

A Newsletter of the Pharmacy and Therapeutics Committee for Nurses, Pharmacists, and Physicians of Children's Hospital

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Chamomile

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New Formulary Drugs

Liposomal lidocaine topical cream 4% (LMX4®)

As compared to lidocaine-prilocaine (EMLA), this new product has a faster onset of action (LMX:30-60 mins; EMLA: 60 mins), less blanching, and carries less risk of methemoglobinemia because it does not contain prilocaine. Effective March 1, 2006, LMX4 will replace EMLA for inpatient and clinic use. However, EMLA will remain available for filling outpatient prescriptions.

Thyrotropin alfa (Thyrogen®)

A recombinant thyroid stimulating hormone, thyrotropin alfa has been added to formulary for the treatment of thyroid carcinoma in conjunction with radioactive iodide, and for monitoring response to imaging.

Other Formulary Issue

Formulary deletion

Pancrease® has been discontinued by manufacturer. Pancrease® MT products are still available.

Ondansetron for ED use

Ondansetron has been approved for use in the ED restricted to the treatment of acute gastroenteritis for patients who meet the following criteria:

Oral ondansetron:

-Patient has been evaluated by a physician.

-Patient has at least one of the following:

- vomited 5 or more times in the past 24 hours.
- hematemesis believed to be secondary to vomiting.
- failed an attempt of oral rehydration in the ED.
- Patient is considered an appropriate candidate for further oral rehydration.

Intravenous ondansetron:

Oral ondansetron is preferred even for patients who have an IV catheter in place. Intravenous ondansetron should be reserved for patients where an oral route of administration is unsafe or clinically inappropriate.

Use ondansetron with caution if:

-Patient has abdominal pain beyond what is expected for gastroenteritis.

-Patient is being evaluated for a surgical diagnosis such as bowel obstruction or appendicitis.

-Patient is pregnant (Category B).

Dosing:

Age	Oral	IV
6 mos. - <1 year	0.2 mg/kg of oral solution x 1 dose in ED	0.15 mg/kg (max. 8 mg) x 1 dose in ED
1 year and older	4mg oral disintegrating tablet (ODT) x 1 dose in ED or 0.2 mg/kg of oral solution (max 4 mg) x 1 dose in ED	

Guidance for redosing:

If the patient vomits within 20 minutes of an oral dose, consider re-dosing either orally or intravenously. If a patient vomits after receiving an IV dose, do not re-dose. If needed, an antiemetic from a different class (eg, prochlorperazine) should be considered.



FDA Approvals 2005

Some pediatric-related highlights:

- ▶ Two new shots are now on the 2006 childhood immunization schedule: Meningococcal Conjugate Vaccine (MCV4) is a new preparation for use in 11-55 years of age; and Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine, Adsorbed (Tdap) will give a boost in pertussis immunity.
- ▶ Therapies approved for rare diseases: mecasermin injection for growth failure; galsulfase injection for mucopolysaccharidosis VI; and sodium phenylacetate 10% and sodium benzoate 10% injection for acute hyperammonemia in patients with urea cycle disorder (previously available as study drug at CHRMC).

NEW DRUGS

Endocrinology

- ⌘ **Exenatide injection (Byetta)** – *glucose control in patients with type 2 diabetes mellitus who are taking metformin, a sulfonylurea, or a combination of metformin and a sulfonylurea but have not achieved adequate glycemic control* – first in a new drug class called incretin mimetics. Mechanism of actions include enhancement of glucose-dependent insulin secretion, suppression of glucose-dependent glucagon secretion, slowing of gastric emptying and food intake reduction. Available as a prefilled pen and dose is given subcutaneously at a fixed dose.
- ⌘ **Ibandronate sodium tablets (Boniva)** – *postmenopausal osteoporosis* – a bisphosphonate taken once-monthly.
- ⌘ **Insulin Detemir injection (Levemir)** – *type 1 or 2 diabetes mellitus* – a long-acting insulin for patients with diabetes mellitus who require basal insulin for glucose control. Given as a once or twice daily subcutaneous injection, this insulin provides up to 24 hours of action duration (mean 5.7-23.2 hrs). It cannot be mixed with other insulin preparations.
- 💡 Insulin glargine (Lantus) is the long-acting insulin agent on CHRMC formulary. Insulin glargine is given once daily and provides glucose coverage for 24 hours without a pronounced peak level.
- ⌘ **Mecasermin injection [rDNA origin] (Increlex)** – *short stature caused by primary IGF-1 deficiency or with growth hormone gene deletion who have developed neutralizing antibodies to growth hormone.*
- ⌘ **Mecasermin rinfabate injection [rDNA origin] (iPlex)** – *severe primary IGF-1 deficiency.*
- 💡 Increlex vs. iPlex: Increlex contains only mecasermin (IGF-1), requires twice daily injection, may cause hypoglycemia (42%) with cases of hypoglycemic seizures, and requires product refrigeration. iPlex contains both mecasermin (IGF-1) and rinfabate (IGFBP-3), requires once daily injection, may cause hypoglycemia (31%) , and requires product to be kept in freezer.
- ⌘ **Pramlintide acetate injection (Symlin)** – *diabetes in conjunction with insulin* - a synthetic analog of human amylin that is given subcutaneously. Amylin is a neuroendocrine hormone secreted by the beta cells of the pancreas and is co-secreted with insulin in response to food intake. This drug works by delaying gastric emptying, preventing postprandial glucagon rise, and producing satiety.

Hematology/Oncology

- ⌘ **Deferasirox dispersible tablets (Exjade)** – *chronic iron overload due to blood transfusions* – once daily iron chelator taken by mouth after tablet is dispersed in drinking beverage.

- ⌘ **Lenalidomide capsules (Revlimid)** – *treatment of transfusion-dependent anemia due to low- or intermediate-1-risk myelodysplastic syndromes associated with a deletion 5q cytogenetic abnormality with or without additional cytogenetic abnormalities* – an analogue of thalidomide, this is an immunomodulatory drug with anti-angiogenic activity. It has several black box warnings include human birth defects, hematologic toxicity, deep venous thrombosis and pulmonary embolism.
- ⌘ **Nelarabine injection (Arranon)** – *T-cell acute lymphoblastic leukemia and T-cell lymphoblastic lymphoma* - a purine nucleoside analogue for use in patients who have failed or relapsed after at least two chemotherapy regimens. Common side effects are fatigue, nausea, vomiting and diarrhea.
- ⌘ **Sorafenib tablets (Nexavar)** – *advanced renal cell carcinoma* – an oral multi-kinase inhibitor that blocks tumor cell proliferation angiogenesis.

Infectious Disease

- ⌘ **Entecavir tablets/oral solution (Baraclude)** – *chronic hepatitis B* – a nucleoside analogue that interferes with viral replication.
- ⌘ **Micafungin sodium injection (Mycamine)** – *candida infections* – like caspofungin, this echinocandin inhibits cell wall synthesis. FDA approved currently for the prophylaxis of Candida infections in patients undergoing hematopoietic stem cell transplantation and the treatment of esophageal candidiasis. It also has activity against Aspergillus spp.
- ⌘ **Tipranavir capsules (Aptivus)** – *HIV infection* – a non-peptidic HIV-1 protease inhibitor that blocks the processing of viral Gag and Gag-Pol polyproteins in HIV-1 infected cells, thus disrupting the replication process. Ritonavir inhibits the metabolism of tipranavir and co-administration is necessary to achieve effective tipranavir plasma concentrations. See package insert for a long list of drug interactions.
- ⌘ **Tigecycline injection (Tygacil)** – *complicated skin and intra-abdominal infections* – a first in a new antibiotic class called glycylicylines. This is a bacteriostatic derivative of minocycline that inhibits bacterial synthesis. However, unlike conventional tetracyclines, tigecycline is not affected by ribosomal protection and efflux, thus effective against tetracycline-resistant and multidrug-resistant organisms (including MRSA).
- ⌘ **Vaccinia immune globulin intravenous (human) (VIGIV)** – *complications of smallpox vaccination*.

Genetic/Metabolic

- ⌘ **Galsulfase injection (Naglazyme)** – *mucopolysaccharidosis VI* – enzyme replacement therapy for a life-threatening lysosomal storage disorder due to a deficiency of the lysosomal enzyme N-acetylgalactosamine 4-sulfatase.
- ⌘ **Sodium phenylacetate 10% and sodium benzoate 10% injection (Ammonul)** – *acute hyperammonemia and associated encephalopathy in patients with urea cycle disorder* – this drug combination helps eliminate nitrogen waste by providing an alternative conjugation pathway in patients who lack or are deficient in one of the enzymes in urea cycle. It must be administered via a central line. A loading dose infusion is followed by an equivalent maintenance infusion.

Nephrology

- ⌘ **Conivaptan hydrochloride injection (Vaprisol)** – *euvolemic hyponatremia* – an arginine vasopressin antagonist for inpatient use.

Neurology

- ⌘ **Ramelteon tablets (Rozerem)** – *insomnia* – a melatonin receptor agonist indicated for the treatment of insomnia due to difficulty in falling asleep. It is not a controlled substance, has not shown to cause abuse, dependence or rebound symptoms, and can be prescribed for long-term use.



Melatonin was reviewed and denied formulary admission in 2004. When a safety review was performed, its activity as a hormone could affect the onset of puberty in children. The P&T Committee felt strongly that melatonin should not be carried on formulary or dispensed by the pharmacy on a non-formulary basis, as safer alternatives exist for children.

Ophthalmology

- ⌘ **Nepafenac ophthalmic suspension (Nevanac)** – *pain and inflammation associated with cataract surgery* – a topical nonsteroidal anti-inflammatory agent.

Rheumatology

- ⌘ **Abatacept injection (Orencia)** – *rheumatoid arthritis* - a selective costimulation modulator which inhibits T cell activation.

NEW FORMULATIONS

Extended Release...

- ⌘ **Azithromycin extended release for oral suspension (Zmax)** – *sinusitis and pneumonia* - one-dose-only (2gm) treatment for mild-to-moderate acute bacterial sinusitis and community-acquired pneumonia in adults.
- ⌘ **Ciprofloxacin extended-release tablets (Proquin XR)** – *uncomplicated urinary tract infection* – once daily dosing with the reduction of GI side effects (nausea and diarrhea).
- ⌘ **Desloratadine and pseudoephedrine ER tablets (Clarinet-D 24 Hour)** – *allergic rhinitis* – a prescription – strength that is given once daily.
- ⌘ **Dexmethylphenidate extended-release capsules (Focalin XR)** – *ADHD* – once-daily dosing.
- ⌘ **Doxazosin extended release tablets (Cardura XL)** – *benign prostatic hyperplasia*.
- ⌘ **Metformin extended-release tablets (Glumetza)** - *type II diabetes*– offers once-daily dosing without significantly increasing GI side effects.
- ⌘ **Tramadol extended-release tablets (Tramadol ER)** – *chronic pain* – once-daily dosing vs. traditional every four to six hours.
- ⌘ **Zolpidem extended-release tablets (Ambien CR)** – *insomnia* – a new bi-layered formulation that first dissolves quickly to induce sleep and the second layer dissolves more slowly to help stay asleep.

Orally disintegrating tablets...

- ⌘ **Alprazolam orally disintegrating tablets (Niravam)** – *anxiety disorders*.
- ⌘ **Citalopram orally disintegrating tablets (Citalopram ODT)** – *depression*.
- ⌘ **Tramadol orally disintegrating tablets (Tramadol ODT)** – *moderate to moderately severe pain*.

Two (or multiple) in one...

- ⌘ **Aledronate sodium and cholecalciferol tablets (Fosamax Plus D)** – *osteoporosis* – once-weekly dosing of a tablet that contains 70 mg aledronate and 2800 units of cholecalciferol (vitamin D₃).
- ⌘ **Drospirenone and estradiol tablets (Angeliq)** – *menopausal symptoms*.
- ⌘ **Isosorbide dinitrate and hydralazine tablets (BiDil)** – *heart failure in black patients* – with approval based on results from the African American Heart Failure Trial (A-HeFT), BiDil contains a fixed-dose of isosorbide dintrate 20 mg and hydralazine 37.5 mg.
- ⌘ **Lidocaine 70 mg and tetracaine 70 mg topical patch (Synera)** – *topical anesthesia for superficial venous access and dermatological procedures*.
- ⌘ **Measles, Mumps, Rubella and Varicella Virus Vaccine Live (Proquad)** – MMR and Varivax in a single shot.
- ⌘ **Pioglitazone and metformin tablets (ACTOplus met)** – *type II diabetes*.
- ⌘ **Risedronate with calcium carbonate tablets (Actonel with Calcium)** – *postmenopausal osteoporosis* – a blister package that contains 4 tablets of 35 mg risedronate (taken on day 1 of a 7-day treatment cycle) and 24 tablets of 1250 mg calcium carbonate (taken on day 2-7).
- ⌘ **Rosiglitazone and glimepiride tablets (Avandaryl)** – *type II diabetes*.
- ⌘ **Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine, Adsorbed Tdap (Boostrix)** – a single booster for individuals 10-18 years of age.
- ⌘ **Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine, Adsorbed Tdap (Adacel)** – a booster immunization indicated for individuals 11 through 64 years of age.



Boostrix vs. Adacel: Since 1996, ACIP has recommended tetanus and diphtheria toxoid vaccine (Td) administration at age

11-12 years and then Td booster every 10 years throughout life. The availability of pertussis containing vaccine for use in adolescents will now add a pertussis component to the routine Td booster series. As compared to pediatric DTaP preparations, both Boostrix and Adacel have a reduced amount of both diphtheria toxoid and acellular pertussis antigens, but the same amount of tetanus toxoid antigens. Boostrix is indicated for adolescents only and contain a different composition of pertussis antigen from Adacel. Adacel can be used in both adolescents and adults. A single Tdap dose (either Boostrix or Adacel) is now recommended for adolescents aged 11-12 years who have completed the childhood DTP/DTaP series but have not received Td booster dose yet. A catch-up dose should be given to adolescents aged 13-18 years. This should be followed by Td boosters every 10 years. In October 2005, the Advisory Committee on Immunization Practices recommended that adults 19-64 years of age should routinely receive a single dose of Tdap to replace the next booster dose of Td. The recommendation is currently under review. Visit the CDC website for more up-to-date information.



Watch out for DTaP and Tdap mix up since they may look and sound alike! Tdap is not indicated for children younger than 10 years of age. It contains reduced amounts of diphtheria toxoid and some pertussis antigens compared to DTaP, and its efficacy in younger children has not been established. Pediatric DTaP contains increased diphtheria toxoid amount and may cause more adverse reactions in older persons.

New strengths...

- ⌘ **Megestrol acetate oral suspension (Megace ES)** – *anorexia, cachexia, and weight loss in AIDS patients* – a concentrated formulation that is dosed at a much reduced volume and can be administered without regard to meals.
- ⌘ **Metronidazole topical gel 1% (Metrogel)** – *rosacea*- a new strength in addition to 0.75%.

Miscellaneous...

- ⌘ **Bromfenac ophthalmic solution** – *ocular inflammation following cataract surgery* - a twice-daily non-steroidal anti-inflammatory agent.
- ⌘ **Clobetasol propionate 0.05% spray** – a potent corticosteroid for *plaque psoriasis*.
- ⌘ **Dapsone gel 5% (Aczone)** – *acne vulgaris*.
- ⌘ **Esomeprazole magnesium injection (Nexium)** – *GERD*.
- ⌘ **Fenofibrate tablets (Triglide)** – *lipid disorders* – new formulation that can be taken without regard to food.
- ⌘ **Fluocinolone acetonide intravitreal implant (Retisert)** – *chronic non-infectious uveitis*.
- ⌘ **Levalbuterol inhalation aerosol (Xopenex HFA)** – *bronchospasm* – now available as a MDI.
- ⌘ **Meningococcal Polysaccharide Diphtheria Toxoid Conjugate Vaccine (Menactra)** – *active immunization against invasive meningococcal disease caused by N meningitidis serogroups A, C, Y, and W-135 in persons 11 to 55 years of age*



How is meningococcal conjugate vaccine MCV4 (Menactra) different from meningococcal polysaccharide vaccine MPSV4 (Menomune)? MPSV4 has been available since the 1970s and contains the serogroups of Neisseria meningitides (A, C, W-135, and Y) bacterial capsular polysaccharides. Routine vaccination with this product has not been recommended due to its relative ineffectiveness in those <2 years of age and short duration of protection. It is, however, recommended for individuals at increased risk, including travelers to countries with epidemic meningococcal, persons with certain medical conditions (persons ≥2 years with terminal complement deficiencies or anatomic or functional asplenia) and other high risk groups (see *MMWR* 2005;54 [RR-7]:1-21). It is given subcutaneously to individuals 2 years of age and older. On the other hand, MCV4 also contains the four above-mentioned serogroup antigens, but each is conjugated to diphtheria toxoid protein. It has been shown that conjugate vaccines induce boostable memory responses, which is also longer-lasting than polysaccharide vaccines. It is given intramuscularly to individuals 11-55 years of age. MCV4 is now recommended as a routine vaccination to all children 11-12 years of age, as well as unvaccinated adolescents at high school entry (15 years old). All college freshmen living in dormitories should also receive this vaccine. MCV4 is preferred for people 11-55 years of age, but MPSV4 is an acceptable alternative if MCV4 is not available. Use MPSV4 for children 2-10 years old, and adults >55.



Several cases of Guillain-Barré Syndrome, a serious nervous system disorder, have been reported among adolescents who received MCV4. The CDC stated that the occurrence rate so far is not greater than would be expected in a population of unvaccinated adolescents. These cases are being investigated by the CDC and FDA.

- ⌘ **Mometasone inhalation powder (Asmanex)** – *asthma* – allows once daily dosing of a potent corticosteroid.

- ⌘ **Paricalcitol capsules (Zemlar)** – *secondary hyperparathyroidism in kidney disease* – formerly only available as injectable.
- ⌘ **Paclitaxel protein-bound particles for injection (Abraxane)** – *metastatic breast cancer* – this new formulation uses albumin as the delivery agent for paclitaxel. As compared to Taxol which contains a toxic solvent called Cremophor, Abraxane allows for a shorter administration time, lowers the risk of hypersensitivity reactions, eliminates premedication need, and produced a higher response rate in clinical trial.
- ⌘ **Tamoxifen oral solution (Soltamox)** – *breast cancer*.

A Dietary Supplement Series:

CHAMOMILE

By Steve Chase, RPh

A number of plants have “chamomile” as part of their common name. For medicinal use, German chamomile (*Matricaria recutita*) is most common, but Roman chamomile (*Chamaemelum nobile*) is also used. These plants belong to the Asteraceae family.

As one of the older known medicinal herbs, chamomile has been used since Roman and Egyptian times for skin inflammation, colic or dyspepsia, anxiety, insomnia, teething, conjunctivitis and laryngitis. Most pharmacologically active constituents of chamomile include the terpenoids. These constituents are derived from essential oil obtained from the flower head of the plant. Other important constituents that are more hydrophilic include the flavanoids, coumarins, and mucilage. The component chamazulene has antibacterial and fungicidal properties. Another component, alpha-bisadlolol (terpenoid), is believed to have anti-inflammatory, antispasmodic, antimicrobial and mild sedative effects. The holistic effect of chamomile is a result of all the extracts working together.

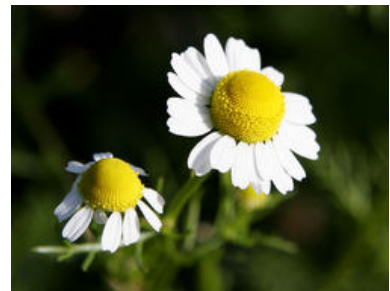
A few controlled trials in healthy, full term infants with colic using a multi-herb teas containing German chamomile (with vervain, licorice, fennel, and lemon balm) verses placebo showed a significant improvement in colic symptom scores. Clinical trials have reported benefits with topical use of chamomile for mucositis and dermatitis. However, many of these trials are open or uncontrolled trials. In open comparative trials a German chamomile cream compared favorably to a hydrocortisone 0.25 – 0.5% cream but no better than a placebo cream.

In general, chamomile is considered a safe herb and adverse effects are mild. It is used widely in foods, beverages and cosmetics. Mild gastroparesis and emesis have been reported with excessive use. Chamomile has anti-allergenic effects, but also has been found to induce allergies. Patients with a history of allergies to ragweed, daisies, sunflowers, and chrysanthemums should avoid chamomile products due to cross-reactivity. Safety during pregnancy or breast feeding has not been evaluated.

Chamomile is available as teas, extracts, salves and as a component of massage oils.

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German chamomile flowers
Source: <http://en.wikipedia.org/wiki/Chamomile>