



PHARM NOTES



Neil Medical Group Pharmacy Services Division

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Anticoagulation: A Focus on Warfarin Therapy

Warfarin (Coumadin®) therapy is a frequently prescribed therapy for those patients in need of anticoagulation. The word anticoagulant literally means “against clotting of blood”. A clot is a thick or sticky clump of blood which can result from or lead to serious health problems. Warfarin works by blocking the body’s ability to make clotting factors that rely on Vitamin K. It prevents clots from forming or stops a clot from enlarging and allows the body to dissolve the clot. Its starts to work in as quickly as one day, but takes several days (4-5) for a therapeutic level to be reached.

Anticoagulation therapy can be used for the prevention and treatment of the following conditions associated with increased risk of blood clots: atrial fibrillation, cerebral vascular attack, myocardial infarction, deep vein thrombosis, pulmonary embolism, cancer, valvular heart disease and heart valve replacement, peripheral vascular disease and pregnancy. Doses are very patient specific and are often adjusted frequently. Lab tests called prothrombin time (PT) and International Normalized Ratio (INR) are checked to see how quickly a patient’s blood is able to clot, with the INR now being the gold standard. These values guide the prescriber on the dose adjustments needed. Typically an INR range of 2-3 is the target, except in cases of mechanical heart valves or patient’s with extremely high risk of clots when the target range is higher. INR’s may be checked frequently (every few days or once a week) until stable and then usually monthly.



Many factors can cause INR values to change including: diet, medications and supplements. If an INR value becomes too high, most often doses are ordered to be held until the INR returns to the treatment range and a new lower dose is then started. If a patient is actively bleeding with an elevated INR, Vitamin K may be given orally or by IM, SC or slow IV infusion to reverse warfarin effects.

Warfarin has many drug-drug interactions. Any medication that also decreases clotting times will potentiate the effect of warfarin. Examples include: Aspirin, NSAIDS, Low-Molecular weight heparins and Plavix®. Certain antibiotics may also increase the effect of warfarin (quinolones, metronidazole, tetracyclines, sulfonamides, macrolides). The increased effect from antibiotic use can be due to the destruction of Vitamin K producing flora in the gi tract or by decreased hepatic metabolism of warfarin depending on the antibiotic. The pharmacy will alert the facility by phone call or letter of the potential interaction.

The facility should then notify the physician. Often, the physician will order more frequent INRs while the antibiotic is being administered.

Sometimes overlooked are the drug-food interactions that can affect warfarin therapy. Remember that warfarin blocks Vitamin K dependent clotting factors. Green leaf vegetables and other vitamin K rich foods (beef or pork liver, margarine, mayo and oils) can decrease the effectiveness of warfarin.

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New Drug Update: Mircera® - the First Continuous Erythropoietin Receptor Activator

Chronic kidney disease (CKD), also known as chronic renal failure (CRF), affects approximately one million people at an annual health care cost surpassing \$20 billion dollars. Inevitably, many of these people wind up on dialysis as a result of one of three central causes; diabetic neuropathy, hypertension, and/or glomerulonephritis. Dialysis is the artificial replacement for compromised kidney function in these patients as the body struggles to compensate. Specifically, Mircera is a novel new drug indicated for the treatment of anemia associated with CKD, including patients on dialysis and those not on dialysis, designed to increase quality of life and ease the daily burden. Patients may be directly switched to once monthly Mircera from traditional agents, whose frequency is often up three times per week. Mircera is the first continuous erythropoietin receptor activator (C.E.R.A.) and due to its continuous activity at receptor sites involved in stimulating red blood cell production, Mircera will offer the ability to provide targeted, stable and sustained control of anemia.

...At a glance

Generic Name: Methoxy polyethylene glycol-epoetin beta

FDA Approval: November 14th 2007

Drug Category: Continuous erythropoietin receptor activator (C.E.R.A.)

Use: Treatment of anemia associated with chronic kidney disease (CKD) in adults, including patients on dialysis and not on dialysis. Safety and efficacy of therapy in other indications have not been established.

Pregnancy Risk Factor: C (There is no adequate experience in human pregnancy.)

Contraindications: Hypersensitivity to the active substance or any of the excipients and patients with uncontrolled hypertension.

Warnings/Precautions: Increased mortality, serious cardiovascular and thromboembolic events, and tumor progression: Renal Failure. Individualize dosing to maintain Hgb levels within the range of 10-12 g/dL. Mircera is not indicated for the treatment of anemia due to cancer chemotherapy.

Adverse Reactions: Mircera compared to shorter-acting erythropoiesis stimulating agents [ESAs].

| Adverse Reaction [$\geq 5\%$] | Mircera | ESAs |
|-----------------------------------|---------|------|
| Hypertension (HTN) | 13 | 14 |
| Diarrhea | 11 | 11 |
| Nasopharyngitis | 11 | 10 |
| Headache (HA) | 9 | 9 |
| Upper respiratory tract infection | 9 | 8 |
| Muscle spasm | 8 | 7 |
| Postural hypotension | 8 | 6 |
| Fluid overload | 7 | 7 |
| Cough | 6 | 5 |
| Back Pain | 6 | 5 |
| Vomiting | 5 | 6 |
| Urinary Tract Infection (UTI) | 5 | 6 |



Mircera continued...

| Adverse Reaction [≥ 5%] | Mircera | ESAs |
|---|---------|------|
| Pain in extremity | 5 | 6 |
| Arteriovenous fistula thrombosis | 5 | 5 |
| Arteriovenous fistula site complication | 5 | 5 |
| Hypotension | 5 | 4 |

Drug Interactions: No interaction studies have been performed. There is no evidence that Mircera alters the metabolism of other medicinal products.

Dosage:

Single-use prefilled syringe – 50 mcg per 0.3 ml, 75 mcg per 0.3 ml, 100 mcg per 0.3 ml, 150 mcg per 0.3 ml, 200 mcg per 0.3 ml, 250 mcg per 0.3 ml, 400 mcg per 0.6 ml, 600 mcg per 0.6 ml, 800 mcg per 0.6 ml.

Single-use vials – 50, 100, 200, 300, 400, 600, 1000 mcg/ml.

Starting Dose:

Patients not currently treated with an ESA: 0.6 mcg/kg body weight administered as a single IV or SC injection once every 2 weeks. Mircera should be dosed to achieve and maintain Hgb between 10 and 12 g/dL. Once attained, Mircera may be administered once monthly using a dose that is twice that of the every-2-week dose (1.2 mcg/kg) and titrated as necessary.

Patients currently treated with an ESA: Mircera can be administered once every 2 weeks or once monthly to patients whose hemoglobin has been stabilized by treatment with an ESA.

Dosing Table:

| Previous epoetin alpha dose (units/wk) | Previous darbepoetin dose (units/wk) | Mircera dose | |
|--|--------------------------------------|--------------------|------------------|
| | | Once monthly (mcg) | Once q2wks (mcg) |
| < 8,000 | < 40 | 120 | 60 |
| 8,000 to 16,000 | 40 to 80 | 200 | 100 |
| > 16,000 | > 80 | 360 | 180 |

Administration: The solution can be administered either SC or IV. Mircera may be injected SC in the abdomen, arm, or thigh; all three injection sites are equally suitable. However, the IV route is recommended for patients receiving hemodialysis because the IV route may be less immunogenic.

Monitoring: Baseline Hgb, every two weeks until stabilized, and then at 2-4 week intervals.

Storage/Stability: The recommended storage temperature is at 2° to 8°C (36° to 46°F). Do not freeze or shake. Protect from light. Storage over the recommended temperature is permissible only for temperatures up to 25°C (77°F) and for no more than 7 days [for vials] and no more than 30 days [for prefilled syringes].

Article by Matthew Hogan, Pharm. D. Candidate at UNC– Chapel Hill School of Pharmacy



Intravenous Bisphosphonate Therapy for Osteoporosis: Boniva® IV

Generic name: ibandronate

Pharmacologic Category: bisphosphonate

Indications: treatment of osteoporosis in postmenopausal women

Mechanism of Action:

Inhibits osteoclast activity and reduces bone resorption and turnover. In postmenopausal women, it reduces the elevated rate of bone turnover, leading to, on average, a net gain in bone mass.

Dosing:

- 3 mg every 3 months administered intravenously over a period of 15 to 30 seconds

No dose adjustment is necessary for patients with mild or moderate renal impairment where creatinine clearance is equal to or greater than 30 mL/min

Administration:

- Boniva injection must only be administered intravenously using the enclosed needle. Prefilled syringes are for single use only. Boniva injection must not be mixed with calcium-containing solutions or other intravenously administered drugs.

Contraindications:

- Known hypersensitivity to Boniva injection, uncorrected hypocalcemia

Warnings/Precautions:

- Boniva may cause a transient decrease in serum calcium values
- Disease related concerns: Hypocalcemia, hypovitaminosis D, and other disturbances of bone and mineral metabolism must be effectively treated before starting Boniva injection therapy. Patients must receive supplemental calcium and vitamin D.
- Use is not recommended with severe renal impairment ($Cl_{cr} < 30$ mL/minute or serum creatinine > 2.3 mg/dL).
- Concerns related to adverse effects:
Bone/joint/muscle pain: Infrequently, severe (and occasionally debilitating) bone, joint, and/or muscle pain have been reported during bisphosphonate treatment. The onset of pain ranged from a single day to several months. Symptoms usually resolve upon discontinuation. Some patients experienced recurrence when re-challenged with same drug or another bisphosphonate; avoid use in patients with a history of these symptoms in association with bisphosphonate therapy.
- Osteonecrosis of the jaw: Bisphosphonate therapy has been associated with osteonecrosis, primarily of the jaw; this has been observed mostly in cancer patients, but also in patients with postmenopausal osteoporosis and other diagnoses. There is no data addressing whether discontinuation of therapy reduces the risk of developing osteonecrosis; however, as a precautionary measure, dental exams and preventative dentistry should be performed prior to placing patients with risk factors on chronic bisphosphonate therapy. Invasive dental procedures should be avoided during treatment.

Side Effects:

Similar to that of the oral formulation: GI Neuromuscular/skeletal

In clinical studies, the injection formulation had a higher incidence of the following adverse effects compared to the oral formulation:

| | |
|---------------------------------------|---------------------------|
| Diarrhea (2.8% vs 2.4%) | Arthralgia (9.6% vs 8.6%) |
| Myalgia (2.8% vs 0.9%) | Headache (3.6% vs 2.6%) |
| Influenza like illness (4.9% vs 1.1%) | |

Local reactions at the injection site, such as redness or swelling, were observed infrequently.

Boniva IV Advantages:

- Patients do not have to sit or stand for 30-60 min or take the medication with a glass of water 1 hr prior to first meal.
- Patients do not have to be able to swallow
- Less incidence of gastrointestinal side effects
- Doctors directly witness medication compliance

Pregnancy Implications: risk factor C: Safety and efficacy have not been established in pregnant women

How Supplied:

3 mg/3 mL single-use, clear glass prefilled syringe. Each syringe is a 5 mL (5 cc) volume syringe supplied with a 23-gauge, 3/4 inch needle with needle-stick protection device.

Continued on page 6...



Inservice: Medication Patch Pointers

General pointers for administration of medicated patches

- Wear gloves or wash hands prior to patient contact and after patient contact.
- Remember to remove previous patch from patient.
- Apply to dry, clean, intact skin on either the abdomen, hip or buttocks. If skin needs to be cleansed, use plain water only. Do not use soaps, oils, lotions, alcohol, or any other agents that might irritate the skin or alter its characteristics. Let area dry completely before applying the patch.
- Use firm pressure to apply – you may need to press for 20-30 seconds.
- Date and initial the patch when applied.
- Refer to facility policy regarding monitoring and verification of patch placement (facilities may require patch placement verification documentation daily or during each nursing shift).
- When disposing, fold the patch in half to avoid contact with skin and to prevent other individuals or animals from coming into contact with the adhesive side of the patch.
- The patch may be worn in the shower, but high heat should be avoided.

Proper Administration of Oxytrol® Patches

Oxytrol® transdermal patches contain oxybutynin for management of bladder incontinence.

- Select a new site for each application and AVOID reapplying to the same site within a 7 day period.
- Apply one patch twice weekly (every 3-4 days).

Proper Administration and Removal of Duragesic® Patches

Duragesic® patches are used to manage pain in patients who need a continuous dosing regimen of opioid therapy.

- **Signatures of two nurses are needed, when documenting the removal and destruction of the used Duragesic® patch. This is documented on the declining count sheet as nurse removing and destroying patch and nurse witnessing removal and destruction.**
- Flush the patch immediately in the toilet.

Coverings for Duragesic patches are available from the manufacturer – but are currently not available for the generic Fentanyl patches. The edges of the patches may be taped down with first-aid tape instead. Note that occlusive dressings should NOT be placed over the patches – they could alter the rate or extent of absorption.

Proper Administration of Exelon® Patches

Exelon® patches are used for treatment of Alzheimer's Disease.

- Patch is intended to be worn for 1 day and sites should be rotated and only used once in a 14 day period.

Inservice by Bobbie Hall, PharmD., CGP, Education Coordinator and Traci Burge, Pharm.D.

Remember to set your clocks forward one-hour on March 9th for Daylight Savings Time!



Meet Our Pharmacy Managers: Doug Hazelgrove, R.Ph. and Jim Rourk, R.Ph.

Neil Medical Group would like to introduce our pharmacy operations managers in the Kinston and Mooresville pharmacies. Doug Hazelgrove, R.Ph. is the new manager in the Kinston location. He spent his early childhood in Kinston, NC before moving to Wilmington, NC. He then attended pharmacy school at the University of North Carolina at Chapel Hill. He first worked as a pharmacist at Revco for 15 years before coming to Neil Medical Group. Doug has been with Neil Medical Group for 11 years before this most recent promotion to manager. He and his

wife of 26 years have three children. His oldest son is a graduate of UNC-Chapel Hill while his daughter and youngest son attended and currently attend NC State. I am sure game days in the Hazelgrove home are quite exciting! In his spare time, Doug enjoys working in his yard, painting, playing golf and spending time with his German shepherd dog. He wants



everyone to know that he considers it a pleasure to provide pharmacy services to the facilities and their residents.

Jim Rourk, R.Ph. has assumed the position of pharmacy manager in the Mooresville pharmacy. Jim grew up in Myrtle Beach, SC and earned his pharmacy degree from the University of North Carolina at Chapel Hill. He then worked at CVS for seven years in the Greensboro, NC area before joining Neil Medical Group. Jim served as the pharmacy manager in the Kinston, NC pharmacy site for 10 years before his recent move to Mooresville. When not at Neil Medical Group, Jim enjoys bike riding, working out at the gym and watching sports.



Article by Traci Burge, Pharm.D.

... Boniva IV—continued from page 4

Storage: Store at 25°C (77°F); excursions permitted between 15° and 30°C

Patient Information:

- Boniva injection should be administered once every 3 months. If the dose is missed, the injection should be administered as soon as it can be rescheduled.
- Patients must receive supplemental calcium and vitamin D.

Studies:

- DIVA Trial

The effectiveness and safety of BONIVA Injection 3 mg once every 3 months was demonstrated in a randomized, double-blind, multinational, noninferiority study (DIVA Study) in 1358 women with postmenopausal osteoporosis (L2-L4 lumbar spine BMD, T-score below -2.5 SD at baseline). The control group received BONIVA 2.5 mg daily oral tablets. The primary efficacy parameter was the relative change from baseline to 1 year of treatment in lumbar spine BMD, which was compared between the intravenous injection and the daily oral treatment groups. All patients received 400 IU vitamin D and 500 mg calcium supplementation per day.

Results: In the ITT efficacy analysis, the least-squares mean increase at 1 year in lumbar spine BMD in patients (n=429) treated with BONIVA Injection 3 mg once every 3 months (4.5%) was statistically superior to that in patients (n=434) treated with daily oral tablets (3.5%). The mean difference between groups was 1.05% (95% CI: 0.53%, 1.57%; p<0.001). The mean increases from baseline in total hip BMD at 1 year were 2.1% in the BONIVA Injection 3 mg once every 3 months group and 1.5% in the BONIVA 2.5 mg daily oral tablet group. Consistently higher BMD increases at the femoral neck and trochanter were also observed following BONIVA Injection 3 mg once every 3 months compared to BONIVA 2.5 mg daily oral tablet.

Article written by Jason Ray, Pharm.D. Candidate Wingate University



Test Your Medication Knowledge

1. Of the following medication orders, which one is complete?

- a. Tylenol 650mg po prn
- b. Mylanta 30 cc po bid prn
- c. Digoxin 0.125 mg po every other day
- d. Amoxicillin 250 mg po for ten days

2. What is the med error in this example?:

Nurse Smith is administering her 9PM meds to a resident. She first administers the Timoptic XE[®] eye gel at 9:02 and follows with Xalatan[®] eye drops immediately after.

- a. The nurse should have waited between the eye medications to assure proper contact with the eye
- b. The nurse should have given the resident's PO medications first
- c. The Timoptic XE[®] should be given after the Xalatan[®] since the XE is a gel.
- d. a and b are correct
- e. a and c are correct
- f. None are correct because the nurse administered the medications correctly

3. What is the expiration date of opened vials of insulin:

- a. 6 months
- b. 45 days if opened
- c. 28 days
- d. 28 days out of refrigerator

4. It is okay to mix medications together when giving them via g-tube.

TRUE/FALSE

5. The fax cut-off time (Monday-Friday) for NEW orders from the pharmacy is:

- a. 3pm
- b. 4pm
- c. 5pm
- d. 6pm

6. Medications should be administered within which time frame?

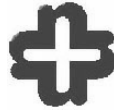
- a. Up to 30 minutes before or after the time ordered
- b. Up to 15 minutes before or after the time ordered
- c. 30 minutes before the time ordered
- d. Up to 1 hour before or after the time ordered
- e. 1 hour after the time ordered

Answers on page 8...

7. A resident has an order for a medication to be given "with food". Which of the following is true?

- a. Administer the medication 30 minutes before and up to 30 minutes after the meal.
- b. Administer the medication while the resident is eating or up to 1 hour after the meal.
- c. Administer the medication with 2 ounces of applesauce.
- d. Administer the medication with milk instead of water.





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Anticoagulation continued from page 1

Patients are encouraged to eat a well balanced diet and to avoid eating larger than their normal amounts of high Vitamin K rich foods.

All medications have potential side effects. Of course, since warfarin decreases clotting factors in the blood, minor bleeding can be expected such as: easy bruising, bleeding gums, nosebleeds and bleeding with minor cuts. Major bleeding symptoms include: red or dark bowel movements, coughing up red colored mucous, severe headache or stomachache or bleeding from a cut that lasts over 10 minutes. Other potential side effects are fever/chills, chest pain, weakness/dizziness, purple toes (rare) or skin necrosis (rare). Due to the potential for serious bleeding, patients that are a high fall risk may not be started on warfarin therapy even if they have increased risk for clots.

In the nursing home, the resident on anticoagulation therapy should be monitored closely. Care should be taken when giving ADL care to avoid cuts and bruising. INR monitoring should be scheduled as ordered and when doses are changed, the old doses of warfarin should be removed immediately from the medication cart to avoid dosing mistakes.

Article by Traci Burge, Pharm.D.

**MARs for
End-of-the-Month
Admissions**

Are you tired of writing out admission orders and the next month's orders for those residents entering the facility at the end of a month?

Just a reminder that Neil Medical Group MAR departments send out monthly MARs based on a date chosen by the facility DON. New admissions often enter the facility after the monthly MARs have been run and delivered to the facility. Both pharmacies (Kinston and Mooreville) run MARs for these new admissions two days before the last day of the month to be delivered to facilities – just another way Neil Medical Group tries to assist the facility!

Answers to the quiz on page 7:

- | | |
|---------|------|
| 1. c | 5. c |
| 2. e | 6. d |
| 3. c | 7. b |
| 4. TRUE | |

Pharm Notes is a bimonthly publication by Neil Medical Group Pharmacy Services Division. Articles from all health care disciplines pertinent to long-term care are welcome. References for articles in Pharm Notes are available upon request. Your comments and suggestions are appreciated. Contact:

Traci Burge

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Note: Periodically, we are asked to add a name to our distribution list. At this time, copies of Pharm Notes newsletters are distributed in bulk to Neil Medical Group customers only.