Oncology Pharmacy Newsletter

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The Oncology Pharmacy Newsletter is publication dedicated to providing useful information for the staff treating patients who come to the Oncology Outpatient Pavilion.

We welcome questions and requests for topics.

References available upon request.

New Emergency Med Kits

Our Emergency Med Kits, found in the Pyxis, have been reformulated to contain Duonebs, as well as albuterol nebs. The other contents remain unchanged. Care must be used in selecting the correct nebulized agent from the bag.

Contents include:

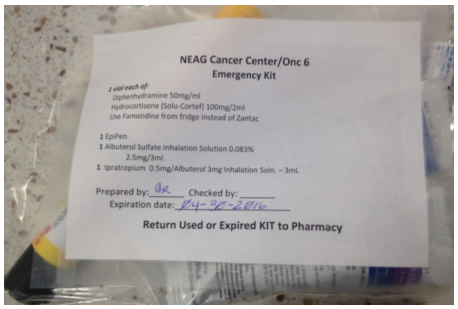
Diphenhydramine 50mg/ml x 1

Hydrocortisone 100mg/2ml x1

EpiPen x 1

Albuterol inhalation solution 0.083% 2.5mg/3ml x 1

Ipratropium 0.5mg/albuterol 3mg/ 3ml x1 (DuoNeb)



Famotidine is obtained from the Pyxis refrigerated stock. The nebulizer set up is found hanging on the Code Cart.

What's-it-Otide? Comparing the Three Somatostatin Analogues

Two newer agents, lanreotide depot, and pasireotide LAR, have joined octreotide LAR for use in treating acromegaly. Lanreotide depot and octreotide LAR are also indicated in other oncologic disease states associated with other hormones affected by somatostatin.

These agents mimic the natural hormone, somatostatin, and bind to somatostatin receptors. They suppress growth hormone, glucagon, insulin, thyroid stimulating hormone and luteinizing hormone. They also decrease release of serotonin, gastrin, vasoactive intestinal peptide, secretin, and motilin.

Acromegaly doses are adjusted based upon growth hormone (GH) and insulin-like growth factor (IGF-1) levels. Doses in the other indicated disease states are based upon clinical response.

Similar pharmacology leads to similar side effect profiles, but octreotide has been available longer, and data on the newer agents are still accumulating. (*See next page*)

Major drug interactions occur with all of these agents. Most commonly, doses of oral antiglycemic medications and insulin may need adjustment due to changes in glucose metabolism. Monitoring of serum glucose levels should continue after discontinuation of octreotide. Cyclosporine levels are known to be decreased, and may lead to organ rejection in transplant patients. Bromocriptine and other drugs that are hepatically metabolized (by CYP3A4) may experience decreased clearance and higher levels. Drugs with cardiac effects such as bradycardia or QT prolongation may see exacerbation of these effects. Due to the effects these agents have on fat and nutrient absorption, some medications may exhibit changes in absorption.

All of these agents MUST be brought to room temperature for 30 minutes before mixing to ensure complete delivery of the medication, so please let Pharmacy know you are expecting a patient. Once mixed must each must be used immediately. They all may be returned to refrigeration for use if never mixed and at room temperature for less than 24 hours.

Before starting Octreotide LAR, patients should have a trial of 2 or more weeks of octreotide acetate to determine if they can tolerate octreotide therapy. If treating Carcinoid tumors or VIPomas, the two agents must be overlapped for at least 2 weeks while the LAR formulation is reaching therapeutic systemic levels or patients' symptoms will reappear. It takes about 3 weeks after a single injection for the concentrations of octreotide LAR or pasireotide LAR to reach stable systemic levels and up to 3 monthly injections to reach steady state. Break through symptoms may occur in otherwise stabilized patients. If this occurs, short term treatment with octreotide acetate may be used to control symptoms in patients receiving monthly Octreotide LAR. Subcutaneous administration of lanreotide depot yields a burst of drug on the day of administration, followed by steady delivery of the remaining dose over the dosing interval. *See next page...*

Comparison of Somatostatin Analogues

Drug	Octreotide LAR	Lanreotide	Pasireotide LAR
Brand Name	Sandostatin® LAR Depot	Somatuline® Depot	Signifor® LAR
Strengths	10mg, 20mg, 30mg	60mg, 90mg, 120mg	20mg, 30mg, 60mg
Indications	-Acromegaly -Carcinoid Tumors -VIPomas (vasoactive intestinal peptide)	-Acromegaly -Gastroenteropancreatic neuroendocrine tumors	-Acromegaly
Off label uses	-Gastroenteropancratic neuroendocrine Tumors		
Doses Doses are modified based on response	**Acromegaly:** 10-40mg every 4 weeks. **Other Indications:** 10-30mg every 4 weeks. Severe Renal or Hepatic impairment: No adjustments for renal impairment unless dialysis dependent. If dialysis dependent or cirrhosis present, start at 10mg every 4 weeks and increase if tolerated.	**Acromegaly:** 60mg, 90mg or 120mg every 4 weeks. Stable patients may tolerate 120mg every 6-8 weeks. CrCl< 60 ml/min or moderate or severe hepatic impairment. May only tolerate 60mg every 4 weeks. Use higher doses with caution. Dose unknown in severe renal dysfunction. **Gastroenteropancratic Neuroendocrine tumors**: 120mg every 4 weeks. CrCl <30ml/min or hepatic impairment: Use with caution, not studied.	**Acromegaly:** 40mg every 4 weeks. Maximum 60mg every 4 weeks. No changes necessary with impaired renal function. Dose unknown in severe renal dysfunction. Moderate Hepatic Impairment: 20mg (max 40mg) every 4 weeks. Do not use in severe hepatic impairment.
Administration	INTRAMUSCULAR only. Bring to room temp before mixing. Administer immediately after mixing in gluteal muscle only alternating sites.	SUBCUTANEOUS only. Bring prefilled syringe to room temp. Administer deep SC in upper outer quadrant of buttocks alternating sites.	INTRAMUSCULAR only. Bring to room temp before mixing. Administer immediately after mixing in gluteal muscle only alternating sites.
ASEs (Not an exhaustive list. If your patient complains of other ASEs, please contact Pharmacy)	-Hyper or hypoglycemia, hypothyroidism, weight loss, other endocrine changes -Bradycardia, peripheral edema, hypertension, arrhythmias, hypokalemia, hypomagnesemia -Itching, rash, alopecia, injection site pain or redness -Abdominal pain, nausea, diarrhea, constipation, gallstones, pancreatitis, steatorrhea -Headache, insomnia, fatigue, anxiety, dizziness, confusion, flu-like symptoms, weakness, arthralgia, myalgia -anemia		
	-antibody to drug (of uncertain clinical significance) -nasopharyngitis - increased LFTs	-antibody to drug (of uncertain clinical significance)	-Elevated INR(slight), hemorrhage or hematoma at injection site -nasopharyngitis - increased LFTs
Status/MAR issues	Formulary for Outpatients	Formulary for Outpatients	INDICATE PATIENT'S OWN SUPPLY on MAR

References: LexiComp Online, September 23, 2015
Sandostatin® LAR Package Insert, Novaritis Pharmaceuticals, UK, 09/2014
Somatuline® Depot Package Insert, Ipsen Pharma Biotech, Signes, France, 12/2014
Signifor® LAR Package Insert, Novartis Pharma AG, Basel, Switzerland, 12/2014

NEW ORAL BREAST CANCER MEDICATION

Heather Kutzler, UConn School of Pharmacy, 2016 PharmD. Candidate

Overview[1]: Palbociclib (Ibrance) is an orally administered targeted oncology drug. It is a small molecule cyclin-dependent kinase (CDK) inhibitor selective for CDK4 and CDK6. Palbociclib was approved in February 2015 and is a first-line option to be used in combination with letrozole for the treatment of postmenopausal women with estrogen receptor (ER) positive, human epidermal growth factor receptor 2 (HER2) negative metastatic breast cancer.

Why this drug is exciting[1]: On average, patients using palbociclib in addition to letrozole have an additional 10 months of progression-free survival compared with letrozole alone (20.2 months compared to 10.2 months). Palbociclib is one of two targeted therapies for ER+/HER2- metastatic breast cancer.

Mechanism[2]: Palbociclib works by arresting the cell cycle in the G1 (growth) phase, preventing it from entering the S (DNA replication) phase.

Dosing[2]: Palbociclib must be used in combination with letrozole. The combination is more effective at preventing the cell from entering the S phase than either agent alone. Palbociclib is supplied as 75 mg, 100 mg, and 125 mg oral capsules. Opening or crushing the capsules is not advised. The recommended dose is one 125 mg capsule taken once daily with food and letrozole 2.5 mg for 21 consecutive days followed by 7 days off treatment. The total cycle is 28 days.

The dose should be taken at approximately the same time each day. If the patient vomits or misses a dose, an additional dose should not be taken that day. The patient should take the next dose the following day at the usual time. There are no dose adjustments for renal or hepatic impairment. For severe (i.e. grade 3-4) adverse effects, reduce the dose to 100 mg daily. The dose can further be reduced to 75 mg daily; however, if any less is required then therapy should be discontinued.

Palbociclib is known to interact with darunavir, carbamazepine, grapefruit juice and other CYP3A substrates, inducers, and inhibitors. Please consult with a pharmacist when a patient starts on any new medications while taking Palbociclib for a full interaction check.

Monitoring[2]: A complete blood count including differential should be taken before initiating therapy, at the beginning of each cycle, on day 14 of the first 2 cycles, and as clinically indicated. Monitor for signs and symptoms of infection and pulmonary embolism.

Adverse Effects[2]: The most common adverse effects experienced with palbociclib are bone marrow suppression (especially neutropenia), infection, fatigue, alopecia, epistaxis, nausea, vomiting, and diarrhea. Pulmonary embolism can also occur. Patients should report any signs of allergic reaction, infection, bleeding, chest pain, or shortness of breath to their provider. No contraindications have been specified at this time.

Patient education[2]: Women of reproductive potential should take care to use effective contraception during treatment and for at least 2 weeks following the last dose. The patient should take this medication with food to enhance absorption with the exception of grapefruit and grapefruit juice. Grapefruit products should be avoided because they can interact with palbociclib. Palbociclib is considered a hazardous agent, so gloves should be worn when anyone except the patient handles the medication. Any leftover medication that is not used should not be thrown in the trash or put down the sink. Instead it should be returned to the pharmacy or clinic for disposal with hazardous wastes.

Please do not hesitate to ask a pharmacist about any medication-related questions that come up. We are happy to assist with any questions that you or a patient may have.

Ibrance (R) [package insert]. New York, NY: Pfizer, Inc; 2015.
Lexi-Comp, Inc. (Lexi-Drugs®). Lexi-Comp, Inc.; January 29, 2015.

Suggestions for topics, questions, and comments are welcome! Just reply to sender of this newsletter or email:

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COMING SOON:

Standard Volume Rituximab Infusions

The rate calculator has passed the test! It will be added to the Pharmacy web-page in the near future and in-servicing will be done for the Infusion Center, MS5, and Oncology 6 RNs. All the nurse needs to do is type in the dose and hit "enter". Please see the sample calculations below.

All of the COS order sets are being modified by Chris Niemann to reflect this new admixture. Anticipated launch date is Thursday, October 15th. All new rituximab orders to start on or after October 15th should be written with the new order sets. If an order is mid-cycle, we can continue to use the 1mg/ml concentration until the cycle is completed.

Due to the way in which rituximab is programmed into the Alaris pump, the pump programming process will not change.

Changes in available Pharmacy technology has made it necessary to mix all rituximab infusions in a total volume of 500ml NS. Many institutions already administer rituximab in this fashion.

Rituximab must be diluted to a final concentration of 1-4mg/ml before infusion, and the final volume of 500ml will accomplish this for the vast majority of doses administered here. For those few patients that we administer doses under 500mg, Pharmacy will mix the rituximab in an appropriately reduced final volume to maintain this concentration.

Enter Dose Ordered **640** mg in 500mL NS **Conc. =** 1.28 mg/mL

Titration for 50mg/hr for initial infusion

Initial rate x 30 minutes	50 mg/hr	=	**39.06 mL/hr**
After 30 minutes increase to	100 mg/hr	=	**78.13 mL/hr**
After 30 minutes increase to	150 mg/hr	=	**117.19 mL/hr**
After 30 minutes increase to	200 mg/hr	=	**156.25 mL/hr**
After 30 minutes increase to	250 mg/hr	=	**195.31 mL/hr**
After 30 minutes increase to	300 mg/hr	=	**234.38 mL/hr**
After 30 minutes increase to	350 mg/hr	=	**273.44 mL/hr**
After 30 minutes increase to	*400mg/hr	=	**312.50 mL/hr**

***400 mg/hr = maximum rate**

Titration for 100mg/hr for subsiquent infusions

Initial rate x 30 minutes	100 mg/hr	=	**78.13 mL/hr**
After 30 minutes increase to	200 mg/hr	=	**156.25 mL/hr**
After 30 minutes increase to	300 mg/hr	=	**234.38 mL/hr**
After 30 minutes increase to	*400 mg/hr	=	**312.50 mL/hr**

***400 mg/hr = maximum rate**