Edurant and Truvada, both of which are one pill once daily.

In regard to pill burden and compliance, there is no consistent, peer-reviewed, high quality evidence of improved compliance with one tablet once-a-day regimens versus two tablets once-a-day regimens. In no case does the Iowa Medicaid PDL require more than a single additional tablet once daily in place of a more expensive combination medication. The HHS Guideline states that "studies have shown that patients taking once-daily regimens have higher rates of adherence than those taking twice-daily dosing regimens." They also go on to state that "the data to support or refute the superiority of fixed dose combination product of one pill versus three pills (of the individual products), once-daily regimens is limited". In no case does the Iowa Medicaid PDL require twice daily dosing as opposed to once daily dosing.

Lastly in consideration of the cost of ARV therapy, conserving resources is important so that more Iowans can be served by the pharmacy benefit with the same dollars when there is equal clinical efficacy amongst the drugs. The Sovereign States Drug Consortium (SSDC) is a collaborative group of Medicaid states of which Iowa is a member. Collectively members are focused on providing quality pharmaceutical care while controlling costs. The primary activity of the SSDC is a Medicaid drug rebate program that negotiates for supplemental rebates (SRs) that are in addition to those required under the federal Medicaid Drug Rebate Program. The SSDC provides all

manufacturers an equal opportunity to submit a SR annually, and interim to the annual as new drugs and formulations are released. In terms of the cost, it is important to point out that unlike other manufacturers of many, newer, ARV drugs, the manufacturer of Triumeq has not offered a SR to the Iowa Medicaid program to make their product more affordable than its preferred components.

The P&T Committee reviewed documentation submitted following the April 2016 P&T meeting by a public speaker, a representative of Viiv Healthcare which manufactures the drug Triumeq. Many of the trials submitted were sponsored by drug manufacturers and indicate controlled, clinical trials that evaluated the clinical benefit of multi-tablet regimens have shown conflicting results, indicating that the benefit of fixed-dose co-formulations over individual components with low pill burdens and once daily dosing has not been clearly proven.

The P&T Committee would like to point out the unique aspects of the ARV drug class including the concern regarding pill burden and adherence to the medication regimen as well as viral resistance have been carefully considered in making our evidence-based recommendations.

Thank you for the opportunity to explain the P&T Committee's rationale for the recommendations to place select ARV medications as non-preferred on the PDL. Please feel free to contact us if you have additional concerns.