TMA DoD Pharmacoeconomic Center
Fort Sam Houston, TX

MTF Quarterly Webcast
December 13, 2012

Introduction

- Greetings from the PEC
- Purpose of the Quarterly MTF Webcast
- DCO Ground Rules
  - Type questions into the DCO system
  - Put on mute, not on hold
  - Contingency plan if DCO system stops working

Outline

- MTF Corner – Update on the DOD PEC Formulary Search Tool
- Review of August 2012 P&T Committee Meeting
- Overview of November 2012 P&T Committee Meeting
- Overview of February 2013 P&T Committee Meeting
- Utilization Management
  - New generics, shortages, BCF clarification
- Questions

MTF Corner

Update on the DOD PEC Formulary Search Tool

Jeremy Briggs, PharmD
Clinical Pharmacist

Review of August 2012 P&T Committee Meeting

Dave Meade PharmD, BCPS
Clinical Pharmacist

August 2012
DoD P&T Committee Meeting

- **Uniform Formulary Class Reviews**
  - Testosterone Replacement Therapies (transdermal and buccal formulations)
  - Low Molecular Weight Heparins

- **New Drugs in Previously Reviewed Classes**
  - Abatacept SC (Orencia)
  - Famotidine/ibuprofen (Duexis)
  - Ketorolac nasal spray (Sprix)
  - Linagliptin/metformin (Jentadueto)
  - Sitagliptin/metformin ER (Janumet XR)
  - Tafluprost ophthalmic solution (Zioptan)

Uniform Formulary Class Reviews

Testosterone Replacement Therapies (transdermal and buccal formulations)

Drugs in the Class

Active Ingredient	Brand (Manufacturer)	Strengths & Formulation	FDA Approval Date	Patent Expiration Date
Testosterone	Androderm (Watson Labs)	2 mg/24 hr, 4 mg/24 hr patches	Sep1995	Oct 2014
	Striant (Actient Pharma)	30 mg buccal tablets	June 2003	Aug 2019
	Androgel 1% (Abbott Labs)	25 mg/2.5 g, 50 mg/5 g gel packets, 12.5 mg /ACT gel pump	Feb 2000	Aug 2020 – Mar 2021
	*Androgel 1.62% (Abbott Labs)	20.25 mg/ACT gel pump	April 2011	Aug 2020
	Axiron (Eli Lilly)	30 mg/ACT lotion pump	Nov 2010	April 2017
	Fortesta (Endo Pharma)	10 mg/ACT (2%) gel pump	Dec 2010	Nov 2018
	Testim (Auxilium Pharma)	50 mg/5 gm gel packets	Oct 2002	April 2023

Oral and injectable products are not in the class

*Androgel 1.62% packets coming soon

ACT= actuation

Overall Clinical Effectiveness Conclusion

- No clinically relevant differences in efficacy among these products.
- Products for transdermal and buccal testosterone replacement effectively raise testosterone levels in hypogonadal men to the normal range when used in accordance with product labeling.
- Risk of transference to children and women with transdermal testosterone should be minimized;
  - Buccal tablets carry the lowest risk;
  - Topical products carry the highest risk.

Overall Clinical Effectiveness Conclusion

- Systemic Adverse Events (AE) are not considered to differ clinically across products
- Most frequent local AE:
  - transdermal application site reactions most frequent with patches, lower with gels;
  - oral application site reactions for buccal tablets; most are mild or transient
- Available evidence suggests no detrimental effect of TRT on prostate cancer or CV risk for most patients
- TRT has not been adequately studied in patients with stable sleep apnea, and should be avoided in patients with untreated or sub-optimally managed sleep apnea
- Physiologic doses of testosterone have not been associated with increased aggression

TRT: Testosterone Replacement Therapies

Testosterone Replacement Therapies Final Decision

BCF	UF	NF	Comments
Testosterone TD 2% gel pump; 10 mg/actuation (Fortesta)	Testosterone 50 mg/5 gm TD gel tubes (Testim) Testosterone 2 mg/24 hr, 4 mg/24 hr TD patches (Androderm) Testosterone 30 mg buccal tablets (Striant)	Testosterone TD solution pump; 30 mg/actuation; (Axiron) Testosterone 1%; 25 mg/2.5 gm, 50 mg/5 gm TD gel packets, and 12.5 mg/ actuation gel pump (Androgel 1%) Testosterone 1.62% TD gel pump; 20.25 mg/actuation (Androgel 1.62%)	All current and new users of topical and buccal testosterone replacement products must go through the PA process to ensure diagnosis of hypogonadism Fortesta 2% gel pump is the preferred product; all users of topical and buccal testosterone replacement products must have trial of Fortesta 2% gel prior to other products

TD: transdermal

TRT- PA CRITERIA

- Manual PA criteria should apply to all current and new users of the testosterone replacement therapies
- Coverage would be approved if the patient met any of the following criteria:
  - Manual PA criteria for all transdermal and buccal testosterone replacement products:
  - Patient is male and has a diagnosis of hypogonadism evidenced by 2 or more morning testosterone levels in the presence of symptoms usually associated with hypogonadism
  - Patient is a female and receiving testosterone for the following uses:
    - Treatment of hypoactive sexual desire in menopausal women (whether natural or surgical); or
    - Treatment of menopausal symptoms in women also receiving FDA-approved estrogen products (with or without concomitant progesterone)
  - Note that use in adolescents under the age of 17 is not approved and will be by appeal only

TRT- PA CRITERIA

- PA criteria would also apply specifically to transdermal gel tubes (Testim), transdermal patch (Androderm), buccal tablets (Striant), transdermal 1% gel pump and gel packets (Androgel 1%), transdermal 1.62% gel pump (Androgel 1.62%), and transdermal solution (Axiron):
  - Patient requires a testosterone replacement therapy that has a low risk of skin-to-skin transfer between family members (for Striant and Androderm only).
  - Patient has tried transdermal 2% gel pump (Fortesta) for a minimum of 90 days AND failed to achieve total testosterone levels above 400ng/dL (lab must be drawn 2 hours after Fortesta application) AND denied improvement in symptoms.
  - Patient has a contraindication or relative contraindication to Fortesta (e.g., hypersensitivity to a component [including alcohol]; concomitant disulfiram use) that does not apply to Testim, Androderm, Striant, Androgel 1%, Androgel 1.62%, or Axiron.
  - Patient has experienced a clinically significant skin reaction to Fortesta that is not expected to occur with Testim, Androderm, Striant, Androgel 1%, Androgel 1.62%, or Axiron.

Low Molecular Weight Heparins

Drugs in the Class

Generic Name	Brand	Formulations	FDA Approval	Patent Expiration
Unfractionated Heparin (UFH)	various	various		Generics
~~Ardeparin~~	~~Normiflow~~	~~Vial~~	~~1997~~	~~D/C'd 2002~~
Dalteparin	Fragmin	Syringe + vial	1994	Expired
Enoxaparin	Lovenox	Syringe + vial (brand)	1993	Generics 2010
Fondaparinux*	Arixtra	Syringe	2001	Generics 2011
~~Tinzaparin~~	~~Innohep~~	~~Vial~~	~~2000~~	~~D/C'd 2011~~

* Pentasaccharide

Overall Clinical Effectiveness Conclusion

- Generic formulations of enoxaparin and fondaparinux are equivalent to Lovenox and Arixtra.
- Fondaparinux has a lower risk of HIT than enoxaparin or dalteparin. Generics are now available.
- Dalteparin is not approved for DVT/PE treatment in the US, which limits the clinical utility.
- All 3 products have similar black box warning for epidural anesthesia; bleeding risks.
- Enoxaparin and fondaparinux require dosage adjustment in renal failure.
- Enoxaparin has the widest clinical utility, due to long history of use, largest number of FDA-approved indications, availability in several dosage strengths, and large number of clinical trials overall and in special populations (pregnancy, pediatrics).

HIT = Heparin-induced thrombocytopenia

Low Molecular Weight Heparins
Final Decisions

BCF	UF	NF	Comments
Enoxaparin (generic)	• Dalteparin (Fragmin) • Fondaparinux (generic)	None	enoxaparin generic designated BCF

New Drugs in Previously Reviewed Classes

Abatacept SC (Orencia)

Abatacept Subcutaneous (Orencia) Background

- Type of Drug:
  - Fusion protein; Selective T cell co-stimulation modulator
  - IV formulation (medical benefit) – available since 2005
    - FDA approved for moderate to severe RA as monotherapy or in conjunction with non-biologic DMARDs
    - Approved for JIA
  - Subcutaneous injection (pharmacy benefit) – approved August 2011
    - FDA approved for moderate to severe RA in adults only as monotherapy or in conjunction with non-biologic DMARDs

JIA: Juvenile Idiopathic Arthritis

Drugs in the Class

Generic	Brand	MoA	Frequency
Adalimumab	Humira	TNF	SQ (qow-qw)
Alefacept	Amevive	CL2	IM (qweek)
Anakinra	Kineret	IL1	SQ (qday)
Certolizumab	Cimzia	TNF	SQ (qow-qmonth)
Etanercept	Enbrel	TNF	SQ (qweek)
Golimumab	Simponi	TNF	SQ (q month)
Abatacept	Orencia	Tmod	SQ (q week)
Excluded from the Pharmacy Benefit			
Abatacept	Orencia	Tmod	IV
Infliximab	Remicade	TNF	IV
Tocilizumab	Actemra	TNF	IV
Ustekinumab	Stelara	TNF	SQ (q 6 months)

Overall Clinical Effectiveness Conclusion

- FDA-approval of SC Orencia was based on its demonstrated non-inferiority to IV Orencia with respect to ACR 20 responses following 6 months of therapy
- In an indirect comparison with Humira, SC Orencia demonstrated non-inferiority in proportion of patients achieving ACR 20 responses following 12 months of therapy
- An indirect comparison of ACR 50 response across major RCTs suggests similar response rates for SC Orencia as the anti-TNF agents

ACR= American College of Rheumatology

Overall Clinical Effectiveness Conclusion

- In general, abatacept's safety profile is similar to that of the anti-TNF biologics. When compared to adalimumab, less injection site reactions were observed
- Although SC abatacept provides a non-TNF biologic option for the treatment of RA and offers patient convenience over the abatacept IV formulation, there is currently insufficient data to conclude that abatacept offers improved efficacy, safety, or tolerability compared to the anti-TNF agents in the TIB class

Famotidine/ibuprofen (Duexis) & Ketorolac nasal spray (Sprix)

Drugs in the Class

Parameter	Duexis	Sprix
Type of Drug	• Fixed-combination of ibuprofen (NSAIDs) and famotidine (H2RA)	• Intranasal formulation of ketorolac
FDA Indications	• Relief of s/sxs of RA and OA • Decrease risk of UGI ulcers	• Short-term (≤5 days) management of moderate to moderately severe acute pain
Strengths	• 800mg/26.6mg Ibuprofen/famotidine tablets	• 15.75 mg/ nasal spray
Dosing	• One tablet three times per day • Famotidine total dose: 80 mg	• Adult patients < 65 years: 31.5 mg (one 15.75 mg spray in each nostril) every 6 – 8 hours • ≥ 65 years, renally impaired patients, and patients < 50 kg (110 lbs): 15.75 mg (one spray in only one nostril) every 6 – 8 hours

NSAIDs: Nonsteroidal anti-inflammatory drug, H2RA: H2-receptor antagonist, RA: rheumatoid arthritis and OA: osteoarthritis

Overall Clinical Effectiveness Conclusion – Duexis

- Duexis is the first fixed-dose combination of a non-selective NSAID with an H2 antagonist
  - Other gastroprotective agents on the UF include Vimovo, Arthrotec, and Celebrex
- In 2 phase III trials enrolling low risk patients, Duexis resulted in significantly reduced incidence of NSAIDs associated ulcer
- No studies evaluating clinically important UGI events (eg., bleeding, perforation, or obstruction)
- Compared to H2RA, coprescribing of PPIs with NSAIDs was associated with a lower risk of DU and GU (AHRQ 2011)
- Compared to misoprostol, coprescribing of PPIs with NSAIDs was associated with lower risk of DU and a similar risk of GU (AHRQ 2011)
- COX-2 inhibitor + PPI offers the greatest GI safety in high risk patients (Cochrane 2010)
- Ibuprofen 200 mg and famotidine 10 mg, 20mg are available OTC

Overall Clinical Effectiveness Conclusion – Duexis

- In REDUCE-1 and REDUCE-2 trials, the incidence of dyspepsia was slightly higher with ibuprofen than with Duexis
- In the follow-on safety study, greater number of patients in the Duexis group experience dyspepsia compared to ibuprofen group
  - Famotidine appeared to decrease the incidence of dyspepsia but this effect did not appear to persist into the safety follow-on population
- Although the fixed-dose combination of famotidine and ibuprofen offers the convenience of a gastroprotective agent with the NSAID, TID dosing may impact compliance
- Additionally, other fixed-dose combination drugs (NSAID with PPI [Vimovo] or NSAID with misoprostol [Arthrotec]) are preferred in systematic reviews or national professional guidelines for reducing GI ulcers
- Duexis offer no distinct clinical advantages to combination NSAIDs/gastroprotective agents already on the UF

Overall Clinical Effectiveness Conclusion – Sprix

- Ketorolac nasal spray is the first intranasal NSAID
- Allows for alternate route of administration for patients who require pain control after surgery and may be unable to tolerate oral medication
- SPID score was significantly higher in the ketorolac group compared with placebo but uncertain clinical relevance
- In 3 placebo comparison studies, morphine use was significantly lower in the ketorolac group for the first 48 hours
  - Debatable whether ketorolac nasal spray is the preferred option. Other opioid-sparing drugs on the UF include other NSAIDs and tramadol

SPID = summed pain intensity difference

Overall Clinical Effectiveness Conclusion – Sprix

- Associated with high incidence of local symptoms such as nasal discomfort or irritation
- Similar to other ketorolac formulations, total duration of Sprix use should not exceed 5 days
- Well known warnings not seen with other NSAIDs, included bleeding and renal dysfunction.
- Sprix offers no distinct clinical advantages to oral NSAIDs already on the BCF and UF

Linagliptin/metformin (Jentadueto) & Sitagliptin/metformin ER (Janumet XR)

Drugs in the Class

Active Ingredient	Brand (Manufacturer)	Strengths	FDA Approval Date
Sitagliptin	Januvia (Merck)	25mg, 50mg, 100mg	10/16/2006
Sitagliptin/ Metformin	Janumet (Merck)	50mg/500mg, 50mg/1000mg	03/30/2007
Sitagliptin/ Metformin ER	Janumet XR (Merck)	50mg/500mg, 50mg/1000mg, 100mg/1000mg	02/02/2012
Sitagliptin/ Simvastatin	Juvisync (Merck)	100mg/10mg, 100mg/20mg, 100mg/40mg	10/07/2011
Saxagliptin	Onglyza (BMS)	2.5mg, 5mg	07/31/2009
Saxagliptin/ Metformin ER	Kombiglyze XR (BMS)	2.5mg/1000mg, 5mg/500mg, 5mg/1000 mg	11/05/2010
Linagliptin	Tradjenta (Boehringer Ingelheim)	5mg	05/02/2011
Linagliptin/ Metformin	Jentadueto (Boehringer Ingelheim)	2.5/500mg, 2.5mg/850mg, 2.5mg/1000mg	01/30/2012

Jentadueto & Janumet XR Background

	Linagliptin/Metformin (Jentadueto)	Sitagliptin/Metformin XR (Janumet XR)
Type of Drug	DPP-4 Inhibitor and metformin immediate-release	DPP-4 Inhibitor and metformin extended-release
FDA Approval Type	505(b)(2)	505(b)(2)
FDA Approval Date	01/30/2012	02/02/2012
Patent Expiration	01/30/2015	2016-2026
FDA Approved Indications	Management of type 2 diabetes mellitus as an adjunct to diet and exercise in patients not adequately controlled on monotherapy	
Off-Label Uses	None	

Overall Clinical Effectiveness Conclusion

- Janumet XR and Jentadueto are indicated as adjunct to diet and exercise to improve glycemic control in patients with T2DM
- Janumet XR is dosed as either one or two tablets once daily, and Jentadueto is given as one tablet BID
- Janumet XR provides a once-daily combination option
- Both agents have similar A1c-lowering effects
- Janumet XR and Jentadueto, like all DPP-4 inhibitors, are considered lipid neutral
- When added to metformin, sitagliptin and linagliptin have shown a decrease in weight ranging from 0.4-1.4kg

Overall Clinical Effectiveness Conclusion

- Although safety and tolerability have not been studied with Janumet XR or Jentadueto, they are generally well-tolerated
- Common side effects are expected to be upper respiratory and GI-related
- Due to metformin and the risk of lactic acidosis, both Janumet XR and Jentadueto require renal dose adjustments, and should be avoided in hepatic insufficiency
- Although no outcomes studies have been performed with Janumet XR or Jentadueto, the TECOS and CAROLINA trials will address long-term outcomes

Tafluprost (Zioptan)

Tafluprost ophthalmic solution

- Background
  - 0.0015% solution
  - Supplied in 30 and 90 count single-use ampules
- Indication
  - Reduces elevated intraocular pressure (IOP) in patients with open-angle glaucoma (OAG) or ocular hypertension (OH)
- Potential Off Label Uses
  - Treatment for hypotrichosis (short eyelashes)

Drugs in the Class

Generic Name	Trade name	Manufacturer	Generic available	Strength, package size	FDA Approval
Bimatoprost	Lumigan	Allergan	No	0.01%, 0.03% 2.5, 5, 7.5 ml	Mar 2001
Travoprost	Travatan Z	Alcon	No	0.004% 2.5 and 5 ml	Sept 2006
Latanoprost	Xalatan	Pfizer	Yes	0.005% 2.5 ml	June 1996
Tafluprost	Zioptan	Merck	No	0.0015% 30, 90 unit dose	Feb 2012

Overall Clinical Effectiveness Conclusion

- Tafluprost ophthalmic solution 0.0015% is effective in reducing IOP; reduces IOP between 6–8 mmHg as do the other prostaglandins
- In one head-to-head trial, IOP-lowering with tafluprost was less than that of latanoprost
- The association of preservative-free tafluprost with decreased AEs remains to be determined
- Theoretically, a preservative-free formulation may enhance compliance, but no studies are available with tafluprost

IOP = intraocular pressure

New Drugs in a Previously Reviewed Class Final Decisions

BCF	UF	NF	Comments
		Abatacept SQ (Orencia)	PA limiting use to FDA-approved indications was approved in Nov 2011 QLs approved in Nov 2011 Retail: 4 syringes/28 days Mail Order: 8 syringes/56 days
		Ibuprofen/famotidine (Duexis) Ketorolac nasal spray (Sprix)	Quantity Limits for ketorolac nasal spray (Sprix): 5 bottles for 30-day supply in both the Retail Network and Mail Order Pharmacy
Sitagliptin/ metformin ER (Janumet XR)	Linagliptin/metformin IR (Jentadueto)		Must try metformin and sulfonylurea 1st before any DPP-4 drug Must try sitagliptin containing product 1st before Tradjenta, Jentadueto, Onglyza, or Kombiglyze XR
		Tafluprost (Zioptan)	

Overview of November 2012 P&T Committee Meeting

November 2012
DoD P&T Committee Meeting

- **Uniform Formulary Class Reviews**
  - Gastrointestinal Antibiotics (GI-2s)
    - Rifaximin, metronidazole, vancomycin, Dificid, Alinia, neomycin
  - Glucagon Like Peptide-1 Receptor Antagonists (GLP-1)
  - Hepatitis C drugs
  - Overactive Bladder (OAB) Drugs
- **New Drugs in Previously Reviewed Classes**
  - Oxycodone Immediate Release (Oxecta)
- **Utilization Management**
  - Ipratropium/albuterol (Combivent Respimat)
  - Azelastine/fluticasone nasal spray (Dymista)
  - Adalimumab (Humira)
  - Enzalutamide (Xtandi); Abiraterone (Zytiga)

Overview of February 2013 P&T Committee Meeting

February2013
DoD P&T Committee Meeting

- **Uniform Formulary Class Reviews**
  - COPD
    - Inhalers
    - Oral
  - Anticoagulants
    - Warfarin
    - Pradaxa
    - Xarelto
  - Topical Pain (non-opioid)
    - Lidoderm
    - Topical diclofenac products

Utilization Management

Utilization Management

- Cost-effective generic formulations now available for
  - Plavix
  - Xalatan ophthalmic solution
  - LMWH (Lovenox and Arixtra)
  - Maximize purchasing of the generic formulations for these medications
- Combivent respimat – not BCF
  - Will be reviewing COPD in Feb 2013
- Smoking cessation
  - Unknown implementation date
  - May P&T meeting decisions still on hold

Tricor Update

Tricor will be available on12/12/12; temporarily unavailable due to production delays

Tricor 145 mg is equivalent to
Antara 130 mg
Fenoglide 120 mg
Fibricor 105 mg
Lipofen 150 mg
micronized Lofibra 200 mg
non micronized Lofibra 160 mg
Triglide160 mg
Trilipix 135 mg

Guidance for Antiplatelet Drugs

- Clopidogrel remains BCF
  - For Acute Coronary Syndrome, stroke and TIA: clopidogrel is 1st–line
- Candidates for prasugrel (PCI only)
  - STEMI
  - DM
  - < 75 yo, > 60 kg, no history of stroke/TIA
- Candidates for ticagrelor
  - PCI and Medical Management
  - Need for CABG

Miscellaneous items

- New PEC website
  - Some technical issues
  - Email questions to PECUF@amedd.army.mil
- PECUF@amedd.army.mil
  - For other questions, formulary clarification, etc
- Next webcast will be held on the 14th of March, 2013 at 0900 and 1700 EST

Questions?

Webcast Evaluations

- Please assist us in improving the webcast presentations by completing an anonymous, 5-question survey
- Link: http://www.zoomerang.com/Survey/WEB22CTVSNWFRP
- Thank you!

PEC Contact Info

- 210-295-1271 (DSN 421-1271)
  - For PEC Clinical Staff
- 1-866-ASK 4 PEC (275-4732)
  - Pharmacy Operation Center
  - PECWEB@amedd.army.mil
    - Website issues
  - pdts.ameddcs@amedd.army.mil
    - Questions, assistance with PDTS, Business Objects
  - PECUF@amedd.army.mil
    - Clinical, formulary questions