Sjögren’s Quarterly

Volume 5, Issue 4 – Fall 2010

The Professionals’ Resource on Sjögren’s Syndrome

Clinicians Face Major Changes in Healthcare – Are You Aware of the Key Issues?

We all know that the way U.S. healthcare professionals do business is rapidly changing. Healthcare plans that reimburse patients for OTC drugs and products will now require prescriptions, Medicare reimbursement once again is on the calendar for major cuts, coding changes also affect the bottom line for medical specialists who treat Sjögren’s patients, and physicians are poised to switch medical records from print to electronic versions. Many of the new rules remain unclear and open to interpretation. Peter Donshik, Clinical Professor of Ophthalmology, University of Connecticut Health Center, sums up the new circumstances in healthcare in one word: “Uncertainty.”

Some physicians have decided to close their offices because of increased expenses and regulations due to Medicare and Medicaid, while others say they will accommodate the changes but continually gauge the business of running their offices. Regardless, changes are afoot that will impact physicians and patients alike. The Sjögren’s Syndrome Foundation (SSF) wants to assure you that it is aware of the impending changes and will work to modify those elements that might affect you negatively.

Did you know that if your patients have access to health reimbursement accounts, your patients will be asking you for a written prescription for OTC products starting January 1?

Continued on page 2

Cognitive Impairment and Neuropsychological Testing in Sjögren’s

by Steven Mandel, MD, Frederick Vivino, MD, Edward Maitz, PhD, Tiffany Jennings, PhD, Kenneth Goldberg, PsyD, Brett Boyer, PhD; Thomas Jefferson University, Jefferson Medical College and PENN Sjögren’s Syndrome Center, Presbyterian Hospital, Philadelphia, Pennsylvania; and Widener University, Chester, Pennsylvania

Continued on page 4
When the New Year arrives, prescriptions will be required for patients seeking refunds from health reimbursement plans for OTC drugs and products. This change affects patients with accounts including Flexible Spending Accounts (FSAs), Health Savings Accounts (HSAs), Archer Medical Savings Accounts (Archer MSAs) and Health Reimbursement Accounts (HRAs). These accounts are provided by employers to allow money from salaries to be set aside tax-free for medical expenses. As a result, your Sjögren’s patients will start asking you for prescriptions for such OTC items as artificial tears, ointments and gels; eyewash and eyelid cleansing solutions; oral moisturizers and mouthwashes; oral remineralizing solutions; nasal sprays, ointments and irrigants; lip moisturizers; dry ear products; vaginal lubricants and moisturizers; and sunscreens.

To complicate matters, it will take awhile to determine precise definitions and variations by state. In the meantime, it will be safest to submit a prescription when in doubt. For example, even though the new rule is a federal Internal Revenue Code, each state has its own legal definition of a prescription, so the rule could be enforced differently depending on the state in which you practice. As a general rule, a letter from a physician does not suffice; prescriptions must be written or electronically submitted by an individual who has authority under state law to do so.

In addition, “equipment” per se appears to be exempt (crutches and bandages are given by the IRS as examples), but since all examples are not included and definitions not clear, if a patient wants to seek healthcare reimbursement for items such as humidifiers, special sox for neuropathy and products such as Thermoeyes™ for eye comfort and hydration, patients and their physicians should try a prescription to see if they will be covered.

Finally, it is unclear whether a new prescription needs to be submitted every time a patient purchases the OTC drug or product. Some health plans spell out that one prescription can be good for a defined period, such as 12 months.

Your patients might be well aware of the changes, but they also might have questions for you. Answers to potential questions that you can share with your patients:

• Prior to January 1, 2011, medically-necessary OTC drugs and products will continue to be covered by these accounts.
• If a patient’s plan allows a grace period for using money left over from one year into the next year, the cut-off of January 1 still applies.
• Health insurance debit cards may no longer be used for OTC products, because current debit card systems cannot substantiate compliance with the new rules requiring a prescription.
• Co-pays and deductibles are still reimbursable through health accounts and plans.

The Patient Protection and Affordable Care Act, enacted in March 2010, revises the definition of medical expenses as it relates to OTC drugs by establishing a new Internal Revenue Code (Section 9003).

Medicare Payments to Decrease Again for Physicians

The Sjögren’s Syndrome Foundation has joined with the American College of Rheumatology (ACR) and other health professional organizations in fighting the impending decreases in Medicare reimbursements to physicians. Currently, physicians face Medicare reimbursement cuts of 23.5% starting December 1, 2010, with another 6% cut scheduled for January 1, 2011, making a total of almost 30% in cuts in the next couple of months if Congress does not take action.

In light of the uncertainty and impending cuts and rising costs, some rheumatologists are closing or considering the closing of their offices. Jeffrey Wilson, MD, of the Lynchburg Rheumatology Clinic in Virginia wrote in a Letter to the Editor, September 30, 2010: “The price-fixing by Medicare over the years prompted many patients to wonder how we could stay in practice with the disparity over reasonable charges and ever decreasing compensation. The answer is, we cannot. While our situation is no different than other small businesses, it portends worrisome results for the Medicare patient.”

The ACR states that it “urges Congress to, at a minimum, pass a 13-month extension prior to November 30, 2010, to ensure physicians are compensated and can continue to provide care to Medicare patients.” It also requests that the SGR formula be fixed, so that further cuts in Medicare reimbursement will not take place and payments to physicians can stabilize to help them run their businesses. Business overhead already is closing in at 70% on average for physician offices, so the question of whether they can continue to care for Medicare patients is paramount. Office closures and rejection of Medicare patients will exacerbate the currently declining number of physicians available to treat patients.

Initiated in the Balanced Budget Act of 1997, Medicare payments became tied to a formula known as the Sustainable Growth Rate (SGR) which links reimbursement
Ask your physician to prescribe Numoisyn today!

Numoisyn Liquid
Prescribing Information
Ingredients: Water, sorbitol, linseed (flaxseed) extract, Chondrus crispus, methylparaben, sodium benzoate, potassium sorbate, dipotassium phosphate, propylparaben.
How Supplied: 30 mL per bottle or 300 mL per bottle.
Therapeutic Group: Numoisyn Liquid is an oral solution formulated for the relief of chronic and temporary xerostomia (dry mouth), which may be a result of disease, medication, oncology therapy, stress, or aging.
Indications: Numoisyn Liquid is indicated for the treatment of symptoms of dry mouth. Numoisyn Liquid relieves the symptoms of dry mouth by enhancing swallowing, improving speech mechanics, and lubricating the oral cavity like natural saliva. Numoisyn Liquid may be used to replace natural saliva when salivary glands are damaged or not functioning. The viscosity is similar to that of natural saliva.
Contraindications: Numoisyn Liquid are contraindicated in patients with a known history of hypersensitivity to any of the ingredients.
Special Precautions for Use: As Numoisyn Liquid contains linseed (flaxseed) extract, patients with irritable bowel syndrome or diverticular disease or those on a high linseed diet may experience abdominal discomfort.
Warning: Federal law restricts Numoisyn Liquid to sale by, or on the order of, a physician or properly licensed practitioner.
Interactions: There are no known interactions between Numoisyn Liquid and any medicinal or other products.
Directions for Use: Shake bottle well. Take 2 mL (about 1/2 teaspoon) of Numoisyn Liquid and rinse around in the mouth before swallowing. Use as needed.
Side Effects: Patients may experience difficulty in swallowing, altered speech, and changes in taste. If side effects persist or become severe, patients should contact a physician.
Storage: Store at room temperature. Do not refrigerate. Use within 3 months of first opening.

Numoisyn Lozenges
Prescribing Information
Ingredients: Sorbitol (0.3 g per lozenge), polyethylene glycol, malic acid, sodium citrate, calcium phosphate dibasic, hydrogenated cottonseed oil, citric acid, magnesium stearate, and silicon dioxide.
Pharmaceutical Form: Oral lozenge
Contents: 100 lozenges per bottle. Net weight of 40 g (0.4 g per lozenge).
Therapeutic Group: Numoisyn Lozenges are oral lozenges formulated to promote lubrication of oral mucosa that may be dry due to a variety of circumstances, including medication, chemotherapy or radiotherapy, Sjögren’s syndrome, or oral inflammation.
Indications: Numoisyn Lozenges are indicated for the treatment of xerostomia (dry mouth). Numoisyn Lozenges provide temporary relief of dry mouth due to damaged salivary function. Numoisyn Lozenges are formulated to support the natural protection of teeth provided by saliva so that no damage occurs to teeth with repeated use of the lozenges.
Contraindications: Numoisyn Lozenges are contraindicated in patients with fructose intolerance or a known history of hypersensitivity to any of the ingredients.
Warning: Federal law restricts Numoisyn Lozenges to sale by, or on the order of, a physician or properly licensed practitioner.
Interactions: There are no known interactions between Numoisyn Lozenges and any medicinal or other products.
Directions for Use: Let one Numoisyn Lozenge dissolve slowly in the mouth when needed. To obtain optimal effect, move the lozenge around in the mouth. Repeat as necessary. Do not exceed 16 lozenges in 24 hours.
Side Effects: Excessive consumption can cause minor digestive problems.
Storage: Store at room temperature. KEEP OUT OF REACH OF CHILDREN.
Overdose: No overdoses have been reported to date.

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changes. If results show cognitive impairment, patients can be taught coping strategies and undergo cognitive remediation therapy. Clinicians and family members can adopt methods of communication that help increase understanding and retention on the part of the patient.

In addition to age and depression many factors can contribute to cognitive function adding to the complex medical picture physicians and researchers already face with Sjögren’s patients. For example, patients might not be diagnosed with depression per se, but might be experiencing sadness, grief or anxiety because of their illness, all of which can affect cognitive function. Lack of adequate good-quality sleep, a problem for many Sjögren’s patients, can contribute to forgetfulness, confusion and ability to focus on mental tasks. Because of fatigue, many patients cannot socialize or engage in stimulating activities; socialization and other stimulating activities can positively affect neuropsychological functioning.

Reports of prevalence rates and degree of CNS involvement and secondary cognitive deficits in Sjögren’s have varied greatly in the literature and range from no findings to dementia. Small sample sizes and different diagnostic criteria used by reporting groups may explain the variance in findings. Deficits primarily have been reported in those skills related to verbal processing, verbal memory and language skills. Some studies have also found problems with attention, concentration and executive functioning. Verbal abilities in Sjögren’s appear to be more highly affected than non-verbal visuospatial abilities, and, interestingly, these findings occur within the context of normal Full Scale IQ scores. However, it should be pointed out that sometimes objective testing finds no memory deficits even when patients report memory problems.

**New insights and new questions about cognitive function in Sjögren’s**

In our recent study, we attempted to better define cognitive functioning in primary Sjögren’s syndrome (pSS). Eighteen pSS patients who met the American-European Consensus Group criteria entered the study along with 17 controls matched for gender, race and education. Table 1 shows the aspects of cognitive functioning that were measured and the tests used frequently in clinical settings for evaluation. Results showed no significant difference between pSS patients and controls in executive function, visual memory (including visual retention and recognition), Performance IQ, Full Scale IQ, and concentration and processing speed. However, verbal memory was significantly lower in the pSS group compared to controls. Because age and evidence of depression affect cognitive function, and because we know that depression occurs more frequently in Sjögren’s patients than in the population at large, these elements were controlled for statistically.

Findings that differed from those cited in previous publications include the fact that Sjögren’s patients demonstrated lower immediate visual recall but no difference in concentration, processing speed or executive functioning. These differences might reflect the diagnostic criteria used, selection bias, or methodological differences. Validation of these findings in additional, larger studies using pSS patients defined by the AECG criteria would be helpful.

| Table 1 |
|-------------------|------------------|
| **Measurement**   | **Test**         |
| Concentration; processing speed | Trail Making Test (TMT) |
| Executive functioning | Wisconsin Card Sorting Test (WCST) |
| Intellectual functioning | Wechsler Abbreviated Scale of Intelligence (WASI) |
| Verbal memory | California Verbal Learning Test-II (CVLT-II) |
| Visual memory | Visual Reproduction Subtest of the Wechsler Memory Scale-III |
| Depression | Symptom Checklist 90-R (SCLR-90) |

**Suggestions for the Clinician**

Clinicians should be aware that cognitive difficulties can occur in Sjögren’s and be prepared to investigate the multiple causes of those difficulties. Recognizing and communicating to patients that this problem exists can help make patients feel validated and lower anxiety levels.

A specialist should provide a full assessment for CNS disease. Baseline neuropsychological testing can be arranged when patients first indicate that they are having difficulty with cognitive tasks. Physicians also should examine patients’ list of medications for potential side effects and drug interactions that could impact cognitive function and perform further studies to rule out metabolic problems.

Several strategies can help patients cope with cognitive dysfunction. Clinicians should consider providing written material and instructions for patients at appointments to reduce the burden of recall. Family members should be encouraged to accompany patients to their appointments to help with recall and ask additional questions. Patients can write down the symptoms they wish to discuss and questions to ask ahead of time and bring them to the physician visit. They can also write down physician answers and keep them in a notebook or file. Finally, clinicians can direct patients to the Sjögren’s Syndrome Foundation for helpful resources in coping with Sjögren’s and its many symptoms and complications. The SSF website at www.sjogrens.org offers Patient Education Sheets on such topics as Brain Fog and Sleep Tips which healthcare professionals can download and distribute.

Patients with moderate to severe deficits should be referred for cognitive remediation therapy. Treatment of concurrent depression may also improve cognitive function in certain individuals. However, clinicians should keep in mind that many such drugs can exacerbate sicca symptoms and therefore choose medications judiciously.

More studies on neuropsychological impairment in Sjögren’s are needed to better delineate the extent and nature of this problem. In the meantime, clinicians should remain alert to cognitive problems in their Sjögren’s patients and investigate the many potential causes. Validation and treatment of major patient symptoms can help people better cope with this debilitating problem and decrease the overall burden of illness among Sjögren’s sufferers.

Continued on page 8 ▼
When moderate to severe Dry Eye patients drop ≥4 times a day, give them

LACRISERT®: All-day relief in a single daily dose*

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LACRISERT® is indicated in patients with moderate to severe Dry Eye syndromes, including keratoconjunctivitis sicca. LACRISERT® is indicated especially in patients who remain symptomatic after an adequate trial of therapy with artificial tear solutions. LACRISERT® is also indicated for patients with exposure keratitis, decreased corneal sensitivity, and recurrent corneal erosions.

LACRISERT® is contraindicated in patients who are hypersensitive to hydroxypropyl cellulose. The following adverse reactions have been reported in patients treated with LACRISERT® but were, in most instances, mild and temporary: blurring of vision, eye discomfort or irritation, matting or stickiness of eyelashes and red eyes. If improperly placed, LACRISERT® may result in corneal abrasion.

Please see brief summary of Prescribing Information on adjacent page.
“Healthcare Changes” Continued from page 2 ▼

to the overall economy. Since the Act’s passage, cuts have been scheduled, sometimes implemented and more often postponed by Congress, and, sometimes, physician payments were not received for long periods while the Centers for Medicare and Medicaid Services placed reimbursements on hold waiting for Congress to address scheduled cuts. At times, Congress enacted cuts retroactively. In 2002, physicians faced a 5.4% cut that was never reversed, and now, further major cuts are slated to occur.

Coding Changes

The Centers for Medicare and Medicaid Services also recently announced the removal of consultation service codes. While this move affects all physicians, rheumatologists are among those who are especially hit hard by the change. A consultation code has traditionally been used by rheumatologists for billing when patients are referred for a comprehensive review of medical records and diagnostic evaluation.

Many patients with complex conditions, such as Sjögren’s, are referred to rheumatologists by physicians who do not have the time or expertise to properly diagnose or treat these conditions. The ACR states that it “is concerned that the elimination of these codes could jeopardize specialty care and result in delayed diagnosis or inferior care to patients with complex conditions. The College believes that specialists should be fairly reimbursed for the level of time, expertise and analysis involved in a consultation.” The Sjögren’s Syndrome Foundation fully supports the ACR and other medical professional groups in the fight to have the codes reinstated.

Mandate for Adoption of Electronic Health Records

Another change in healthcare practice is the move from paper to electronic medical records (EMRs). EMRs are viewed as improving patient care (for example, cutting down on medical error and duplication of tests and providing more time for physicians with patients) and easy access to patient data by all parties who treat a patient. At the same time, the price tag for implementing new systems is daunting. The American Recovery and Reinvestment Act of 2009 (ARRA) provides financial incentives to those who implement the use of EMRs by 2014. Funds are provided for those who make the switch, but as many physicians point out to us, it will not begin to cover the costs. In addition, healthcare professionals who do not transfer to EMRs by 2015 face severe cuts in Medicare and Medicaid.

Changes for Clinicians

Prescriptions required for OTC products and drugs if patient is eligible for reimbursement through special health plans

Physicians face additional cuts scheduled for Medicare reimbursements

Medical specialists, including rheumatologists, hit by coding changes

Electronic Medical Records mandated

New Sjögren’s Clinic Opens at University of Rochester Medical Center

A new weekly clinic dedicated to managing Sjögren’s patients has opened at the University of Rochester Medical Center in Rochester, New York. The clinic will offer coordinated access to the many specialists involved in patient care facilitating the complex management of Sjögren’s patients. Having a center specifically on Sjögren’s also will provide a patient base to enable URCM to lead investigations into Sjögren’s to increase our understanding of the disease and test new potential therapeutic agents.

Andrea Coca, MD, a URCM rheumatologist, is overseeing the new clinic, which, in addition to rheumatology, includes physicians in ENT, ophthalmology and neurology. Dr. Coca says that the center has data accessed over the last four years on about 100 patients with sicca symptoms, and about 45-50% of those have been determined to have Sjögren’s. To contact the clinic, call 585-341-7900.

SSF Announces Research Grant Recipients

The Sjögren’s Syndrome Foundation awarded seven research grants in July 2010, holding the line on its research program despite the current economic climate. This year’s grantees will delve into new areas in Sjögren’s including genetics and epigenetics as well as hot topics in immunology. Grants were awarded in the amount of $35,000 a year; all grants are provided for two years depending on satisfactory progress. Twenty medical and scientific experts from the U.S. and around the world contributed their time and expertise this year as reviewers for the SSF research program.

“We would not have such a robust research program without the generosity of SSF members. This factor coupled with this year’s gesture from a current researcher to donate back to research is amazing,” says Steven Taylor, SSF CEO. The Galewood Foundation provided funding for two grants for a second year. In addition, for the first time in SSF history, a grantee relinquished their second year of grant money so that another grant could be funded. Sara Michie, MD, whose mother had suffered from Sjögren’s, will continue the second year of her research grant by carrying over funding from her first year and using funding from other sources.

Grantees are listed below along with shortened versions of their scientific abstracts. Full abstracts as well as guidelines and a list of review priorities for applications may be accessed online at http://www.sjogrens.org/research.

2010 Research Grants

Research Grant – Mechanisms in Developing Dry Eye
Sunil Chauhan, DVM, PhD
Schepens Eye Research Institute, Boston, Massachusetts

“Mechanism and Functional Relevance of Corneal Lymphangiogenesis in Dry eye Disease”

SSF Scientific Reviewers called Dr. Chauhan’s proposal a novel idea that could lead to a new treatment for the inflammation associated with dry eye or even a preventive therapy for dry eye. Dr. Chauhan recently was promoted to Investigator/Instruction at Schepens Eye Research Institute and is just launching his career in dry eye disease research.

Scientific Abstract

We have recently demonstrated that the draining lymphoid tissues are the primary site for generation of autoreactive-T cells in dry eye diseases (DED). However, the mechanisms by which corneal antigen-presenting cells (APC) migrate to the lymphoid compartment and prime autoreactive naive T cells, primary steps for induction of autoimmunity, are still not well understood.

We hypothesize and provide preliminary data that immunopathogenesis of DED is associated with the selective induction of corneal neo-lymphatic vessels which facilitate trafficking of mature corneal APC toward the draining lymph nodes. To validate our hypothesis, we propose three specific aims –Aims 1 and 2 involve confirmation and determination of cellular and molecular factors that contribute to lymphangiogenesis in DED cornea; and Aim 3 will test the efficacy of in-vivo blockade of select pro-lymphangiogenic molecules on DED. These studies will assist in identifying potentially important therapeutic targets in the ocular surface disease associated with Sjögren’s.
Results of a Sjögren’s Syndrome Foundation-funded research grant on cognitive impairment in Sjögren’s are due out soon and will be reported in a future Sjögren’s Quarterly. The study was carried out by Lynn Epstein, MD and Athena Papas, DMD, PhD at Tufts University.

**References**


**Research Grant – Epigenetics**

Lindsey Criswell, MD, MPH, Dsc
University of California, San Francisco
San Francisco, California

“Epigenetic Profiling of Multiple Cell and Tissue Types in Sjögren’s Syndrome”

Reviewers praised Dr. Criswell for investigating a new and promising area of research – epigenetics. It also was pointed out that the project might help identify important reasons for male/female differences in disease susceptibility.

**Scientific Abstract**

Epigenetic modifications such as DNA methylation do not affect the genetic sequence; however, they do play a critical role in transcriptional regulation of genes and subsequent gene expression. Methylation of DNA can be detected on a large scale basis using recently developed high-throughput technologies.

We propose to perform a comprehensive screen of 27,578 highly informative CpG sites spanning 14,495 genes across the genome using DNA derived from peripheral blood mononuclear cells (PBMCs), saliva and labial salivary gland biopsy tissue from 30 Sjögren’s cases and 30 controls to identify epigenetic profiles associated with disease susceptibility (Aim 1). We will also collect fresh blood samples to perform epigenetic studies in specific cell types following utilization of sophisticat-ed cell sorting techniques (Aim 2). The identification of unique epigenetic profiles in Sjögren’s will significantly transform our understanding of disease etiology and may lead to more effective approaches to prevention, diagnosis and treatment.

**Research Grant – Genetics**

Kathy L. Moser, PhD
Oklahoma Medical Research Foundation
Oklahoma City, Oklahoma

“The Genetic Basis of Human Sjögren’s Syndrome”

Reviewers were impressed with the proposed use of GWAS technology in the largest sample ever studied of SS subjects to elucidate possible loci linked to pathologic pathways. They concluded that the search for candidate genes in pSS analysing 700 SNPs with strong prior evidence of association with autoimmune diseases is an outstanding line of research in SS.

**Scientific Abstract**

Sjögren’s syndrome (SS) is a complex disorder influenced by both genetic and environmental factors. However, the genetics of human SS are virtually unexplored. Recent large-scale genetic studies in lupus, rheumatoid arthritis (RA) and other related diseases have pinpointed hundreds of important disease genes and revealed novel disease pathways.

Continued on page 12 ▼
HOW ARE YOUR SJÖGREN’S PATIENTS BALANCING THEIR DRY-MOUTH SYMPTOMS?

EVOXAC® CAN HELP.
Dry-mouth symptoms of Sjögren’s aren’t always recognized as a medical problem until they start disrupting daily lives.¹,² Yet adequate salivary flow is essential for good oral health, initiating enzymatic food digestion, facilitating taste bud sensation, and more.³,⁴ If your patients are having trouble with their dry-mouth symptoms due to Sjögren’s syndrome, learn how EVOXAC (cevimeline HCl) can help.⁵-⁷

Learn how EVOXAC can help increase salivary flow in patients with dry-mouth symptoms associated with Sjögren’s syndrome at EVOXAC.com.

IMPORTANT SAFETY INFORMATION
EVOXAC (cevimeline HCl) is indicated to treat the symptoms of dry mouth in patients with Sjögren’s syndrome.

- Cevimeline HCl is contraindicated in patients with uncontrolled asthma, known hypersensitivity to the drug, and when miosis is undesirable, e.g., in acute iritis and narrow-angle (angle-closure) glaucoma
- Cevimeline HCl can potentially alter cardiac conduction and heart rate and produce transient changes in hemodynamics. Cevimeline HCl should be administered with caution and under close medical supervision to patients with a history of cardiac disease, controlled asthma, chronic bronchitis, or chronic obstructive pulmonary disease
- Cevimeline HCl should be administered with caution to patients taking beta-adrenergic antagonists because of the possibility of conduction disturbances and to patients with a history of nephrolithiasis or cholelithiasis
- If a patient sweats excessively while taking cevimeline HCl, dehydration may develop
- Caution should be advised while driving at night or performing hazardous activities in reduced lighting
- Safety and effectiveness in pediatric patients have not been established

- Cevimeline HCl is metabolized by the P-450 isozymes CYP2D6 and CYP3A3/4. Thus, there may be potential for interaction between cevimeline HCl and other compounds
- Special care should be exercised when cevimeline HCl is taken by geriatric patients, considering the greater frequency of decreased hepatic, renal, or cardiac function
- The most frequently reported adverse events associated with the pharmacologic action of a muscarinic agonist (>10% incidence) in clinical trials of cevimeline HCl were: excessive sweating, nausea, rhinitis, and diarrhea. Consult the full Prescribing Information for other adverse events

References:
FDA Panel Recommends Lupus Drug

The first therapy for the treatment of systemic lupus erythematosus (SLE or lupus) in over 50 years has just made a major advance in the FDA approval/registration (NDA) process. On November 16, the Food and Drug Administration (FDA) Arthritis Advisory Committee voted overwhelmingly (13 to 2) to recommend the biologic Benlysta® for approval in SLE. The FDA will consider regulatory approval in early December; the agency usually follows the recommendation of the panel’s outside experts, but there is no guarantee. Human Genome Sciences (HGS), based in Rockville, Maryland, developed the anti-BLyS monoclonal antibody in collaboration with GlaxoSmithKline (GSK). The first of its kind in a class of B-lymphocyte stimulator (BLyS) inhibitors, Benlysta successfully met its primary endpoint in two Phase 3 trials.

The Sjögren’s Syndrome Foundation (SSF) was present for the full-day meeting involving physicians, researchers and patient representatives. HGS Vice President of Clinical Research, William Freimuth, MD, presented the Phase 2 and 3 Benlysta® (belimumab) SLE clinical trial data during the SSF Annual Luncheon Meeting held during the American College of Rheumatology last year. Elaine Alexander, MD, PhD, Chair of the SSF Medical and Scientific Advisory Board, the SSF Clinical Trials Consortium and moderator for that meeting says, “Our sincerest congratulations are extended to Human Genome Sciences and its partner. We have long faced a challenge in treating effectively such complex diseases as SLE and Sjögren’s, and this latest news marks a major potential breakthrough in addressing the clear need for treatment for many lupus patients, and hopefully, in the future, Sjögren’s patients.” Two centers in Europe currently are conducting small, exploratory trials in Sjögren’s with belimumab. The only anti-B cell therapy that has been FDA-approved for autoimmune disease so far is Rituxan® (rituximab), an anti-CD20 monoclonal antibody, for rheumatoid arthritis. ■

Transitions – NIDCR Director Tabak Assumes Position of Second-in-Command at NIH

After ten years at the helm of the National Institute of Dental and Craniofacial Research (NIDCR), Lawrence (Larry) Tabak, DDS, PhD has assumed the position of Principal Deputy Director of the National Institutes of Health (NIH). “Larry Tabak is an exceptional choice for the position of NIH Principal Deputy Director and one that the SSF and its extended scientific and clinical family applauds and celebrates,” says Elaine Alexander, MD, PhD, Chair of the SSF Medical and Scientific Advisory Board. “Larry’s ten-year tenure as NIDCR Director has been studded with multiple major accomplishments across a broad range of important scientific venues, including Sjögren’s. Uniquely, Larry has demonstrated the insight and vision for expanding the understanding of the pathobiology of Sjögren’s from an autoimmune exocrinopathy, prominently involving the exocrine glands of the mouth and eyes, to recognition of the complex and diverse multi-system manifestations and complications of this prevalent autoimmune/lymphoproliferative disorder. The SSF is extremely grateful to Larry and his NIDCR team for catalyzing translational medicine between basic and clinical research, fostering/supporting interactive collaborations between intramural and extramural scientists that have resulted in major advances in the field that, in some cases, may have important ramifications for the development of new therapeutics. Although we will miss his interactive and supportive leadership at the helm of NIDCR, we look forward to working closely with him in his new capacity and continuing our partnership with NIDCR Acting Director Isabel Garcia.”

Dr. Tabak has long been a highly valued friend to the Sjögren’s Syndrome Foundation and Sjögren’s patients. Under his leadership at NIDCR, the NIDCR accelerated its support of Sjögren’s research by providing an initial $11.5 million dollars for the International Registry on Sjögren’s and additional monies for an extension of that major project; a $3.5 million Request for Applications in Sjögren’s research; numerous Concept Clearances in Sjögren’s, the most recent being in May 2010; and ongoing support for the Sjögren’s Syndrome Clinic at the NIH which offers expert treatment for patients and clinical studies in Sjögren’s to expand our knowledge about the natural history of SS, disease complications and potential therapeutics. NIDCR took the lead on NIH sponsorship of several workshops and conferences hosted by the SSF, including a CME symposium for clinicians, a workshop on outcome measures, another on lymphoma and SS, and the IXth International Symposium on Sjögren’s.

Dr. Tabak always has highlighted the needs of patients who suffer from a broad range of medical conditions and diseases and continually has emphasized the fact that the NIH and medical and scientific community at large exist to help patients. In his farewell letter as he left his NIDCR post in August, Dr. Tabak mentioned the
We propose using powerful genome-wide association approaches to screen >1.1 million genetic variants for association with SS. Significant associations will be confirmed through replication studies in independent subjects. This project is a large, multidisciplinary international effort to discover the fundamental cause of human SS. Every gene and pathway established as causal in SS has significant potential for providing rapid advances in our understanding of disease mechanisms. These results will lay important groundwork for developing accurate diagnostic tools and identifying therapeutic targets tailored to disease relevant pathways in SS.

**Scientific Abstract**

Sjögren’s syndrome (SS), a chronic systemic autoimmune disease affecting primarily the salivary/lacrimal glands, is characterized by formation of lymphocytic foci (LF). We identified the presence of CD4+TH17 memory cells within LF of human patients, raising the question whether TH17 cells are responsible for subsequent glandular destruction. I propose to further characterize the different cell populations within LF of Sjögren’s patients, focusing heavily on possible regulatory T cells that suppress pro-inflammatory activities of CD4+TH17 cells, especially IL-27-secreting cells. In addition, I will examine the efficacy of gene therapy to down-regulate CD4+TH17 cell activity, and possibly disease, in salivary glands of a murine SS model, using an IL-27-expressing rAAV2-viral vector. Results are expected to show lack of regulatory cells within LF and the capability of suppressing SS disease progression utilizing this gene therapy approach, thereby establishing the basis for CD4+TH17 cells being pathogenic and providing proof-of-concept for future translational research.

**Research Grant – Immunology, Lymphocytic Infiltration and Gene Therapy**

Cuong Nguyen, PhD
University of Florida, Gainesville, Gainesville, Florida

“Suppression of TH17 cells using IL-27 gene therapy: A potential therapeutic approach for the treatment of Sjögren’s syndrome patients”

Supported by the Galewood Foundation

SSF Reviewers described Dr. Nguyen as a productive and talented young immunologist who should be encouraged and supported to further his interest in Sjögren’s. They emphasized the importance of investigating current theory of autoimmune pathology, the excellent collaborations and high likelihood of successful completion.

**First-Year Grant:**

**Research Grant – Gland Biology and Regeneration**

Helen P. Makarenkova, PhD
Neurosciences Research Foundation
San Diego, California

“Molecular mechanisms of lacrimal gland development and regeneration”

Supported by the Galewood Foundation

Dr. Makarenkova was awarded a second-year renewal grant in 2010.

**Second-Year Goals:**

Dr. Makarenkova is striving to understand the regulatory mechanisms underlying lacrimal gland (LG) development and repair and hopes the experiments will provide new insights and potentially lead to the development of new treatments to promote LG regeneration. During the first year, she delineated the cause for functional differences between Fibroblast Growth Factors (FGF) 7 and 10; determined that FGFR2b is necessary for LG morphogenesis; and discovered that Barx2 is important for LG morphogenesis and cooperates with FGF10 to regulate expression of Matrix Metalloproteinases, epithelial cell migration and LG bud elongation. She published an article in *Science Signaling* and presented at the American Society for Cell Biology meeting in December 2009.

**First-Year Grant:**

Dr. Makarenkova was awarded a second-year renewal grant in 2010.

**Second-Year Goals:**

During the second year of her SSF grant, Dr. Makarenkova will investigate how the molecular structure of different FGFs is translated into specific LG cell functions such as cell survival, migration, proliferation and differentiation and how FGFs cooperate with other factors in regulation of LG development and repair.

**Research Grant – Regulatory T Cells in Sjögren’s**

Jean Oak, MD, PhD
University of California, Irvine, Irvine, California

“Regulatory T Cell Function in a Mouse Model of Sjögren’s Syndrome”

Dr. Oak was noted by SSF Reviewers to be another young and excellent investigator who should be encouraged to de-
Patients should learn to manage it 3 ways

Helping patients understand that their dry mouth needs to be managed 3 ways is key to counseling. Why? Because if left untreated, dry mouth can lead to some fairly serious dental problems. While sipping water may help, it doesn’t lubricate and protect the mouth the way saliva does. The Biotène system, with its protein-enzyme formulations, offers products in each of the 3 management areas.

1. Soothe & Moisturize: Only Biotène offers the choice of a portable spray for on-the-go comfort, a soothing liquid and an effective gel that offers relief, especially at night.

2. Daily Cleaning: Only Biotène has 2 mouthwashes to reduce bad breath, and 3 cavity-preventing fluoride toothpastes that are specifically designed for dry mouth sufferers. Plus, our products are alcohol and SLS-free.

3. Saliva Stimulation: To help stimulate salivary flow throughout the day, Biotène provides 2 breath-freshening gums.

Recommend the Biotène system of products to all your patients with dry mouth symptoms.

Soothe & Moisturize (gel, spray, liquid)  Daily Cleaning (toothpaste, mouthwash)  Saliva Stimulation (chewing gum)

www.biotene.com
Dr. Michie was awarded a second-year renewal grant in 2010. As noted above, she will continue with her second year but allow her funding to be redirected for additional research through the SSF research program.

First-Year Grant:
By the end of the first year, Dr. Michie completed her first aim to determine which endothelia adhesion molecules and their lymphocyte receptors are highly expressed in inflamed lial salivary glands of pSS patients. After evaluating the glands from SS patients and controls for expression of a wide range of chemokines and chemokine receptors, she found that chemokines fell into 2 groups: 1) Chemokines that are expressed by epithelia (first group noted above) and compare the results with those of their ongo-

ing studies in NOD mice to determine if these mice are good models for in vivo studies of salivary gland chemokines and chemokine receptors.

The SSF thanks the expert reviewers who give generously of their time and knowledge. The following include those who in 2010 reviewed applications for SSF grants as well as SSF-sponsored Student Fellowships and abstracts at professional meetings for the SSF Outstanding Abstract Award: Austin Mircheff, PhD; Elaine Alexander, MD, PhD; Pablo Argueso, PhD; Olga Baker, DDS, PhD; Jill Buyon, MD; Philip L. Cohen, MD; Denise Faustman, MD, PhD; Philip C. Fox, DDS; Sarah Hamm-Alvarez, PhD; Roland Jons-son, DMD, PhD; Michael A. Lemp, MD; Eva Mezey, MD, PhD; J. Daniel Nelson, MD; Jerry Niederkorn, PhD; Ammon Peck, PhD; Andres Pinto, DMD; Manuel Ramos-Casals, MD, PhD; Hal Scofield, MD; Daniel J. Wallace, MD; and Driss Zoukhri, PhD.

First-Year Goals:
- **Research Grant – Cellular and Molecular Immunology**
  Sara Michie, MD
  Stanford University, Palo Alto, California

  “Lymphocyte migration to inflamed salivary glands in Sjögren’s syndrome”

**SSF and Vice President of Research Kathy Hammitt in his inclusion of thanks to those who made a difference during his tenure. The Sjögren’s Syndrome Foundation is grateful for Dr. Tabak’s leadership and appreciation for the patients, their families and the patient advocacy community. Isabel Garcia, DDS, MPH has assumed the role of Acting Director of the Institute while a search is conducted for a permanent Director. The Foundation has enjoyed immensely the opportunity to work closely with Dr. Garcia in her position as NIDCR Deputy Director and prior to that as Director of the Office of Science Policy and Analysis at NIDCR. ■

**New Products Released this Fall:**
**TOBRADEX® ST Suspension and SYSTANE® Balance Lubricant Eye Drops**

Two new treatments have become available this fall: TOBRADEX® ST Suspension and SYSTANE® Balance Lubricant Eye Drops.

**TOBRADEX® ST Suspension** is a fixed combination antibiotic (tobramycin) and steroid (dexamethasone) for the management of anterior blepharitis. It is formulated with xanthan gum and contains half the concentration of dexamethasone compared with the original formulation of TOBRADEX® Suspension. Both antibiotic and anti-inflammatory components penetrate the eyelid extremely well. The thicker drop allows patients to place it more accurately on affected lids to ensure the medicine is getting right to the area of need.

**SYSTANE® Balance** is a new artificial tear formulation for patients with MGD and posterior blepharitis. It contains a lipid emulsion system and a HP Guar-based molecule to create a gel to adhere to the eye’s surface. Studies indicate this product significantly improves the length of time that a lipid layer covers the eye and increases tear break-up time.
If a sharp and stabbing pain occurs in one of your salivary glands right before or while eating or drinking, the cause might be an obstruction (a stone or mucous plug). In rare cases, associated gland swelling can accompany the discomfort. Here are some tips for massaging or “milking” the gland that might help:

Additional Tips:

- Stay well hydrated to encourage the flow of saliva through the gland.
- Temporarily avoid foods and beverages that cause the pain and possible swelling.
- Apply warm compresses to the area to increase comfort.
- Ibuprofen may be taken temporarily to decrease pain and inflammation.
- Talk to your doctor about use of a mucolytic agent for 5-10 days to thin the saliva and allow it to easily pass through the salivary ducts.

In all cases of salivary gland swelling and associated pain a medical professional should be consulted as soon as possible to determine the cause.
Announcing the 11th International Symposium on Sjögren’s Syndrome

September 28 – October 1, 2011
Athens, Greece

Organized by: The Department of Pathophysiology, School of Medicine, University of Athens
Chair: Athanasios G. Tzioufas, MD
Honorary President: Harry M. Moutsopoulos, MD FACP, FRCP

Deadlines:
Abstracts – June 30, 2011; Open online submission of abstracts from April – June 2011
Early Registration – August 1, 2011
Early Registration Cost: Delegates: 450 Euros
Fellows and students: 250 Euros
Accompanying persons: 100 Euros

For information, contact:
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