Alabama Medicaid DUR Board Meeting Minutes
January 22, 2014

Members Present: Paula Thompson, Kelli Littlejohn, Bernie Olin, Denyse Thornley-Brown, Frank Pettyjohn, , Dan McConaghy, Jimmy Jackson, Rhonda Harden, Robert Moon

Also Present: Tiffany Minnifield, Heather Vega, Lori Thomas, Clemice Hurst

Present via Conference Call: Kristian Testerman

Members Absent: Donald Marks, Jared Johnson

Call to Order: The DUR meeting was called to order by P. Thompson at approximately 1:00p.m.

Review and Adoption of Minutes: The minutes of the October 23, 2013 meeting were presented and reviewed. P. Thompson pointed out one item that was omitted from the minutes. L. Thomas notated this and will amend the minutes. D. Thornley-Brown made a motion to approve the minutes as amended and F. Pettyjohn seconded the motion. The motion was approved unanimously.

Prior Authorization and Overrides Update: L. Thomas began the Prior Authorization and Overrides Update with the Monthly Manual Prior Authorizations and Overrides Report for the month of August 2013. She reported 9,086 total requests. L. Thomas directed the board members to the overrides section of the report. She pointed out that the compounds have been moved under the override section due to these requests requiring a maximum cost override. She then reported 18,619 electronic requests for the same time frame. From the Prior Authorization and Override Response Time Ratio report for August 2013, L. Thomas reported that approximately 89-90% of all manual PAs and overrides were responded to in less than two hours, about 99% in less than four hours and 99% in less than eight hours. For the month of September 2013, L. Thomas reported 9,336 manual PA requests and 18,184 electronic PA requests. She reminded the board members that Synagis requests could be sent into HID beginning September 1st. She reported that more than 76% of PAs were responded to in less than two hours, approximately 95% in less than four hours and 99% in less than eight hours. For the month of October 2013, L. Thomas reported 9,433 manual PA requests and 19,972 electronic PA requests. For October, L. Thomas reported over 76% of requests were reviewed in less than two hours, approximately 90% in less than four hours and over 98% reviewed in less than eight hours.

Program Summary Review: L. Thomas briefly reviewed the Alabama Medicaid Program Summary. She reported 4,342,675 total prescriptions, 220,433 average recipients per month using pharmacy benefits and an average paid per prescription of $62.26 for the months of April 2013 through September 2013.

Cost Management Analysis: L. Thomas reported an average cost per claim of $62.96 for September 2013. From the 3rd Quarter 2013 Drug Analysis, L. Thomas reported 77.4% generic utilization, 9.7% brand single-source, 4.6% brand multi-source (those requests which required a DAW override) and 8.3% OTC and "other". From the Top 25 Drugs Based on Number of Claims from 07/01/2013 – 09/30/2013, L. Thomas reported the top five drugs: hydrocodone-acetaminophen, montelukast sodium, amoxicillin, omeprazole, and ProAir® HFA. She then reported the top five drugs from the Top 25 Drugs Based on Claims Cost from 07/01/2013 – 09/30/2013: Abilify®, Vyvanse®, Focalin XR®, Invega® Sustenna®, and ProAir® HFA. From the Top 15 Therapeutic Classes by Total Cost of Claims for the same time frame, L. Thomas reported the top five classes: Antipsychotic Agents, Corticosteroids (Respiratory Tract), Amphetamines, Hemostatics, and Miscellaneous Anticonvulsants.

UPDATES

RDUR Intervention Report: L. Thomas presented the RDUR Activity Report for October 2013. She reported 500 profiles reviewed and 591 letters sent with 106 responses received as of the date of the report. She reported 43 of 66 physicians indicated that they found the RDUR letters "useful" or "extremely useful". The criteria for the cycle of intervention letters was therapeutic appropriateness of anti-epileptics in patients with depression or suicidality.

Proposed Criteria: L. Thomas presented the proposed set of 67 criteria to the Board. T. Minnifield instructed the Board members to mark their ballots. Of the 67 criteria, results from the criteria vote returned 67 approved.

Medicaid Update: T. Minnifield began the Medicaid Update by reminding the Board members that all Medicaid information discussed is available online, as well as any new Medicaid ALERTs. T. Minnifield discussed the changes that were implemented on January 1, 2014. K. Littlejohn reminded Board members that Medicaid had been preparing for these changes since September 2013. J. Jackson asked if children were excluded from the prescription limit. K. Littlejohn explained that children < 21 years of age were excluded. D. McConaghy asked if IV meds were excluded from the prescription limit. K. Littlejohn explained that those medications could be billed once per month as long as State Board of Pharmacy laws were followed. K. Littlejohn advised the Board members that the Pharmacy Study Commission had their last meeting in November and sent their final report to Governor Bentley at the end of December. K. Littlejohn acknowledged R. Harden and D. McConaghy for their hard work as members of the Pharmacy Study Commission. K. Littlejohn mentioned that the legislative session began earlier in January this year and will end earlier, as well.

P & T Committee Update: C. Hurst began the P & T Update by informing the Board that the last meeting was held on November 13, 2013 and covered the Skeletal Muscle Relaxants, Opiate Agonists, Antiemetics, and Proton Pump Inhibitors. The next P and T meeting is scheduled for February 12, 2014 at 9am and will cover the Skin and Mucous Membrane Agents. C. Hurst also discussed the January 2014 PDL changes, which included name brand Pulmicort becoming the non-preferred agent.

New Business: T. Minnifield notified the Board that the next DUR meeting will be held on April 23, 2014. P. Thompson made a motion to adjourn the meeting. The motion was seconded by D. Thornley-Brown. A voice vote to adjourn was unanimous. The meeting was adjourned at 2:03p.m.

Next Meeting Date: The next DUR Board meeting will be held on April 23, 2014.

Respectfully submitted,

Lori Thomas, PharmD

Lori Thomas, PharmD

ALABAMA MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

1. Telaprevir / Peginterferon Alfa and Ribavirin (Negating) ___√___ _____ _____

Alert Message: A review of the patient's recent drug history does not indicate the concurrent use of Incivek (telaprevir) with peginterferon alfa and ribavirin. Telaprevir must not be used as monotherapy due to the risk of the selection of resistant mutants which may be followed by viral breakthrough. Combination therapy with peginterferon alfa and ribavirin reduces the frequency of resistance development.

Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Telaprevir		Peginterferon alfa
		Ribavirin

References:

Sarrazin C, Zeuzem S. Resistance to Direct Antiviral Agents in Patients with Hepatitis C Infection. Gastroenterology. 2010 Feb;138(2):447-62.

Sarrazin C, Kieffer TL, Bartels D, et al. Dynamic Hepatitis C Virus Genotypic and Phenotypic Changes in Patients Treated with the Protease Inhibitor Telaprevir. Gastroenterology. 2007;132:1767-77

Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.

Clinical Pharmacology, 2013 Elsevier/Gold Standard.

Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

2. Telaprevir / Pregnancy / Miscarriage-Delivery-Abortion ___√___ _____ _____

Alert Message: Incivek (telaprevir) in combination with peginterferon alfa and ribavirin is contraindicated in pregnant women and in men whose female partners are pregnant (Pregnancy Category X). Women of childbearing potential and men must use at least two forms of effective contraception during treatment and for at least 6 months after treatment has concluded.

Conflict Code: MC – Drug (Actual) Diagnosis Precaution

Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Telaprevir	Pregnancy	Miscarriage
		Delivery
		Abortion

References:

Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.

Clinical Pharmacology, 2013 Elsevier/Gold Standard.

Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

3. Telaprevir / Drugs Highly Dependent on CYP3A for Clearance ___√___ _____ _____

Alert Message: The concurrent use of Incivek (telaprevir) is contraindicated with drugs that are highly dependent on CYP3A4/5 for clearance, and for which elevated plasma concentrations are associated with serious and/or life threatening reactions. Telaprevir is a potent CYP3A4 inhibitor and co-administration with drugs requiring CYP3A4 for metabolism may cause large increases in serum concentrations of the CYP3A4/5 substrate.

Conflict Code: DD - Drug/Drug interaction
Drugs/Diseases

Util A	Util B	Util C
Telaprevir	Alfuzosin	
	Dihydroergotamine	
	Ergotamine	
	Methylergonovine	
	Lovastatin	
	Simvastatin	
	Sildenafil (Revatio)	
	Tadalafil (Adcirca)	
	Pimozide	
	Triazolam	
	Midazolam-oral	

References:
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

4. Telaprevir / Potent CYP3A Inducers ___√_____ _____ _____

Alert Message: The concurrent use of Incivek (telaprevir) with the potent CYP3A4 inducer rifampin is contraindicated. Telaprevir is a CYP3A4 substrate and co-administration with rifampin significantly reduces telaprevir plasma concentrations and may lead to loss of virologic response.

Conflict Code: DD - Drug/Drug interaction
Drugs/Diseases

Util A	Util B	Util C
Telaprevir	Rifampin	

References:
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

5. Ketoconazole & Itraconazole / Telaprevir ____√____ _____ _____

Alert Message: The concurrent use of Incivek (telaprevir) with ketoconazole or itraconazole may result in increased plasma concentrations of telaprevir and the antifungal, as all are substrates and inhibitors of CYP3A4. When co-administered with telaprevir the dosages of itraconazole or ketoconazole should not exceed 200 mg /day.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C (Include)
Ketoconazole		Telaprevir
Itraconazole		

Max Dose of Antifungal: 200mg/day

References:
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

6. Telaprevir / Posaconazole ____√____ _____ _____

Alert Message: The concurrent use of Incivek (telaprevir) with Noxafil (posaconazole) may result in elevated plasma concentrations of both telaprevir and posaconazole, increasing the risk of adverse effects which includes posaconazole-related QT interval prolongation and torsade de pointes. Clinical monitoring is advised during concurrent use of these agents.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Telaprevir	Posaconazole	

References:
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

7. Telaprevir / Voriconazole ____√____ _____ _____

Alert Message: The concurrent use of Incivek (telaprevir) with voriconazole is not recommended unless an assessment of the benefit /risk ratio justifies its use. Co-administration may result in increased plasma concentrations of telaprevir and increased risk of telaprevir-related adverse effects. Voriconazole levels can be increased or decreased leading to either increased risk of voriconazole adverse effects (e.g., QT prolongation or torsade de points) or decreased voriconazole efficacy.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Telaprevir	Voriconazole	

References:
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

8. Telaprevir / P-gp, CYP3A4 and/or OATP1B1 & 2 Substrates ___√___ _____ _____

Alert Message: Incivek (telaprevir) is a strong CYP3A4 inhibitor and an inhibitor of P-glycoprotein (P-gp), OATP1B1 and OATP2B1. Concurrent use of telaprevir with drugs that are substrates of these pathways may result in increased plasma concentrations of the substrate, resulting in increased risk of adverse effects. Dosage adjustment of the substrate may be required during telaprevir therapy and readjustment after completion of telaprevir therapy.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Telaprevir	Afatinib (P-gp)	Trazodone (3A4)
	Aliskiren (3A4)	Ziprasidone (3A4)
	Fexofenadine (3A4 OATP1B1)	Escitalopram (3A4)
	Ondansetron (P-gp & 3A4)	Citalopram (3A4)
	Acetaminophen (3A4)	Repaglinide (3A4 & OATP1B1)
	Almotriptan (3A4)	
	Buprenorphine (3A4)	

References:
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

9. Telaprevir / Digoxin ___√___ _____ _____

Alert Message: The concurrent use of Incivek (telaprevir), a P-gp inhibitor, and digoxin, a P-gp substrate, may cause elevated digoxin concentrations, increasing the risk of digoxin-related adverse events. If concurrent use is required the lowest dose of digoxin should be prescribed initially. The serum digoxin concentrations should be monitored and used for titration of digoxin to obtain the desired clinical effect.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Telaprevir	Digoxin	

References:
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

10. Telaprevir / Antiarrhythmics ___√___ _____ _____

Alert Message: The concurrent use of Incivek (telaprevir), a potent CYP3A4 inhibitor, and CYP3A4-metabolized antiarrhythmics may result in serious and/or life threatening adverse events. Caution is warranted and clinical monitoring is recommended when these agents are used concomitantly with telaprevir.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Telaprevir	Amiodarone	
	Flecainide	
	Propafenone	
	Quinidine	

References:
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

11. Telaprevir / Warfarin ___√___ _____ _____

Alert Message: The concurrent use of Incivek (telaprevir) and warfarin may cause alterations (increases or decreases) in the warfarin plasma concentrations. When these drugs are co-administered monitor INR closely and adjust warfarin dose if necessary.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Telaprevir	Warfarin	

References:
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

12. Telaprevir / Carbamazepine ___√___ _____ _____

Alert Message: The concurrent use of Incivek (telaprevir) and carbamazepine may result in increased carbamazepine plasma concentrations and decreased telaprevir plasma concentrations. Clinical or laboratory monitoring of carbamazepine concentrations and dose titration are recommended to achieve the desired clinical response.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Telaprevir	Carbamazepine	

References:
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

13. Telaprevir / Phenytoin & Phenobarbital ___√___ _____ _____

Alert Message: The concurrent use of Incivek (telaprevir) and phenytoin or phenobarbital may result in altered phenytoin and phenobarbital plasma concentrations (increase or decrease) and decreased telaprevir plasma concentrations. Clinical or laboratory monitoring of the anticonvulsant concentrations and dose titration are recommended to achieve the desired clinical response.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Telaprevir	Phenytoin	
	Phenobarbital	

References:
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

14. Telaprevir / Trazodone ____√____ _____ _____

Alert Message: The concurrent use of Incivek (telaprevir), a potent CYP3A4 inhibitor, and CYP3A4 substrate trazodone may result in elevated trazodone plasma concentrations, increasing risk of adverse events. Dosage adjustment of trazodone may be necessary during concurrent therapy with telaprevir.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Telaprevir	Trazodone	

References:
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

15. Telaprevir / Colchicine / Renal or Hepatic Impairment Negating ____√____ _____ _____

Alert Message: The concurrent use of Incivek (telaprevir), a potent CYP3A4 inhibitor, and the CYP3A4 substrate colchicine may result in elevated colchicine plasma concentrations, increasing the risk of fatal colchicine toxicity. A reduction in colchicine dosage or an interruption of colchicine treatment is recommended in patients with normal renal or hepatic function. Please see the manufacturer's specific dosing information for the use of colchicine.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Telaprevir	Colchicine	Renal Impairment
		Hepatic Impairment

References:
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

16. Telaprevir / Colchicine / Renal or Hepatic Impairment (Include) ____√____ _____ _____

Alert Message: The concurrent use of Incivek (telaprevir), a potent CYP3A4 inhibitor, and the CYP3A4 substrate colchicine may result in elevated colchicine plasma concentrations, increasing the risk of fatal colchicine toxicity. Patients with renal or hepatic impairment should not be prescribed colchicine with telaprevir.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C **(Include)**
Telaprevir	Colchicine	Renal Impairment
		Hepatic Impairment

References:
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

17. Telaprevir / CYP3A4 Substrate CCBs ___√___ _____ _____

Alert Message: The concurrent use of Incivek (telaprevir), a potent CYP3A4 inhibitor, and a CYP3A4 substrate calcium channel blocker (CCB) may result in elevated CCB plasma concentrations, increasing risk of CCB-related adverse events. Caution is warranted and clinical monitoring is recommended. Dosage reductions may be necessary if the CCB co-administered is amlodipine.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Telaprevir	Amlodipine	
	Felodipine	
	Nicardipine	
	Nifedipine	
	Nisoldipine	
	Diltiazem	
	Verapamil	

References:
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

18. Telaprevir / Prednisone & Methylprednisolone ___√___ _____ _____

Alert Message: The concurrent use of Incivek (telaprevir) with prednisone or methylprednisolone is not recommended. The systemic corticosteroids are CYP3A4 substrates and co-administration with telaprevir, a potent CYP3A4 inhibitor, may result in significantly increased corticosteroid plasma concentrations.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Telaprevir	Prednisone	
	Methylprednisolone	

References:
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

19. Telaprevir / Dexamethasone ___√___ _____ _____

Alert Message: The concurrent use of Incivek (telaprevir), a CYP3A4 substrate, and dexamethasone, a CYP3A4 inducer, may result in decreased telaprevir plasma concentrations and loss of virologic activity. The combination of telaprevir and dexamethasone should be used with caution or alternatives should be considered.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Telaprevir	Dexamethasone	

References:
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

20. Telaprevir / Inhaled & Nasal Corticosteroids Fluticasone & Budesonide ___√_____ _____ _____

Alert Message: The concurrent use of Incivek (telaprevir) with the inhaled or nasal corticosteroids budesonide or fluticasone may cause increased plasma concentrations of the corticosteroid, resulting in significantly reduced serum cortisol concentrations. Co-administration of these agents is not recommended unless the potential benefit to the patient outweighs the risk of systemic corticosteroid side effects.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Telaprevir	Fluticasone-Inhaled & Nasal	
	Budesonide-Inhaled & Nasal	

References:
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

21. Telaprevir / Bosentan ___√_____ _____ _____

Alert Message: The concurrent use of Incivek (telaprevir) with Tracleer (bosentan) may result in elevated bosentan plasma concentrations leading to increased risk of bosentan-related adverse events. Caution is warranted and clinical monitoring is recommended.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Telaprevir	Bosentan	

References:
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

22. Telaprevir / Efavirenz ___√_____ _____ _____

Alert Message: The concurrent use of Incivek (telaprevir) and Sustiva (efavirenz) may result in decreased exposure to both telaprevir and efavirenz. HIV guidelines recommend that the telaprevir dose be increased to 1125 mg every 8 hours along with close clinical monitoring during co-administration due to potential for HIV and hepatitis C treatment failure.

Conflict Code: LR – Low Dose
Drugs/Diseases

Util A	Util B	Util C (Include)
Telaprevir		Efavirenz

Dose/day: < 1125mg/day of telaprevir

References:
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.
Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in HIV-1 Infected Adults and Adolescents. Department of Health and Human Services. February 12, 2013;1-167. Available at http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

23. Telaprevir / Atripla ___√___ _____ _____

Alert Message: The concurrent use of Incivek (telaprevir) and Atripla (efavirenz/ emtricitabine/tenofovir) may result in the decreased exposure to both efavirenz and telaprevir and increased exposure to tenofovir. HIV guidelines recommend that the telaprevir dose be increased to 1125 mg every 8 hours along with close clinical monitoring during co-administration due to potential for HIV and hepatitis C treatment failure and tenofovir adverse effects.

Conflict Code: LR – Low dose
Drugs/Diseases

Util A	4804	Util B	Util C (Include)
Telaprevir			Atripla

Dose/day: < 1125mg/day of telaprevir

References:
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

24. Telaprevir / Tenofovir-Containing Agents ___√___ _____ _____

Alert Message: The concurrent use of Incivek (telaprevir) and a tenofovir-containing agent (i.e., Viread, Truvada, Complera or Atripla) may result in increased tenofovir exposure and risk for tenofovir-related adverse effects. Increased clinical and laboratory monitoring is warranted.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	4804	Util B	Util C
Telaprevir		Tenofovir	
		Tenofovir/Emtricitabine	
		Tenofovir/Emtricitabine/Efavirenz	
		Tenofovir/Rilpivirine/Emtricitabine	

References:
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

25. Telaprevir / Atorvastatin ___√___ _____ _____

Alert Message: The concurrent use of atorvastatin-containing agents (Lipitor, Caduet and Liptruzet) with Incivek (telaprevir) should be avoided. Telaprevir is a strong CYP3A4 inhibitor and concurrent use with atorvastatin, a CYP3A4 substrate, may lead to elevated atorvastatin levels and increase the risk of statin-related myopathy and rhabdomyolysis.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Telaprevir	Atorvastatin	

References:
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

26. Telaprevir / Immunosuppressants ___√___ _____ _____

Alert Message: The concurrent use of Incivek (telaprevir), a potent CYP3A4 inhibitor, with a CYP3A4 substrate immunosuppressant may result in elevated plasma concentrations of the CYP3A4 substrate, increasing the risk of immunosuppressant-related adverse events. Close monitoring of immunosuppressant blood levels is recommended.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Telaprevir	Cyclosporine	
	Tacrolimus	
	Sirolimus	

References:
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

27. Telaprevir / Salmeterol ___√___ _____ _____

Alert Message: The concurrent use of Incivek (telaprevir) with a salmeterol-containing agent is not recommended due to the risk of adverse cardiovascular events associated with salmeterol. Telaprevir is a potent CYP3A4 inhibitor and use with the CYP3A4 substrate salmeterol can result in elevated salmeterol plasma concentrations.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Telaprevir	Salmeterol	

References:
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

28. Telaprevir / Methadone ___√___ _____ _____

Alert Message: The concurrent use of methadone with Incivek (telaprevir) may result in reduced plasma concentrations of methadone. Clinical monitoring is recommended as the dose of methadone during maintenance therapy may need to be adjusted in some patients.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Telaprevir	Methadone	

References:
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

29. Telaprevir / Ethinyl Estradiol Contraceptives ___√___ _____ _____

Alert Message: The concurrent use of Incivek (telaprevir) and ethinyl estradiol contraceptives may result in decreased ethinyl estradiol plasma concentrations with the potential of birth control failure in women with childbearing potential. Systemic hormonal contraception must be augmented by 2 alternative effective forms of contraception and may include intrauterine devices and barrier methods during therapy and for 6 months following therapy.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Telaprevir	EE- containing contraceptives	

References:
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

30. Telaprevir / PDE5 for ED ___√___ _____ _____

Alert Message: The concurrent use of Incivek (telaprevir) and a PDE5 inhibitor for the treatment of ED may result in increased PDE5 inhibitor plasma concentrations and risk of serious PDE5 inhibitor-related adverse events. Do not exceed the following doses for PDE5 inhibitors when used with telaprevir: sildenafil - 25 mg every 48 hours, tadalafil -10 mg every 72 hours and vardenafil - 2.5 mg every 24 hours.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Telaprevir	Vardenafil 5, 10 & 20mg (Levitra only Staxyn has separate criteria presented in June) Sildenafil 50& 100 mg (Viagra only Revatio contraindicated) Tadalafil 20mg (Cialis only Adcirca contraindicated)	

References:
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

31. Telaprevir / Alprazolam ___√___ _____ _____

Alert Message: The concurrent use of Incivek (telaprevir) with alprazolam may result in elevated alprazolam serum concentrations and risk of alprazolam-related adverse events. Clinical monitoring is warranted.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Telaprevir	Alprazolam	

References:
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

32. Telaprevir / Zolpidem ___√___ _____ _____

Alert Message: The concurrent use of Incivek (telaprevir) with zolpidem may result in decreased zolpidem exposure. Clinical monitoring and dose titration of zolpidem is recommended to achieve the desired clinical response.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Telaprevir	Zolpidem	

References:
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

33. Telaprevir / Rifabutin ___√___ _____ _____

Alert Message: The concurrent use of Incivek (telaprevir) with rifabutin is not recommended. Co-administration of these agents may result in elevated rifabutin plasma concentrations and decreased telaprevir concentrations. Both agents are CYP3A4 substrates and telaprevir is a potent CYP3A4 inhibitor while rifabutin is a CYP3A4 inducer.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Telaprevir	Rifabutin	

References:
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

34. Telaprevir / Darunavir / Ritonavir ___√___ _____ _____

Alert Message: Concurrent use of Incivek (telaprevir) with ritonavir-boosted Prezista (darunavir) is not recommended. Co-administration of these agents has been shown to result in reduced steady-state exposure to both telaprevir and darunavir.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C **(Include)**
Telaprevir	Darunavir	Ritonavir

References:
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

35. Telaprevir / Fosamprenavir / Ritonavir ___√___ _____ _____

Alert Message: Concurrent use of Incivek (telaprevir) with ritonavir-boosted Lexiva (fosamprenavir) is not recommended. Co-administration of these agents has been shown to result in reduced steady-state exposure to both telaprevir and fosamprenavir.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C **(Include)**
Telaprevir	Fosamprenavir	Ritonavir

References:
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

36. Telaprevir / Lopinavir-Ritonavir ___√___ _____ _____

Alert Message: Concurrent use of Incivek (telaprevir) with Kaletra (lopinavir/ritonavir) is not recommended. Co-administration of these agents has been shown to result in reduced steady-state exposure to telaprevir.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Telaprevir	Lopinavir/Ritonavir	

References:
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

37. Telaprevir / Atazanavir / Ritonavir ___√___ _____ _____

Alert Message: Concurrent use of Incivek (telaprevir) with ritonavir-boosted Reyataz (atazanavir) has been shown to result in reduced steady-state exposure to telaprevir while steady-state atazanavir exposure was increased. Monitor patient for decreased telaprevir efficacy and atazanavir-related adverse effects.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C **(Include)**
Telaprevir	Atazanavir	Ritonavir

References:
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

38. Telaprevir / Clarithromycin, Erythromycin & Telithromycin ___√___ _____ _____

Alert Message: Concurrent use of Incivek (telaprevir) with the antibacterials, clarithromycin, erythromycin or telithromycin, may result in increased plasma concentrations of telaprevir and the antibacterial agent. Caution is warranted and clinical monitoring is recommended when agents are co-administered. All three antibacterials have been shown to increase QT prolongation and clarithromycin and erythromycin are reported to cause torsade de pointes.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Telaprevir	Clarithromycin	
	Erythromycin	
	Telithromycin	

References:
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

39. Telaprevir / Certain Statins ___√___ _____ _____

Alert Message: Concurrent use of Incivek (telaprevir) with fluvastatin, pitavastatin, pravastatin or rosuvastatin may result in increased plasma concentrations of the statin, increasing the risk of statin-related adverse effects. Caution is warranted and clinical monitoring is recommended when telaprevir is co-administered with one of these statins. Telaprevir is an inhibitor of OATP1B1 and OATP2B1 transporters.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Telaprevir	Fluvastatin	
	Pravastatin	
	Pitavastatin	
	Rosuvastatin	

References:
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Incivek Prescribing Information, April 2013, Vertex Pharmaceuticals Inc.

40. Eletriptan / Potent CYP3A4 Inhibitors ___√___ _____ _____

Alert Message: Relpax (eletriptan) is a CYP3A4 substrate and should not be used within at least 72 hours of treatment with drugs that have demonstrated potent CYP3A4 inhibition and have this effect described in the contraindications, warning and precaution section of labeling.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B		Util C
Eletriptan	Ketoconazole	Saquinavir	Tipranavir
	Itraconazole	Ritonavir	
	Nefazodone	Indinavir	
	Clarithromycin	Nelfinavir	
	Telithromycin	Atazanavir	
	Boceprevir	Fosamprenavir	
	Telaprevir	Lopinavir/Ritonavir	

References:
Relpax Prescribing Information, Jan. 2012, Pfizer US Pharmaceutical Group.
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

41. Topiramate ER / Overutilization ___√___ _____ _____

Alert Message: Trokendi XR (topiramate extended-release) may be over-utilized. The manufacturer's recommended maximum dose of extended-release topiramate is 400 mg once daily.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C
Topiramate XR		

Max Dose: 400mg/day

References:
Trokendi UX Prescribing Information, August 2013, Supernus Pharmaceuticals.

42. Topiramate IR / Migraine / Negating Seizures & Anticonvulsants ___√___ _____ _____

Alert Message: The manufacturer's recommended maximum daily dose of topiramate as treatment for adults for prophylaxis of migraine headache is 100 mg per day in two divided doses.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Topiramate IR 100	Migraine	Seizures/Epilepsy
Topiramate IR 200		Anticonvulsants

References:
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Topamax Prescribing Information, Oct. 2012, Janssen Pharmaceuticals, Inc.

43. Axitinib / Therapeutic Appropriateness ___√___ _____ _____

Alert Message: The safety and effectiveness of Inlyta (axitinib) have not been established in patients less than 18 years of age.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Axitinib		

Age Range: 0 – 17 yoa

References:
Inlyta Prescribing Information, September 2013, Pfizer, Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

44. Axitinib / Overuse ____√____ _____ _____

Alert Message: Inlyta (axitinib) may be over-utilized. The manufacturer's maximum recommended dose is 10mg twice daily, approximately 12 hours apart.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C **(Negating)**			
Axitinib		Chronic Liver Disease	Ketoconazole	Itraconazole	Clarithromycin
		Cirrhosis	Nefazodone	Ritonavir	Saquinavir
		Nelfinavir	Indinavir	Telithromycin	Voriconazole
		Atazanavir	Carbamazepine	Phenytoin	Rifabutin
		Phenobarbital	Pioglitazone	Rifampin	Efavirenz
		Dexamethasone	Modafinil	Oxcarbazepine	Nevirapine
		Bosentan	Nafcillin	Etravirine	Boceprevir
		Telaprevir	Delavirdine		

Max Dose: 20mg/day

References:
Inlyta Prescribing Information, September 2013, Pfizer, Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.
Flockhart DA. Drug Interactions: Cytochrome P450 Drug Interaction Table. Indiana University School of Medicine. Available at: http://medicine.iupui.edu/clinpharm/ddos/table.asp.

45. Axitinib / Moderate Hepatic Impairment ____√____ _____ _____

Alert Message: Inlyta (axitinib) may be over-utilized. Patients with moderately impaired hepatic function (Child-Pugh class B) should have their starting dose decreased by approximately half and subsequent doses increased or decreased based on safety and tolerability. Axitinib has not been studied in patients with severe hepatic impairment (Child-Pugh class C).

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C (Include)
Axitinib		Chronic Liver Disease
		Cirrhosis

Max Dose: 20mg/day

References:
Inlyta Prescribing Information, September 2013, Pfizer, Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

46. Axitinib / Strong CYP3A4/5 Inhibitors ___√___ _____ _____

Alert Message: Inlyta (axitinib) may be over-utilized. The concomitant use of of axitinib and strong CYP3A4/5 inhibitors should be avoided. If these agents must be co-administered, it is recommended that the dose of axitinib be reduced by approximately half and subsequent doses increased or decreased based on safety and tolerability.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C (Include)
Axitinib		Ketoconazole
		Itraconazole
		Voriconazole
		Nefazodone
		Nelfinavir
		Saquinavir
		Ritonavir
		Indinavir
		Atazanavir
		Clarithromycin
		Telithromycin
		Boceprevir
		Telaprevir
		Delavirdine

Max Dose: 20mg/day

References:
Inlyta Prescribing Information, September 2013, Pfizer, Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.
Flockhart DA. Drug Interactions: Cytochrome P450 Drug Interaction Table. Indiana University School of Medicine. Available at: http://medicine.iupui.edu/clinpharm/ddos/table.asp. Accessed 10/2013.

47. Axitinib / Strong or Moderate CYP3A4/5 Inducers ___√___ _____ _____

Alert Message: The manufacturer recommends that concurrent use of Inlyta (axitinib) with strong or moderate CYP3A4/5 inducers be avoided. In clinical studies co-administration of axitinib with rifampin, a strong inducer of CYP3A4/5, reduced plasma exposure of axitinib in healthy volunteers.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B				Util C
Axitinib	Carbamazepine	Phenytoin	Rifabutin	Phenobarbital	
	Pioglitazone	Rifampin	Efavirenz	Dexamethasone	
	Modafinil	Oxcarbazepine	Nevirapine	Bosentan	
	Nafcillin	Etravirine			

References:
Inlyta Prescribing Information, September 2013, Pfizer, Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.
Flockhart DA. Drug Interactions: Cytochrome P450 Drug Interaction Table. Indiana University School of Medicine. Available at: Http://medicine.iupui.edu/clinpharm/ddos/table.asp.
Pithavala YK, Tortorici M, Toh M, et al. Effect of Rifampin on the Pharmacokinetics of Axitinib (AG-013736) in Japanese and Caucasian Healthy Volunteers. Cancer Chemother Pharmacol. 2010 February;65(3):563-570.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

48. Axitinib / Non-adherence ___√___ _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Inlyta (axitinib). Non-adherence to the prescribed dosing regimen may result in sub-therapeutic effects, which may lead to decreased patient outcomes and additional healthcare costs.

Conflict Code: LR – Non-adherence
Drugs/Diseases

Util A	Util B	Util C
Axitinib		

References:

Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005; 353:487-497.
Ruddy K, Mayer E, Partridge A. Patient Adherence and Persistence With Oral Anticancer Treatment. CA Cancer J Clin 2009;59:56-66.
Hershman DL, Shao T, Kushi LH, et al. Early discontinuation and non-adherence to adjuvant hormonal therapy are associated with increased mortality in women with breast cancer. Breast Cancer Res Treat (2011) 126:529-537.

49. Axitinib / Pregnancy / Pregnancy Negating ___√___ _____ _____

Alert Message: Inlyta (axitinib) is FDA pregnancy category D. If axitinib is used during pregnancy, or if the patient becomes pregnant while receiving this drug, the patient should be apprised of the potential hazard to the fetus.

Conflict Code: MC – Drug/Diagnosis Precaution/Warning/Contraindication
Drugs/Diseases

Util A	Util B	Util C(**Negating**)
Axitinib	Pregnancy ICD-9s	Delivery
		Miscarriage
		Abortion

References:

Inlyta Prescribing Information, September 2013, Pfizer, Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

50. Axitinib / Hypertension & Hypertensive Crisis ___√___ _____ _____

Alert Message: In a controlled clinical study with Inlyta (axitinib), hypertension was reported in 40% of patients and hypertensive crisis reported in <1%. In the case of severe and persistent hypertension despite use of anti-hypertensive medication and axitinib dose reduction, consider discontinuing axitinib.

Conflict Code: DB – Drug-Drug Marker and/or Diagnosis
Drugs/Diseases

Util A	Util B	Util C
Axitinib	Hypertension	
	Hypertensive Crisis	
	Antihypertensive Medications	

References:
Inlyta Prescribing Information, September 2013, Pfizer, Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

51. Axitinib / Thromboembolic Events ___√___ _____ _____

Alert Message: In clinical trials with Inlyta (axitinib), thromboembolic events were reported, including deaths. Axitinib should be used with caution in patients who are at risk for, or who have a history of, these events.

Conflict Code: MC – Drug/Diagnosis Precaution/Warning/Contraindication
Drugs/Diseases

Util A	Util B	Util C
Axitinib	TIA	
	Cerebrovascular Accident	
	Myocardial Infarction	
	Retinal Artery/Vein Occlusion	
	Retinal Vein Thrombosis	
	Pulmonary Embolism	
	Deep Vein Thrombosis	

References:
Inlyta Prescribing Information, September 2013, Pfizer, Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

52. Axitinib / Hemorrhage ___√___ _____ _____

Alert Message: In clinical trials with Inlyta (axitinib), hemorrhagic events were reported in 16% of patients. Axitinib has not been studied in patients who have evidence of untreated brain metastasis or recent active gastrointestinal bleeding and should not be used in these patients.

Conflict Code: MC – Drug/Diagnosis Precaution/Warning/Contraindication
Drugs/Diseases

Util A	Util B	Util C
Axitinib	Cerebral Hemorrhage	
	Hematuria	
	Hemoptysis	
	Lower GI hemorrhage	
	Melena	

References:
Inlyta Prescribing Information, September 2013, Pfizer, Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

53. Axitinib / Reversible Posterior Leukoencephalopathy Syndrome ___√___ _____ _____

Alert Message: In clinical trials with Inlyta (axitinib), reversible posterior leukoencephalopathy syndrome (RPLS) was reported in <1% of patients. If symptoms of RPLS develop (headache, seizure, lethargy, etc.), and magnetic resonance imaging confirms the diagnosis, therapy with axitinib should be discontinued.

Conflict Code: MC – Drug/Diagnosis Precaution/Warning/Contraindication
Drugs/Diseases

Util A	Util B	Util C
Axitinib	Seizure	
	Confusion	
	Blindness	

References:
Inlyta Prescribing Information, September 2013, Pfizer, Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

54. Axitinib / Hyper/Hypothyroidism ___√___ _____ _____

Alert Message: In clinical trials with Inlyta (axitinib), hypothyroidism was reported in 19% of patients and hyperthyroidism in 1% of patients. Thyroid function should be monitored before initiation of, and periodically throughout, treatment with axitinib.

Conflict Code: MC – Drug/Diagnosis Precaution/Warning/Contraindication
Drugs/Diseases

Util A	Util B	Util C
Axitinib	Hyperthyroidism	
	Hypothyroidism	

References:
Inlyta Prescribing Information, September 2013, Pfizer, Inc.
Clinical Pharmacology, 2013 Elsevier / Gold Standard.

55. Abilify Maintena / Oral Aripiprazole ___√___ _____ _____

Alert Message: The concurrent use of Abilify Maintena (aripiprazole extended-release injection) and oral Abilify (aripiprazole) for greater than the recommended overlapping 14 day conversion period may represent an unintended duplication of therapy that could result in increased aripiprazole exposure, adverse effects and unnecessary additional cost.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Aripiprazole Injection	Aripiprazole Oral	

References:
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Facts & Comparisons, 2013 Updates, Wolters Kluwer Health.
Abilify Maintena Prescribing Information, Feb 2013, Otsuka Pharmaceutical, Inc.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

56. Dolutegravir / Non-adherence ___√___ _____ _____

Alert Message: Non-adherence to antiretroviral therapy may result in insufficient plasma levels and partial suppression of viral load leading to the development of resistance, HIV progression and increased mortality.

Conflict Code: LR – Non-adherence
Drugs/Diseases

Util A	Util B	Util C
Dolutegravir		

References:
Tivicay Prescribing Information, August 2013, ViiV Healthcare.
Hoffman C, Mulcahy F, Goals and Principles of Therapy, Eradication, Cost, Prevention and Adherence. In: Hoffman C, Rockstroh J, Kamps BS, eds. HIV Medicine, Flying Publishers-Paris, Cagliari, Wuppertal, Sevilla, 2005:167-173.
Cheever LW, Chapter V: Adherence to HIV Therapies. In: A Guide to Clinical Care of Women with HIV/AIDS, 2005 Edition, HIV/AIDS Bureau, US Department of Health and Human Services.
http://hab.hrsa.gov/publications/womencare05/WG05chap5.htm
Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in HIV-1 Infected Adults and Adolescents. Department of Health and Human Services. Feb 12, 2013.
Available at: http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf.

57. Dolutegravir / Overutilization ___√___ _____ _____

Alert Message: Tivicay (dolutegravir) may be over-utilized. The manufacturer's maximum recommended dose of dolutegravir in treatment-naïve or treatment-experienced INSTI-naïve patients, not receiving potent UGT1A/CYP3A inducers, is 50 mg once daily.

Conflict Code: ER – Overutilization
Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Dolutegravir		Efavirenz
		Fosamprenavir/ritonavir
		Tipranavir/ritonavir
		Rifampin

Max Dose: 50 mg/day
Age Range: 12-999 yoa

References:
Tivicay Prescribing Information, August 2013, ViiV Healthcare.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

58. Dolutegravir / Overutilization ____√____ _____ _____

Alert Message: Tivicay (dolutegravir) may be over-utilized. The manufacturer's maximum recommended dose of dolutegravir in treatment-naïve or treatment-experienced INSTI-naïve patients when co-administered with the following potent UGT1A/CYP3A inducers: efavirenz, fosamprenavir/rtv, tipranavir/rtv or rifampin is 50 mg twice daily. The safety and efficacy of doses above 50 mg twice daily have not been evaluated.

Conflict Code: ER – Overutilization
Drugs/Diseases

Util A	Util B	Util C **(Include)**
Dolutegravir		Efavirenz
		Fosamprenavir/ritonavir
		Tipranavir/ritonavir
		Rifampin

Max Dose: 100 mg/day
Age Range: 12-999 yoa

References:
Tivicay Prescribing Information, August 2013, ViiV Healthcare.
Cottrel ML, Hadzic T, Kashuba AD. Clinical Pharmacokinetic, Pharmacodynamic and Drug-Interaction Profile of the Integrase Inhibitor Dolutegravir. Clin Pharmacokinet. 04 July 2013 (Online). [Epub ahead of print].

59. Dolutegravir / Therapeutic Appropriateness ____√____ _____ _____

Alert Message: Single agent antiretroviral therapy is not recommended in HIV-1-infected patients. Monotherapy does not demonstrate potent and sustained antiretroviral activity when compared to combination therapy with three or more antiretrovirals.

Conflict Code: TA - Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Dolutegravir		All Other HIV Antiretroviral Meds

References:
Tivicay Prescribing Information, August 2013, ViiV Healthcare.
Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in HIV-1 Infected Adults and Adolescents. Department of Health and Human Services. Feb 12, 2013.
Available at: http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf.
Panel on Antiretroviral Therapy and Medical Management of HIV-Infected Children. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. November 5, 2012;pp1-333.
Available at: http://aidsinfo.nih.gov/contentfiles/lvguidelines/pediatricguidelines.pdf

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

60. Dolutegravir / Therapeutic Appropriateness – Age < 12 yoa ___√___ _____ _____

Alert Message: Safety and effectiveness of Tivicay (dolutegravir) have not been established in pediatric patients younger than 12 years or weighing less than 40 kg, or in pediatric patients who are INSTI-experienced with documented or clinically suspected resistance to other INSTIs (raltegravir, elvitegravir).

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Dolutegravir		

Age Range: 0-11 yoa

References:
Tivicay Prescribing Information, August 2013, ViiV Healthcare.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

61. Dolutegravir / Dofetilide ___√___ _____ _____

Alert Message: Co-administration of Tivicay (dolutegravir) with Tikosyn (dofetilide) is contraindicated due to the potential for increased dofetilide plasma concentrations and the risk of serious and/or life-threatening events (e.g., QT prolongation and torsades de pointes). Dolutegravir inhibits the renal organic transporter OCT2 which is responsible for dofetilide elimination.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Dolutegravir	Dofetilide	

References:
Tivicay Prescribing Information, August 2013, ViiV Healthcare.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

62. Dolutegravir / Hepatitis B & C ___√___ _____ _____

Alert Message: Patients with underlying hepatitis B or C may be at increased risk for worsening or development of transaminase elevations with use of Tivicay (dolutegravir). Appropriate laboratory testing prior to initiating therapy and monitoring for hepatotoxicity during dolutegravir therapy are recommended in patients with underlying hepatic disease such as hepatitis B or C.

Conflict Code: MC – Drug (Actual) Disease Precaution
Drugs/Diseases

Util A	Util B	Util C
Dolutegravir	Hepatitis B	
	Hepatitis C	

References:
Tivicay Prescribing Information, August 2013, ViiV Healthcare.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

63. Dolutegravir / Inducers of CYP3A, UGT1A1, UGT1A3, UGT1A9, BCRP & P-gp ___√_____ _____ _____

Alert Message: Co-administration of Tivicay (dolutegravir) with drugs that induce CYP3A4, UGT1A1, UGT1A3, UGT1A9, BCRP or P-gp should be avoided because there is insufficient data to make dosing recommendations. Concurrent use of dolutegravir with drugs that induce the above enzymes and transporters may decrease dolutegravir plasma concentrations reducing the therapeutic effect.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Dolutegravir	Carbamazepine	
	Phenytoin	
	Oxcarbazepine	
	Phenobarbital	
	Modafinil	
	Dexamethasone	
	Nevirapine	

References:
Tivicay Prescribing Information, August 2013, ViiV Healthcare.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

*No marketed BCRP or UGT1A3 inducers at this time – will be added if/when inducers are marketed. Inducers which have specific dosing recommendations are not included in this criterion (see #4).

64. Dolutegravir / Etravirine / Negating Combo PI Therapy ___√_____ _____ _____

Alert Message: Co-administration of Tivicay (dolutegravir) and etravirine should be avoided, unless also administered with atazanavir/ritonavir, darunavir/ritonavir or lopinavir/ritonavir. The concurrent use of etravirine and dolutegravir, without these ritonavir-boosted protease inhibitors, significantly reduces the plasma concentrations of of dolutegravir resulting in decreased therapeutic effect.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Dolutegravir	Etravirine	Atazanavir
		Darunavir
		Ritonavir
		Lopinavir/Ritonavir

References:
Tivicay Prescribing Information, August 2013, ViiV Healthcare.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Cottrel ML, Hadzic T, Kashuba AD. Clinical Pharmacokinetic, Pharmacodynamic and Drug-Interaction Profile of the Integrase Inhibitor Dolutegravir. Clin Pharmacokinet. 04 July 2013 (Online). [Epub ahead of print].

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

65. Dolutegravir / Metformin ___√_____ _____ _____

Alert Message: Close monitoring is recommended when starting or stopping Tivicay (dolutegravir) and metformin together as metformin dose adjustment may be required. Concurrent use of these agents may result in increased metformin concentrations due to inhibition by dolutegravir of the renal organic cation transporter OCT2 which is responsible for metformin elimination.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Dolutegravir	Metformin	

References:
Tivicay Prescribing Information, August 2013, ViiV Healthcare.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.

66. Dolutegravir / Medications Containing Polyvalent Cations ___√_____ _____ _____

Alert Message: Tivicay (dolutegravir) should be administered 2 hours before or 6 hours after taking medications containing polyvalent cations. Polyvalent cations can bind dolutegravir in the GI tract and reduce its bioavailability.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Dolutegravir	Buffered Aspirin	
	Aluminum Hydroxide	
	Oral Calcium Supplements	
	Magnesium Hydroxide	
	Oral Iron Supplements	
	Sucralfate	
	Cation-containing Laxatives	
	Multivitamins	

References:
Tivicay Prescribing Information, August 2013, ViiV Healthcare.
Clinical Pharmacology, 2013 Elsevier/Gold Standard.
Cottrel ML, Hadzic T, Kashuba AD. Clinical Pharmacokinetic, Pharmacodynamic and Drug-Interaction Profile of the Integrase Inhibitor Dolutegravir. Clin Pharmacokinet. 04 July 2013 (Online). [Epub ahead of print].

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

67. Dolutegravir / Inhibitors of CYP3A, UGT1A1, UGT1A3, UGT1A9, BCRP & P-gp ___√___ _____ _____

Alert Message: Co-administration of Tivicay (dolutegravir) with drugs that inhibit CYP3A4, UGT1A1, UGT1A3, UGT1A9, BCRP or P-gp may result in increased dolutegravir plasma concentration as dolutegravir is a substrate of these enzymes and transporters. Potential for interaction is low and no dosage adjustment is recommended but monitoring may be appropriate.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Dolutegravir	Cyclosporine (3A4 & P-gp & BCRP)	
	Gemfibrozil (UGT1A1 & UGT1A3)	
	Ketoconazole (3A4 & UGT1A1 & P-gp)	
	Itraconazole (3A4 & P-gp)	
	Voriconazole (3A4 & P-gp)	
	Posaconazole (3A4 & P-gp)	
	Diltiazem (3A4 & P-gp)	
	Nicardipine (3A4 & P-gp)	
	Verapamil (3A4 & P-gp)	
	Nefazodone (3A4 & P-gp)	
	Clarithromycin (3A4 & P-gp)	

References:
Tivicay Prescribing Information, August 2013, ViiV Healthcare.
The Liverpool HIV Pharmacology Group (LHPG). Drug Interaction Charts. The University of Liverpool. Accessed Oct 15, 2013. Available at: http://www.hiv-druginteractions.org/Interactions.aspx
Pharmacology Weekly's Medication and Herbal Table of Substrates, Inhibitors and Inducers of UGT Enzymes in Phase II Metabolism. UGT Drug Reference Table. Accessed 10 2013.
Available at:
http://www.pharmacologyweekly.com/content/pages/drug-reference-table-cyp-p450-ugt-enzymes-transporters-ab

* Dolutegravir (DTG) is primarily metabolized via UGT1A1 with CYP3A4 as a secondary metabolic pathway (approximately 10%). DTG is also a substrate for UGT1A3, UGT1A9, BCRP or P-gp. Dolutegravir is a substrate for P-gp but because of its high permeability, significant alterations in absorption due to inhibition or induction is not expected (except with the HIV protease inhibitors). Interaction studies were conducted with boceprevir and telaprevir (potent CYP3A4 & P-gp inhibitors) and the increased DTG exposure was not considered clinically significantly as adverse events of DTG were mild and not exposure-dependent. There is no known UGT1A9 inhibitor, yet.

Stephanie McGee Azar, Acting Commissioner (X) Approve ( ) Deny 3-14-14 Date

R Moon
Robert Moon, M.D., Deputy Commissioner and Medical Director (X) Approve ( ) Deny 3-12-14 Date

Kathy Hall, Deputy Commissioner (✓) Approve ( ) Deny 3/10/14 Date