

## Solutions Summary

Drug	Indication/ Dosage	Incidence/Cost	Highlights
<b>Somatuline<sup>®</sup> Depot</b> (lanreotide) Injection  Approved August 30, 2007  Tercica, Inc.	Acromegaly  Subcutaneous Injection	Affects approximately 15,000 people in the United States and Canada and is most commonly found in middle-aged adults.  Pricing is currently unavailable.	<b>New Drug Approval:</b> Somatuline is the only 28-day acromegaly therapy available in a prefilled syringe; it does not require reconstitution.
<b>Hycamtin<sup>®</sup></b> (topotecan)  Approved October 12, 2007  GlaxoSmithKline	Relapsed Small Cell Lung Cancer (SCLC)  Oral	An estimated 213,380 new cases of lung cancer in 2007; SCLC has the most aggressive course of any type of pulmonary tumor if untreated.	<b>New Drug Approval:</b> Hycamtin is the only oral single-agent chemotherapy approved for the treatment of SCLC after failure of first- line therapy.
<b>Ixempra<sup>™</sup></b> (ixabepilone)  Approved October 16, 2007  Bristol-Myers Squibb	Advanced Breast Cancer  Intravenous Infusion	Breast cancer is the most common cancer among women and the second leading cause of cancer death; the National Cancer Institute estimates 178,480 women will have been diagnosed with breast cancer in 2007.	<b>New Drug Approval:</b> Ixempra could potentially be less susceptible to mechanisms of multiple drug resistance than currently available agents.
<b>Tasigna<sup>®</sup></b> (nilotinib)  Approved October 29, 2007  Novartis	Chronic Myelogenous Leukemia (CML)  Oral	Accounts for 10% to 15% of all leukemias; an estimated 4,570 new cases of CML will have been diagnosed in the United States in 2007.	<b>New Drug Approval:</b> Approved for all phases of Ph+ CML in patients intolerant or resistant to prior therapies including Gleevec.
<b>Norditropin<sup>®</sup></b> (somatropin [rDNA origin] injection)  Indication approved September 20, 2007  Novo Nordisk	Short stature associated with Turner syndrome  Subcutaneous Injection	A rare chromosomal condition affecting females. It occurs in approximately 1 in 2,500 live female births, and in as many as 10 percent of all miscarriages worldwide.	<b>New Indication:</b> This new indication for <i>Norditropin</i> expands on the drug's previously approved indications for the treatments of pediatric and adult growth hormone deficiency, the treatment of SGA, and short stature in Noonan syndrome.

# Specialty Solutions

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## Featured Items

- Solutions Summary
- New Drug Approvals
  - Somatuline<sup>®</sup> Depot
  - Oral Hycamtin<sup>®</sup>
  - Ixempra<sup>™</sup>
  - Tasigna<sup>®</sup>
- Product Update
  - Norditropin<sup>®</sup>
- In The News
  - Tysabri<sup>®</sup> for the Treatment of Crohn's Disease
  - Treatment options for Hereditary Angioedema
- Pipeline Watch

Questions?  
Contact Rena McClain at 201-269-6555

## New Drug Approval

### **Somatuline® Depot (lanreotide) Injection Approved for the Treatment of Acromegaly**

On August 30, 2007, the Food and Drug Administration (FDA) approved a new subcutaneous product, *Somatuline Depot*, for the long-term treatment of acromegaly in patients who have had an inadequate response to surgery and/or radiotherapy, or for whom surgery and/or radiotherapy is not an option. Acromegaly is a condition in which patients have persistent hypersecretion of growth hormone (GH), which is most often the result of a pituitary tumor. This excess secretion of GH results in the release of insulin-like growth factor (IGF-1) from the liver, stimulating bone and tissue growth. The condition occurs in approximately 60 per million persons; there are an estimated 15,000 individuals in the United States and Canada affected. Signs and symptoms include enlarged hands, feet, and head; facial changes such; enlargement of the heart, liver, kidneys, spleen, and other organs; joint pain and fatigue; reduced sex drive; and loss of concentration.

## Specialty Solutions

### Product Update

#### **What's New?**

*Somatuline* is a somatostatin analogue. It works to decrease growth hormone secretion, can reduce tumor size, and improve signs and symptoms of acromegaly. *Somatuline Depot* is a sustained-release product that is given every 28 days. Initial recommended dosing for *Somatuline* is 90 mg given by deep subcutaneous injection at 4-week intervals for 3 months. Following 3 months at this dosing, the dose may be adjusted based on GH and IGF-1 levels. *Somatuline Depot* is available in 60-, 90-, and 120-mg single-use, prefilled syringes. It is the only somatostatin analogue available in prefilled syringes and that will not require reconstitution.

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Based on AWP, the cost of therapy with *Somatuline Depot* can range from \$2,138 to \$3,821 for a 1-month supply (approximately \$27,000 to \$42,000 annually). *Somatuline Depot* has been presented to Medco's Pharmacy & Therapeutics Committee; coverage rules have been developed. *Somatuline Depot* will be available under limited distribution; Accredo will have access once it is made available.

### **Oral Hycamtin® (topotecan) Approved for the Treatment of Relapsed Small Cell Lung Cancer**

On October 12, 2007, the Food and Drug Administration (FDA) approved a new oral dosage form for a currently approved intravenous cancer drug, *Hycamtin*. Oral *Hycamtin* is approved for the treatment of relapsed small cell lung cancer (SCLC). SCLC makes up approximately 10% to 15% of all lung cancer cases. If left untreated, it has the most aggressive course of the pulmonary tumors. Distant metastasis is common in NSCL, often making localized therapy an unsuitable option; the most common form of treatment is chemotherapy.

Questions?

Contact Rena McClain at 201-269-6555



## Specialty Solutions

### Product Update

#### What's New?

Oral *Hycamtin* is the only oral single-agent chemotherapy approved for the treatment of SCLC after failure of first-line therapy. *Hycamtin* is a member of a class of drugs known as topoisomerase I inhibitors. Topoisomerase I is important in that it maintains the correct conformation of DNA in cells. By inhibiting this enzyme, *Hycamtin* use results in permanent damage to the cell's genetic material and the death of dividing cells.

The recommended dose of oral *Hycamtin* is 2.3 mg/m<sup>2</sup>/day once daily for 5 consecutive days repeated every 21 days. *Hycamtin* carries a black box warning; bone marrow suppression is a dose-limiting toxicity, and, therefore, blood cell counts should be monitored. Reductions in dose should be given to patients whose neutrophil, platelet, and erythrocyte levels falls below acceptable levels.

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Oral *Hycamtin* will be available in 0.25-mg and 1-mg capsules; pricing is currently unavailable. Oral *Hycamtin* is expected to be made available for distribution in 2008, it is anticipated that Accredo will have access. *Hycamtin* will be presented to the Medco P&T Committee; development of coverage rules is being considered. Pricing is unavailable at this time.

#### ***Ixempra*<sup>™</sup> (ixabepilone) Approved for the Treatment of Advanced and Metastatic Breast Cancer**

On October 16, 2007, the FDA approved a new intravenous agent, *Ixempra*, for the treatment of locally advanced and metastatic breast cancer. As a single agent, *Ixempra* is approved for treating patients after failure with a taxane, an anthracycline, and capecitabine. It is also approved for use in combination with capecitabine after treatment failure with a taxane and anthracycline. Breast cancer is the most common cancer among women and the second leading cause of cancer death; the National Cancer Institute estimates 178,480 women will have been diagnosed with breast cancer in 2007. Unfortunately, once breast cancer has metastasized, it cannot be cured; however, it can be treated.

#### What's New

*Ixempra* belongs to a new class of agents known as epothilones. It works inside cells to induce programmed cell death or apoptosis. It has a distinct binding mode within the cells, which may prove it to be less susceptible to mechanisms of multiple drug resistance than currently available agents. *Ixempra* is administered via IV infusion; the recommended dose is 40 mg/m<sup>2</sup> given over 3 hours every 3 weeks.

#### Specialty Solutions

Based on AWP, the estimated cost per infusion for an average adult is \$5,760. *Ixempra* will be presented to Medco's P&T Committee. Accredo will have access to *Ixempra*, and will coordinate delivery with prescribers and infusion centers as part of its therapy management program.

Questions?  
Contact Rena McClain at 201-269-6555



## Specialty Solutions

### Product Update

### ***Tasigna*<sup>®</sup> (nilotinib) Approved for the Treatment of Chronic Myelogenous Leukemia**

On October 29, 2007, the FDA approved a new oral cancer drug, *Tasigna*, for the treatment of chronic phase and accelerated phase Philadelphia chromosome positive (Ph+) chronic myelogenous leukemia (CML) in adult patients resistant or intolerant to prior therapy including *Gleevec*<sup>®</sup> (imatinib mesylate). CML is a rare form of cancer that causes rapid growth of blood forming cells, and accounts for 10% to 15% of all leukemias. This form of leukemia affects mostly adults, with the average age of diagnosis being 67. It is estimated that in 2007, 4,570 new cases of CML will have been diagnosed in the United States.

#### **What's New?**

*Tasigna* is an inhibitor of tyrosine kinase; it works by reducing the activity of one or more proteins responsible for the uncontrolled growth of the leukemia cells. The recommended dosing of *Tasigna* is 400 mg twice daily. Treatment with *Tasigna* should be continued until disease progression or the patient becomes intolerant to therapy. *Tasigna* labeling carries a black box warning; there is a risk of QT prolongation and sudden death with its use. QT prolongation is a serious cardiac condition in which there is a delay in the electrical pulses responsible for the heart beating; this can lead to further complications including syncope, seizure, and death. Patients with low levels of potassium or magnesium, or who have long QT syndrome should not use *Tasigna*. Electrocardiograms (ECGs) should be taken at the start of therapy, 7 days after its initiation and periodically throughout treatment, as well as after any dosage adjustments.

#### **Specialty Solutions**

*Tasigna* will be available in blister packs containing 28 200-mg capsules. Each blister pack contains 2 blister cards of 14 capsules each, for dosing two capsules in the morning and two more in the evening at 12-hour intervals over a 7-day period. Pricing for *Tasigna* is unavailable at this time. Accredo will be a providing pharmacy for *Tasigna*. Medco's P&T committee will be reviewing *Tasigna*; coverage rules are under development.

Questions?  
Contact Rena McClain at 201-269-6555



## Product Update

### ***Norditropin*<sup>®</sup> (somatropin [rDNA origin] injection) Approved for the Treatment of Short Stature Associated With Turner Syndrome**

On September 20, 2007, the FDA extended approval to *Norditropin* for the treatment of short stature in children with Turner syndrome. Turner syndrome, the most common sex-chromosome abnormality in female conceptions, affecting approximately 3% of all female conceptions, is the result of a partial loss or complete loss of an X chromosome.

Females with Turner syndrome have a number of symptoms associated with their condition including short stature, amenorrhea (the absence of menstruation), and incomplete or absent development at puberty. Short stature, the most common clinical feature is often treated with the administration of exogenous growth hormone to maximize height. Therapy should be initiated when the child's height falls below the fifth percentile for their age, typically between the ages of 2 and 5.

A dosage of up to 0.067 mg/kg/day should be given to Turner patients. *Norditropin* is also approved for the treatment of children with short stature associated with Noonan syndrome, the treatment of children with growth failure due to inadequate secretion of endogenous growth hormone, and for replacement of endogenous growth hormone in adults with growth hormone deficiency (GHD) who meet specific criteria. Based on average wholesale price (AWP), indication, patient age, and associated weight, annual treatment with *Norditropin* may cost approximately \$13,000 to \$30,000.

## In the News

### ***Tysabri*<sup>®</sup> for the Treatment of Crohn's Disease Recommended by Advisory Committee**

In December 2006, the manufacturers of *Tysabri* submitted a supplemental Biologics License Application (sBLA) to the FDA seeking approval of *Tysabri* for the treatment of patients with moderately to severely active Crohn's disease, a chronic inflammatory bowel disease that causes inflammation or swelling along the gastrointestinal tract. *Tysabri*, an infused product, is currently approved for use in relapsing forms of multiple sclerosis. Included in the sBLA were data from a number of trials that evaluated the safety and efficacy of *Tysabri* in Crohn patients. Also included was information on a risk management plan and proposed labeling. There is currently a risk management plan in place due to the risk of PML, a serious opportunistic infection of the brain that often leads to disability or death.

In July 2007, the Gastrointestinal Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee met to evaluate the potential for use of *Tysabri* in this indication. The panel did recommend its approval; the FDA though is not bound agree to the recommendation. The FDA is currently reviewing the proposed risk management plan for Crohn's disease. They have extended their review time by up to 3 months; a decision is expected by January 13, 2008. Accredo will continue to monitor *Tysabri* as it moves along the FDA approval review process. Products currently approved to treat Crohn disease include *Remicade*<sup>®</sup> and *Humira*<sup>®</sup>.

# Specialty Solutions

## Product Update

Questions?  
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## In the News (Continued)

### Patients Suffering From Hereditary Angioedema May Receive Treatment Options

Hereditary angioedema (HAE) is a rare genetic disorder whose prevalence is estimated at 1 individual per 50,000. HAE results from a dysfunction or deficiency in C1 inhibitor (C1-INH). Under normal circumstances, C1-INH functions as a regulatory protein inhibiting inflammation. When there is an inadequate amount of C1-INH, patients experience recurrent episodes of angioedema, or severe swelling of the skin. This swelling results from fluid leakage into the narrow spaces between body tissue and/or parts of one's organs. This swelling can affect the face, lips, mouth, throat, larynx, extremities, and genitalia. Swelling of the larynx is especially troubling in that it can cause asphyxiation.

There are no FDA-approved agents to treat HAE. Treatments employed—including steroids, antihistamines, and epinephrine—are often ineffective. Other options include the use of androgens and fresh frozen plasma. In clinical trials today, there are three agents that may prove promising in treating HAE—icatibant, ecallantide, and *Cinryze*<sup>™</sup>.

Icatibant works by blocking a receptor to bradykinin, a hormone that plays a role in inflammation. It has been shown that patients with HAE have elevated levels of bradykinin leading to edema formation during attacks. By blocking the receptor, icatibant trials have shown that it reduces the time to onset of symptom relief during an attack. A New Drug Application (NDA) has been filed with the FDA for approval of this agent.

Ecallantide works by blocking kallikrein and its byproduct bradykinin, discussed above. Like icatibant, it would be indicated for emergency treatment of HAE attacks. It is currently in Phase III clinical trials; a BLA has been submitted to the FDA.

*Cinryze*, the last of the agents being investigated, is a C1-INH concentrate. Clinical trials have shown that the administration of C1-INH can both prevent attacks and treat acute attacks. A BLA has been submitted to the FDA; a decision is anticipated by January 30, 2008.

Accredo will continue to monitor the specialty drug pipeline for this and other rare diseases for which there have been limited treatment options.

## Specialty Solutions

### Product Update

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## Pipeline Watch

Product	Indication	Incidence /Prevalence	Highlights
<b>Actemra™</b> (tocilizumab)  Intravenous  8 mg/kg every 4 weeks  Hoffman-La Roche, Inc.	Rheumatoid Arthritis	Almost 22 million people around the world suffer from RA. Approximately 75% to 80% of the 2.5 million US RA patients are women.	The first humanized interleukin-6 (IL-6) receptor-inhibiting monoclonal antibody representing a novel mechanism of action to treat RA.  Phase III
<b>Denufosol Tetrasodium</b>  Inhalation  60 mg three times daily  Inspire Pharmaceuticals	Cystic Fibrosis	An inherited chronic disease that affects the lungs and digestive system of about 30,000 children and adults in the United States (70,000 worldwide).	Designed to enhance the lung's innate mucosal hydration and mucociliary clearance mechanisms. Its unique approach to this is different from the approach of other approved CF products and may be important in intervening in the early clinical course of CF lung disease.  Phase III
<b>Picoplatin</b>  Intravenous  Dosing N/A  Poniard Pharmaceutical	Small Cell Lung Cancer	Approximately 1.2 million patients afflicted with lung cancer annually. SCLC is the most deadly and aggressive form of lung cancer and accounts for more than 20% of all lung cancer cases.	A new generation platinum chemotherapy agent designed to overcome platinum resistance and to prolong the time to relapse after chemotherapy in the treatment of solid tumors, and to have an improved safety profile compared with existing platinum-based chemotherapeutics.  Phase III
<b>Prestara™</b>  Oral  200 mg/day  Genelabs	Systemic Lupus Erythematosus	The reported prevalence of SLE in the population is 40 to 150 cases per 100,000.	Contains prasterone, a synthetic form of the human hormone dehydroepiandrosterone (DHEA); lupus patients with active disease generally have low blood levels of DHEA, therefore, oral use of DHEA may be beneficial in the treatment of SLE.  NDA/BLA filed

Specialty Solutions

Product Update

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## Pipeline Watch (Continued)

Product	Indication	Incidence /Prevalence	Highlights
<b>Provenge<sup>®</sup></b> (Sipuleucel-T)  Intramuscular  Dosage N/A  Dendreon Corporation	Prostate Cancer	An estimated 218,890 new cases of prostate cancer are anticipated to have been diagnosed in 2007.	<i>Provenge</i> may represent the first in a new class of active cellular immunotherapies (ACIs) that are uniquely designed to stimulate a patient's own immune system.  NDA/BLA filed
<b>Tanespimycin</b>  Intravenous  50 mg/m <sup>2</sup> , 175 mg/m <sup>2</sup> or 340 mg/m <sup>2</sup> twice weekly on a cycle of 2 weeks of treatment every 3 weeks  Kosan Biosciences	Refractory Multiple Myeloma	There will be an estimated 19,900 new cases of multiple myeloma in the United States in 2007.	Tanespimycin has been shown to induce cellular self-destruction of drug-sensitive and drug-resistant multiple myeloma cell lines. It also inhibits expression of various cell surface cytokines involved in growth, survival and drug resistance of multiple myeloma cells  Phase III
<b>Treanda<sup>®</sup></b> (bendamustine)  Intravenous  Dosing N/A  Cephalon	Chronic Lymphocytic Leukemia  Non-Hodgkin Lymphoma	An estimated 15,000 new cases of CLL are diagnosed every year in the United States.	<i>Treanda</i> induces rapid, sustained DNA damage, which results in apoptosis, or programmed cell death, in the tumor.  If approved, <i>Treanda</i> would be the first new therapy approved by the FDA for the treatment of CLL since 2001.  Trials evaluating its safety and efficacy in patients with indolent NHL who have relapsed after <i>Rituxan<sup>®</sup></i> therapy.  Phase III

# Specialty Solutions

## Product Update

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