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PHARMACY NEWS CAPSULE

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Infliximab (Remicade®) for Treatment Failure

Since infliximab's original FDA approval, it has been on formulary for outpatient use for various inflammatory disorders such as Crohn's disease, ulcerative colitis, rheumatoid arthritis, and ankylosing spondylitis without restrictions. Infliximab currently represents the second highest overall drug expenditure at Memorial Healthcare System and is essentially a "break-even" when the cost was compared to actual reimbursement. Therefore, MHCS will no longer accept NEW infliximab orders UNLESS prior treatment with Humira® or other TNF-antagonist has been made and it has been documented that the patient does not tolerate the alternative agents. This will not impact patients currently being treated with infliximab. It is not the intent to remove infliximab from formulary but only to designate this as an agent to be used AFTER failure with other TNF antagonist agents.

Ketorolac (Toradol®) Dose Limit

Ketorolac is an NSAID most commonly used peri-operatively and post-operatively to assist in the management of post-op pain. The current recommendations designate that the total systemic therapy should not exceed 5 days, due to the increased risk of developing severe gastrointestinal events that can result from prolonged courses of therapy. Therefore if no duration of therapy has been indicated by the prescriber, pharmacy will automatically schedule the ketorolac order to discontinue following 5 total days of therapy and the prescriber will be notified via written communication of this change.

INSIDE THIS ISSUE

Remicade for Treatment Failure	1
Toradol Dose Limit	1
Zofran QT Prolongation	1
Sedative/Hypnotic Policy Update	1
Formulary Approvals	2
Formulary Denials	2
Therapeutic Substitutions	2
Xarelto – New indication	3-4

Ondansetron (Zofran®) QT Prolongation

Due to the recent FDA warning, Memorial Healthcare System will no longer dispense IV ondansetron doses exceeding 16 mg per dose for the prevention of chemotherapy induced nausea and vomiting. This warning is based on a recently completed study suggesting a single 32 mg dose may prolong the QT interval, which could pre-dispose patients for Torsades de Pointes.

Sedatives/Hypnotics for Sleep Policy Update

This policy was amended to allow the use of diphenhydramine (Benadryl®) for sleep if a patient takes it at home. The maximum dose will be limited to 25mg. This addition was to prevent patients from being transitioned to zolpidem (Ambien®) when diphenhydramine works for the patient.

Approval of New Drugs:

1. Roflumilast (Daliresp®) – Roflumilast is indicated to reduce the risk of COPD exacerbations in patients with severe COPD associated with chronic bronchitis and a history of exacerbations. Roflumilast is not a bronchodilator and does not have a role in the treatment of acute bronchospasms associated with COPD. When used in combination with salmeterol or tiotropium, it produces a better improvement in FEV_1 compared with monotherapy with salmeterol or tiotropium. Roflumilast is not included in the current guidelines for the treatment of COPD.

2. Mirabegron (Myrbetriq®) – Mirabegron is a potent and selective beta-3 adrenoceptor agonist indicated for treatment of overactive bladder (OAB) with symptoms of urinary incontinence, urgency, and urinary frequency. Most drugs approved for the treatment of OAB are anticholinergic agents. Mirabegron may be useful for patients who are unable to tolerate the side effects associated with anticholinergic agents or patients for whom anticholinergic-induced mydriasis may increase intraocular pressure. The recommended initial dosage is 25mg once daily with or without food.

3. Romiplostim (Nplate®) – Romiplostim is a unique thrombopoiesis-stimulating agent for use in patients with thrombocytopenia and chronic ITP who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy. Its use has been associated with a reduced incidence of bleeding and a reduction in the need for administration of immunoglobulin and corticosteroids. Romiplostim will be restricted to Hematology specialists only.

4. Penicilloyl Polylysine (Pre-Pen®) – Pre-Pen® is a skin test antigen reagent indicated for the assessment of sensitization to penicillin in patients suspected to have clinical penicillin hypersensitivity. Initially, the ordering of Pre-Pen will be limited to the infectious disease specialists until more experience is gained with the use of this product.

Denial of New Drugs:

1. Aclidinium bromide (Tudorza®) – Aclidinium bromide is a long acting anticholinergic approved for maintenance treatment of bronchospasm associated with COPD, including chronic bronchitis and emphysema. Based on similar efficacy and safety between tiotropium (Spiriva®) and aclidinium the products can be considered therapeutically equivalent but the current lack of an institutional size limits the use of aclidinium to the outpatient setting and all orders for it will be substituted to a therapeutically equivalent dose of tiotropium (Spiriva®).

2. Tafluprost (Zioptan®) – Tafluprost is a prostaglandin agonist approved for reducing elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension. Tafluprost has no apparent advantage in terms of efficacy, tolerability, or adverse reactions over existing prostaglandin agonists. Orders for tafluprost will be automatically interchanged to latanoprost.

Therapeutic Substitutions

Direct Thrombin Inhibitors:

Due to the recent significant cost increase of lepirudin (Refludan®), a formulary interchange was approved to substitute lepirudin to argatroban for heparin induced thrombocytopenia (HIT). A very limited supply of lepirudin will be on hand for patients with severe hepatic impairment.

- Lepirudin (Refludan®) → Argatroban

Rivaroxaban (Xarelto®) Formulary Update

BACKGROUND: Rivaroxaban is an oral anticoagulant that inhibits platelet activation and fibrin clot formation via direct, selective and reversible inhibition of factor Xa in both the intrinsic and extrinsic coagulation pathways. Factor Xa catalyzes the conversion of prothrombin to thrombin. Thrombin both activates platelets and catalyzes the conversion of fibrinogen to fibrin.

Rivaroxaban was originally approved for formulary addition at the October 2011 P&T meeting following its initial approval for prevention of DVT following knee or hip surgery. Since this initial approval Rivaroxaban has also gained approval for stroke prophylaxis in patients with non-valvular atrial fibrillation (July 2011) and most recently for treatment of DVT or PE and for the reduction in the risk of recurrent DVT and/or PE (November 2012).

COMPARATIVE DOSING & ADJUSTMENTS PER INDICATION:

1) Nonvalvular Atrial Fibrillation

Creatinine Clearance	Recommended Dose
> 50 ml/min	20 mg QDAY (with evening meal)
15-50 ml/min	15 mg QDAY (with evening meal)
< 15 ml/min or HD patient	Avoid Use

2) Postoperative Thromboprophylaxis (Knee or Hip)

- Dose = 10 mg daily (Avoid use if CrCl < 30 ml/min.)
- **Initiate therapy after hemostasis has been established (~10 hours postoperatively).**
- Use for 12 to 14 days for knee replacement.
- Use for 35 days for hip replacement.

3) DVT/PE Treatment

Creatinine Clearance	Recommended Dose
> 30 ml/min	15mg BID for 21 days, Then 20mg QDAY (Take with food.)
< 30 ml/min	Avoid Use

RECOMMENDATION FOR DISCONTINUATION PRIOR TO SURGERY:

- Discontinue 24 hours prior to surgery

REVERSAL AGENTS:

- No specific antidote (not dialyzable)
- Prothrombin Complex Concentrate (PCC), APCC, or recombinant factor VIIa can be used

CONVERSION GUIDANCE:

Rivaroxaban to Warfarin

- Discontinue rivaroxaban and initiate both warfarin and a parenteral anticoagulant at the time the next rivaroxaban dose would have been administered (12 or 24 hours)

Warfarin to Rivaroxaban

- Discontinue warfarin and start Rivaroxaban when INR < 3.0

Lovenox to Rivaroxaban

- Initiate Rivaroxaban 0-2 hours before time of next scheduled dose of Lovenox would have been administered

Fondaparinux to Rivaroxaban

- Initiate Rivaroxaban 0-2 hours before time of next scheduled dose of Fondaparinux would have been administered

Dabigatran to Rivaroxaban

- Initiate Rivaroxaban 0-2 hours before time of next scheduled dose of Dabigatran would have been administered

Heparin to Rivaroxaban

- Stop heparin infusion and initiate rivaroxaban simultaneously

Rivaroxaban to Heparin drip/LMWH/Fondaparinux

- Initiate heparin drip/LMWH/Fondaparinux when next dose of rivaroxaban would have been administered (12 or 24 hours)

*****Remember that rivaroxaban can contribute to INR elevation; therefore, initial INR measurements after initiating warfarin may be unreliable*****