

New chronic illness paradigm puts patient at centre

Conference highlights importance of close interprofessional collaboration, and patients being experts on their own care

by Alison DeLory

HALIFAX | It's time to invite patients back in.

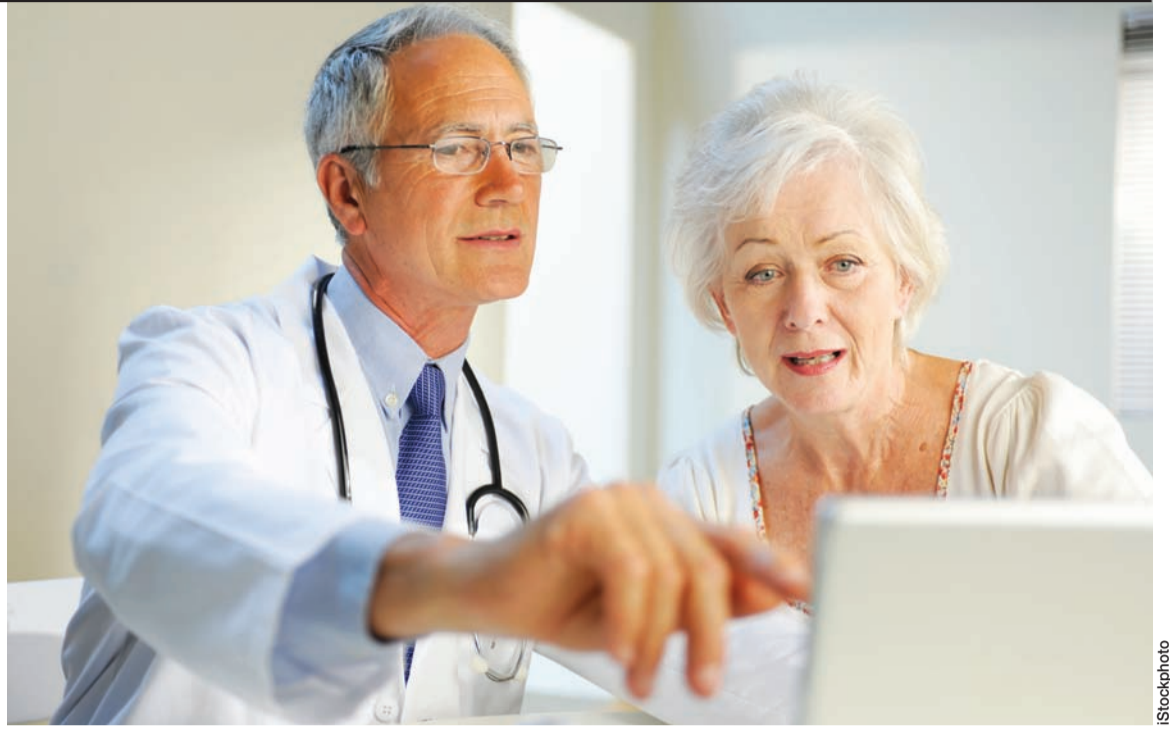
That was one of the key messages at the Chronic and Complex Health Care conference held in Halifax last month, where conference co-chair Dr. David Butler-Jones called for a strong primary health-care model where physicians work closely with other professionals and their patients to manage chronic diseases.

Dr. Butler-Jones applauded Canada's success in dealing with infectious health crises such as the H1N1 pandemic last year. Our health-care system, he said, also responds appropriately when patients suffer

acute problems that land them in emergency departments.

Yet while it excels in a crisis, the system breaks down in the long-term care of patients with complex, chronic health issues. "We need to step back, think about what we want the system to accomplish. Self-management will depend on a system that supports it," he said.

Self-management, or patient-centred care, was a recurring theme here, as was how physicians fit into this new paradigm. Self-management refers to informed, "activated" patients, who have the knowledge, skills, resources and confidence to manage their own health. But there is concern that if patients are at the centre



Self-management in chronic illness refers to informed, "activated" patients who have the knowledge, resources and confidence to manage their own health and work with members of a health-care team. New self-management programs in Canada empower patients but make sure they have support.

of their own care, physicians will become peripheral.

That won't happen, according to Dr. Butler-Jones. He said guidance and technical competence are essential in chronic care management and there is no substitute for medical training and expertise to facilitate that. Besides, patients need help separating fact from fiction. Dr. Butler-Jones said there is terrible misinformation on the Internet, including assertions that doctors, dentists, nurses and big pharma are all out to get patients. "We (physicians) have to think about how we articulate and communicate science. It's hard to do that in

10-second sound bites."

When chronically ill patients come into the examining room there are two experts present, said Dr. Robert Boulay, president of the College of Family Physicians of Canada. There is the physician, who is the medical expert, and the patient, who knows his or her own health better than the physician. "They (patients) have been pushed out of the way. We have to invite them back in," Dr. Boulay said.

But that doesn't diminish the important work physicians do treating chronically ill patients. "They're needed more than ever to co-ordinate care."

Dr. Boulay said this coordination would be most effective if every Canadian had a patient-centred medical home. The "medical home" could be a regular physician's office or place of care such as a health-care team in which the physician and staff are familiar with regular patients and their medical histories. Patients could connect with their medical homes by phone during regular office hours and receive communication and co-ordinated care from other physicians or sources, even after hours. Yet despite Canadian Institute for Health Information

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approximately 12 and 3% of those taking placebo. However, the incidences of decreases in serum calcium to $\leq 8.0\text{ mg/dL}$ (2.0 mM) and serum phosphate to $\leq 2.0\text{ mg Elemental Phosphorus/dL}$ (0.65 mM) were similar in both treatment groups.

In a small, open-label study, at higher doses (80 mg/day) some patients had elevated transaminases. However, this was not observed at 40 mg/day. No clinically significant toxicity was associated with these laboratory abnormalities.

Rare cases of leukemia have been reported following therapy with other bisphosphonates. Any causal relationship to either the treatment or to the patients' underlying disease has not been established.

Post-Market Adverse Drug Reactions

The following adverse reactions have been reported in post-marketing use with alendronate:

Body as a Whole: Hypersensitivity reactions including urticaria and rarely angioedema. As with other bisphosphonates, transient symptoms as in an acute-phase response (myalgia, malaise, asthma and rarely, fever) have been reported with alendronate, typically in association with initiation of treatment. Rarely, symptomatic hypocalcemia has occurred, both in association with predisposing conditions and in patients without known predisposing conditions. Rarely, peripheral edema.

Dental: Localized osteonecrosis of the jaw (ONJ) has been reported rarely with oral bisphosphonate treatment. ONJ is generally associated with local infection (including osteomyelitis), tooth extraction with delayed healing (see WARNINGS AND PRECAUTIONS, General).

Gastrointestinal: Esophagitis, esophageal erosions, esophageal ulcers, rarely esophageal stricture or perforation, and oropharyngeal ulceration. Some of these have been serious and required hospitalization. Rarely, gastric or duodenal ulcers, some severe and with complications (see WARNINGS AND PRECAUTIONS AND DOSAGE AND ADMINISTRATION).

Musculoskeletal: bone, joint, and/or muscle pain, rarely severe and/or incapacitating (see WARNINGS AND PRECAUTIONS); joint swelling; low-energy femoral shaft fracture (see WARNINGS AND PRECAUTIONS).

Nervous System: dizziness, vertigo, dysgeusia.

Skin: Rash (occasionally with photosensitivity), pruritus, alopecia, rarely severe skin reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis.

Special Senses: Rarely uveitis, scleritis or episcleritis.

DRUG INTERACTIONS

(see Prescribing Summary and Product Monograph for full listing)

Alendronate is not expected to interact with other drugs based on effects on protein binding, renal excretion, or metabolism of other drugs.

Concomitant use of hormone replacement therapy (HRT [estrogen \pm progestin]) and FOSAMAX[®] was assessed in two clinical studies of one or two years' duration in postmenopausal osteoporotic women. Combined use of FOSAMAX[®] and HRT resulted in greater increases in bone mass, together with greater decreases in bone turnover, than seen with either treatment alone. In these studies, the safety and tolerability profile of the combination was consistent with those of the individual treatments (see ADVERSE REACTIONS, Clinical Trial Adverse Drug Reactions, Concomitant Use with Estrogen/Hormone Replacement Therapy in the Product Monograph). The studies were too small to detect antifracture efficacy; no significant differences in fracture incidence among the treatment groups were found. Specific interaction studies were not performed. FOSAMAX[®] was used in osteoporosis studies in men, postmenopausal women, and glucocorticoid users, with a wide range of commonly prescribed drugs without evidence of clinical adverse interactions.

In a three-year, controlled, clinical study (n=2027) during which a majority of patients received concomitant NSAIDs, the incidence of upper gastrointestinal adverse events was similar in patients taking FOSAMAX[®] 5 or 10 mg/day compared to those taking placebo. However, since NSAID use is associated with gastrointestinal irritation, caution should be used during concomitant use with FOSAMAX[®].

Drug-Food and Drug-Herb Interactions - Food and beverages other than plain water, and herbal products, may markedly reduce the absorption and effectiveness of alendronate. FOSAMAX[®] must be taken at least one-half hour before the first food, beverage, or medication of the day with plain water only (see DOSAGE AND ADMINISTRATION, Information to Be Provided to the Patient in the Product Monograph).

Drug-Laboratory Interactions - Interactions with laboratory tests have not been established.

Drug-Lifestyle Interactions - No studies on the effects on the ability to drive and use machines have been performed. However, certain adverse reactions that have been reported with FOSAMAX[®] (e.g., dizziness, vertigo, visual disturbances, and severe bone, muscle or joint pain) may affect some patients' ability to drive or operate machinery. Individual responses to FOSAMAX[®] may vary.

OVERDOSAGE

No specific information is available on the treatment of overdosage with alendronate. Hypocalcemia, hypophosphatemia, and upper gastrointestinal adverse events, such as upset stomach, heartburn, esophagitis, gastritis, or ulcer, may result from oral overdosage. Milk or antacids should be given to bind alendronate. Vomiting should not be induced and the patient should remain fully upright. Dialysis would not be beneficial.

Vitamin D toxicity has not been documented during chronic therapy in generally healthy adults at a dose less than 10,000 IU/day. In a clinical study of healthy adults, a 4000 IU daily dose of vitamin D₃ for up to five months was not associated with hypercalcemia or hypercalcaemia. For management of a suspected drug overdose, contact your regional Poison Control Center.

Please see the Product Monograph for information on DOSAGE FORMS, COMPOSITION AND PACKAGING

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Product Monograph available at
www.merckfrosst.com
or upon request at 1-800-567-2594



Member



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Change funding models for chronic care: CFPC president

by Alison DeLory

HALIFAX | Dr. Robert Boulay, president of the College of Family Physicians of Canada and an FP in Miramichi, N.B., answered some questions posed by the *Medical Post* on the changing role of the FP in chronic disease care at the Chronic and Complex Health Care Conference here last month.

Q: With primary-care models emphasizing patient-centred care, some FPs may feel they are being squeezed out. Is this justified?

I can understand the fear. Under the fee-for-service system, it's a realistic fear. Chronic diseases take a lot of time to manage. We need to keep pressing governments to change funding models to enable us to treat chronic diseases.

Q: Should doctors fear losing responsibility for the care of their patients?

Doctors want security for themselves. It's not a fear of losing turf. We want to continue to be providers for our families and our patients. We (at the CFPC) want to make sure they get what they need. To ask doctors to leap wholeheartedly into new systems breeds reluctance: Show them the path and show them the destination and they'll be more willing to take it. That's why



Dr. Boulay

we need more pilots (projects).

Q: Are family physicians still the best professionals to treat chronic disease?

I think so. Others, including nurse practitioners, pharmacists, certified diabetes educators, dietitians and social workers should also be part of

team, but there has to be a sustained long-term relationship with a physician. The physician may or may not be the team leader, but the physician has to assume a lot of the clinical lead and take responsibility for establishing relationships.

Q: What about the legal responsibility? Physicians are concerned they will be liable for treatment provided by another member of a patient's care team.

In a team there is shared responsibility. This (liability) is a red flag that's often raised. Yet in my experience it's never happened. It's a myth. It's a unicorn.

Q: What is your main goal as president?

To get physicians to step up. To promote physician leadership. To have people assume a leadership role in the transformation of health care. To be enablers of change, not barriers to change.

Half of Canadians have chronic illness

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figures that show Canada spent \$191.6 billion on health care last year, approximately one in five Canadians does not have a family physician. “Most Canadians have had some difficulty accessing health-care for themselves and their family members,” Dr. Boulay said.

Dr. Butler-Jones said the answer lies in primary-care teams that include a variety of disciplines with a mix of expertise. “Many elements of medical care or prevention can be carried out by other disciplines. The key is building teams suited to patient needs, with complementary skills, but always with a comprehensive and integrative view and approach,” he said.

Cost control essential

According to the Toronto-based Institute for Optimizing Health Outcomes (IOHO), more than half of all Canadians (16.5 million) have one or more chronic conditions and the number is increasing as the population ages.

Besides premature death and a lower quality of life for the patient, chronic diseases create large adverse economic effects on families and communities. Both direct costs (such as hospital care, specialized treatment, physician care and prescription drugs) and indirect costs (the value of economic output lost because of illness, disability or premature death) are enormous. The economic burden on Canada caused by mental illness alone is estimated at more than \$14.3 billion annually, according to a June 2010 report from the Institute of Health Economics. The Canadian Diabetes Association reports the economic burden of diabetes in Canada was \$12.2 billion for 2010.

Caring for chronically ill patients is time consuming. They receive on average 12 hours of professionally managed health-care visits a year according to the IOHO, and their complex needs require patience. Dr. Butler-Jones said physicians need sufficient time to sort through the issues with them. “We say: ‘What’s your issue?’ How do they know which of the five things they are suffering from is ‘the issue?’” he asked.

Dr. Stanley Kutcher, a pediatric psychiatrist at the IWK Health Centre in Halifax, said the cost of treating chronic diseases can be reduced through novel primary-care models. It’s not always necessary, cost-effective or in the patient’s best interest to have a physician in

charge of patient care, he said.

“There are overlaps in provider competencies among different professionals. (We must) try to ensure that physicians are being used to deliver those competencies that cannot be more cheaply and as effectively delivered by other providers.” Focus on what is doable in primary health-care, Dr. Kutcher advised, and make it competency driven, not professionally driven. He suggested giving people on the front lines (such as peer mediators trained in mental health-care) the core competencies to deal with patients.

Dr. Butler-Jones also advo-



Dr. Butler-Jones Dr. Kutcher

cated proactivity: “We think of vaccines and prevention differently than we think about treatment. We don’t question paying for lipid drugs in the same way we question new vaccines or recreation programs for kids.” Other cost-effective interventions he cited are diabetes prevention,

colorectal cancer screening, promotion of healthy eating and HIV/AIDS prevention.

Across Canada, provinces are increasingly using the Stanford Chronic Disease Self-Management Program to help patients gain confidence in their ability to control their symptoms. Through adapted Stanford models, small groups meet once a week for six weeks. A pair of trained lay leaders, with health problems of their own, facilitate the meetings that are highly interactive and focused on building skills and sharing experiences.

New Brunswick’s version is called My Choices—My Health. Bronwyn Davies is the director of primary health-care

and chronic disease prevention and management strategy for the N.B. department of health. Speaking at the Chronic and Complex Health Care conference, she said the program “empowers patients but makes sure they have support. Self-management support needs to go along with self-management for patients.” Since the program began in 2008, some 105 small groups have formed, but administrators say it is a challenge to get physicians to refer patients to the program.

Davies also said electronic medical records are essential to improving the care of patients with chronic diseases, but until their use is more widespread, her province has had to try



Proven efficacy. Single-dose convenience.

PRESCRIBING SUMMARY

IMPORTANT: For complete prescribing information, please refer to the full Product Monograph at www.pfizer.ca.

Patient Selection Criteria

THERAPEUTIC CLASSIFICATION

Antibacterial Agent

INDICATIONS AND CLINICAL USE

In adults

Zmax SR (azithromycin sustained-release granules for oral suspension) is indicated in adults for treatment of respiratory tract infections caused by susceptible strains of the designated microorganisms in the following diseases and specific conditions: acute bacterial exacerbations of chronic bronchitis due to *Haemophilus influenzae*, *Moraxella catarrhalis* or *Streptococcus pneumoniae*; acute bacterial sinusitis due to *Haemophilus influenzae*, *Moraxella catarrhalis* or *Streptococcus pneumoniae*; community-acquired pneumonia of mild severity due to *Chlamydia pneumoniae*, *Haemophilus influenzae*, *Mycoplasma pneumoniae* or *Streptococcus pneumoniae*.

Azithromycin should not be used in patients with pneumonia who are judged to be inappropriate for outpatient oral therapy because of moderate to severe illness or risk factors such as any of the following: patients with cystic fibrosis, patients with nosocomial acquired infections, patients with known or suspected bacteremia, patients requiring hospitalization, or patients with significant underlying health problems that may compromise their ability to respond to their illness including immunodeficiency or functional asplenia.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Zmax SR and other antibacterial drugs, Zmax SR should be used only to treat infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information is available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Because some strains are resistant to azithromycin, when applicable, appropriate specimens should be obtained before Zmax SR treatment, for initiation of culture, susceptibility and serology tests to determine the causative organism(s) and susceptibility to azithromycin. Therapy with Zmax SR may be initiated before results of these tests are known; once the results become available, antibacterial treatment should be modified accordingly.

CONTRAINDICATIONS

Zmax SR (azithromycin sustained-release granules for oral suspension) is contraindicated in patients with hypersensitivity to azithromycin, erythromycin, any macrolide or ketolide antibiotic or to any ingredient in the formulation or component of the container. For a complete listing, see **DOSAGE FORMS, COMPOSITION AND PACKAGING** section of the product monograph.

Safety Information

WARNINGS AND PRECAUTIONS (also see Supplemental Product Information)

General

Serious allergic reactions, including angioedema, anaphylaxis and dermatological reactions including Stevens-Johnson syndrome and toxic epidermolysis have been reported rarely (with rare reports of fatalities) in patients on azithromycin therapy (see **CONTRAINDICATIONS**).

As with any antibacterial preparation, observation for signs of superinfection with nonsusceptible organisms, including fungi is recommended.

Cardiovascular

Prolonged cardiac repolarisation and QT interval, imparting a risk of developing cardiac arrhythmia and *torsades de pointes*, have been seen in treatment with other macrolides. A similar effect has been reported with azithromycin and cannot be completely ruled out. There is information that “QT Related Adverse Events” may occur in some patients receiving azithromycin. There have been spontaneous reports from post-marketing experience of prolonged QT interval and *torsades de pointes* (see **ADVERSE REACTIONS – Post-Market Adverse Drug Reactions** section of the product monograph).

Gastrointestinal

A higher incidence of gastrointestinal adverse events (8 of 19 subjects) was observed when azithromycin was administered to a limited number of subjects with GFR < 10 mL/min (see **WARNING AND PRECAUTIONS, Renal Impairment** section of the product monograph).

Sensitivity/Resistance

Prescribing Zmax SR in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

For additional information on Warnings and Precautions, see the Supplemental Product Information section.

Special Populations

Pregnant Women: There are no adequate and well-controlled studies in pregnant women. Zmax SR should not be used during pregnancy unless the expected benefit to the mother outweighs any potential risk to the fetus.

Nursing Women: Azithromycin has been reported to have been secreted into human breast milk. Therefore, Zmax SR should not be used in the treatment of nursing women unless the expected benefit to the mother outweighs the possibility of any potential risk to the infant. Azithromycin may accumulate in breast milk over time with Zmax SR single dose therapy.

Pediatrics (<18 years of age): Zmax SR is not recommended in pediatric patients, i.e., patients below 18 years of age.

ADVERSE REACTIONS

During Phase III pivotal clinical studies, 23% of adult subjects receiving Zmax SR experienced treatment-related adverse reactions, as judged by the Investigator to be possibly, probably or definitely related to Zmax SR. Most gastrointestinal events were mild to moderate in severity, occurred on the day of dosing and resolved within 1-2 days. Discontinuations from study due to treatment-related adverse events were comparable between the pooled Zmax SR studies (0.2%, 3/1292) and comparator groups (0.5%, 6/1304).

Clinical Trial Adverse Drug Reactions

Because clinical trials are conducted under very specific conditions, the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates seen in clinical trials of another drug. Adverse drug reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.

Adverse drug reactions (adverse reactions) are new or worsening medical events that are judged by the Investigator to be possibly, probably or definitely related to the study drug. Adverse reactions that could occur with Zmax SR are derived from several sources: (i) adverse reactions observed in the pivotal clinical trials of Zmax SR; (ii) adverse reactions observed in other Zmax SR trials, including studies performed in other indications or in other target populations; and (iii) adverse reactions that are known to occur with immediate-release azithromycin, but were not observed in clinical trials of Zmax SR (azithromycin sustained-release granules for oral suspension).

The most common treatment-related adverse reactions occurring in ≥1% of Zmax SR-treated adult patients receiving a single 2 g dose of Zmax SR in pivotal clinical trials (pooled results of 5 studies) were diarrhea (10.9%), nausea (3.9%), abdominal pain (2.7%), headache (1.3%) and vomiting (1.1%).

For additional information on adverse reactions, see the Supplemental Product Information section. See the Zmax SR product monograph for complete information on adverse reactions.

other things. For example, recently a program was introduced in the Moncton, N.B., area where diabetics with high blood glucose had their test results printed on bright pink paper to help grab their physicians' attention.

Dr. Kutcher reminded the conference to stay focused on meeting the needs of the population and not the needs of professionals. He said some clinics do not stay open past 4:30 p.m., and asked rhetorically whether people who get sick at night deserve treatment.

"Their (patient) needs should drive how we provide care. We're moving in the right direction but we have a tremendous way to go."

Self-management requires support of 'health coach'

by Alison DeLory

HALIFAX | Patients who actively manage their own health feel better and have better health outcomes, said Dr. Durhane Wong-Rieger (PhD), president of the Toronto-based Institute for Optimizing Health Outcomes at the Chronic and Complex Health Care Conference here last month. But they can't do it alone. "Without the health professional, patient self-management skills don't



Dr. Wong-Rieger

last long . . . (only) six months to two years."

Patients need evidence-based information, resources and confidence. Without those elements, adherence is sub-optimal, she said.

Dr. Wong-Rieger's data showed 14% to 21% of patients never fill their prescriptions, 30% to 50% don't take medication in the recommended manner, 66% with hypertension have poor blood pressure control due to non-adherence, and 21% of type 1 diabetics never

Traditional care model vs. health coaching

Traditional care	Health coaching
Health-care professional is expert	Health-care professional offers evidence-based options
Patient told what to do	Patient is expert in life and chooses options
One size fits all solutions	Individually tailored solutions
Extrinsic motivators	Intrinsic motivators
Patient required to facilitate change	Collaboration and assistance in facilitating change
Ignores barriers to change	Addresses barriers to change
Resistance to change rises	Resistance to change lowers
Goal-setting overload	Number and magnitude of goals suit patient

check their blood glucose levels.

'Health coaching'

Dr. Wong-Rieger's ideas for integrated chronic disease self-management involve a high level of self-management support or "health coaching."

The role of the health coach, she said, is to provide patients with knowledge, motivation and problem-solving skills within proactive practice team environments. Health coaching may also involve brief motivational interviews to help patients explore and resolve their ambivalence.

No single approach—neither patient-centred nor professionally managed care—works in isolation, said Dr. Wong-Rieger. "We must build a system that integrates and supports both."

To report an adverse event, please contact: 1-866-234-2345.

DRUG INTERACTIONS

Overview

Caution is warranted when azithromycin is administered to a patient with a history of a significant cardiac repolarization disorder or who is taking other medicinal products that cause a prolonged QT interval (see **WARNINGS AND PRECAUTIONS, Cardiovascular** and **ADVERSE REACTIONS, Post-Market Adverse Drug Reactions** sections of the product monograph).

Azithromycin does not interact significantly with the hepatic cytochrome P450 system. It is not believed to undergo the cytochrome P450-related drug interactions seen with erythromycin and other macrolides. Hepatic cytochrome P450 induction or inhibition via cytochrome metabolite complex does not occur with azithromycin.

See the product monograph for a complete list of potential drug-drug interactions.

Administration

DOSE AND ADMINISTRATION (also see Supplemental Product Information)

Dosing Considerations

A single 2 g dose of Zmax SR is not bioequivalent and is not interchangeable with a single 2 g dose of azithromycin immediate-release (tablets or powder for oral suspension).

A single 2 g dose of Zmax SR is not bioequivalent and is not interchangeable with any regimens employing azithromycin immediate-release oral formulations (tablets or oral suspension) due to a different pharmacokinetic profile (see **ACTION AND CLINICAL PHARMACOLOGY, Pharmacokinetics** and **DETAILED PHARMACOLOGY, Human Pharmacology**, and **Pharmacokinetics** sections of the product monograph).

Recommended Dose and Dosage Adjustment

The recommended dose for adults is a single 2 g dose of Zmax SR given as a suspension.

Zmax SR provides a full course of antibacterial therapy in a single oral dose.

It is recommended that Zmax SR be taken on an empty stomach (at least 1 hour before or 2 hours following a meal).

Geriatrics: No dose adjustment is necessary in elderly patients requiring Zmax SR therapy (see **ACTION AND CLINICAL PHARMACOLOGY, Pharmacokinetics, Special Populations and Conditions** sections of the product monograph).

Pediatrics (<18 years of age): Zmax SR is not recommended in pediatric patients, i.e., patients below 18 years of age.

SUPPLEMENTAL PRODUCT INFORMATION

WARNINGS AND PRECAUTIONS

General

Allergic reactions may occur during and soon after treatment with azithromycin. Despite initially successful symptomatic treatment of the allergic symptoms, when symptomatic therapy was discontinued, the allergic symptoms recurred soon thereafter in some patients without further azithromycin exposure. These patients required prolonged periods of observation and symptomatic treatment. If an allergic reaction occurs, the drug should be discontinued and appropriate therapy should be instituted. Physicians should be aware that reappearance of the allergic symptoms may occur when symptomatic therapy is discontinued.

Azithromycin and ergot derivatives should not be co-administered due to the possibility that ergot toxicity may be precipitated by macrolide antibiotics.

Severe neutropenia (WBC <1000/mm³) may adversely affect the distribution of azithromycin and its transport to the site of infection. Antibacterials with proven efficacy in this population should be used, as outlined by relevant guidelines for the treatment of patients with severe neutropenia. No studies of Zmax SR have been conducted in patients with severe neutropenia and the efficacy and safety of Zmax SR has not been established in this patient population.

Infantile hypertrophic pyloric stenosis (IHPS) has been reported in 2 premature siblings treated after birth with azithromycin; a causal relationship between azithromycin and IHPS could not be concluded from this report, but the theoretical possibility for such a relationship exists.

Zmax SR contains 19.36 g of sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrose-isomaltase insufficiency should not take this medicine, due to the sucrose content. In addition, patients with diabetes mellitus should pay appropriate attention to the sugar content of Zmax SR.

Gastrointestinal

Clostridium difficile-associated disease

Clostridium difficile-associated disease (CDAD) has been reported with use of many antibacterial agents, including azithromycin. CDAD may range in severity from mild diarrhea to fatal colitis. It is important to consider this diagnosis in patients who present with diarrhea, or symptoms of colitis, pseudomembranous colitis, toxic megacolon, or perforation of colon subsequent to the administration of any antibacterial agent. CDAD has been reported to occur over 2 months after the administration of antibacterial agents.

Treatment with antibacterial agents may alter the normal flora of the colon and may permit overgrowth of *Clostridium difficile*. *Clostridium difficile* produces toxins A and B, which contribute to the development of CDAD. CDAD may cause significant morbidity and mortality. CDAD can be refractory to antimicrobial therapy.

If the diagnosis of CDAD is suspected or confirmed, appropriate therapeutic measures should be initiated.

Hepatic/Biliary/Pancreatic

Since the liver is the principle route of elimination for azithromycin, the use of Zmax SR should be undertaken with caution in patients with impaired hepatic function (see **ACTION AND CLINICAL PHARMACOLOGY, Pharmacokinetics** section of the product monograph).

See the Zmax SR product monograph for complete warnings and precautions on the following: drug-drug interactions, lysosomal lipid storage diseases, ergot derivatives coadministration, severe neutropenia, infantile hypertrophic pyloric stenosis, carcinogenesis and mutagenesis, cardiovascular effects, *Clostridium difficile*-associated disease, hepatic/biliary/pancreatic effects, neurologic effects, renal impairment, and effects on sexual function/reproduction.

ADVERSE REACTIONS

Post-Market Adverse Drug Reactions

The following adverse experiences have been reported in patients receiving azithromycin under conditions (e.g., open trials, marketing experience) where a causal relationship is uncertain or in patients treated with significantly higher than the recommended doses for prolonged periods.

In addition, because these reactions are reported voluntarily from a population of uncertain size, reliably estimating their frequency is not always possible.

The following post-market adverse reactions have been reported in patients receiving azithromycin: blood and lymphatic system disorders (agranulocytosis, haemolytic anaemia, thrombocytopenia); cardiac disorders (arrhythmia [including ventricular tachycardia], palpitations. There have been reports of electrocardiogram QT prolonged and *torsade de pointes* in patients receiving therapeutic doses of azithromycin, including a pediatric case report of QT interval prolongation which reversed to normal upon discontinuation [see **Warning & Precautions, Cardiovascular**]; congenital, familial and genetic disorders (pyloric stenosis); ear and labyrinth disorders (hearing impaired [including deafness and vertigo]*); eye disorders (visual impairment); gastrointestinal disorders (constipation, diarrhea, pancreatitis, tongue discoloration, vomiting, ageusia, dysgeusia); general disorders and administration site conditions (asthenia, fatigue, edema); hepato-biliary disorders (hepatitis fulminant, hepatitis, hepatic function abnormal, jaundice cholestatic. There have also been cases of hepatic necrosis and hepatic failure, which have resulted in death); immune system disorders (anaphylactic reaction [with fatalities], serum sickness, angioedema); infections and infestations (pseudomembranous colitis, vaginal infection); metabolism and nutrition disorders (dehydration, decreased appetite, hypoglycaemia); musculoskeletal, connective tissue and bone disorders (arthralgia, myalgia); nervous system disorders (anosmia, convulsion, dizziness, hyposensitivity, parosmia, paraesthesia, psychomotor hyperactivity, syncope); psychiatric disorders (aggression, agitation, anxiety, nervousness); renal and urinary disorders (nephrotic syndrome, renal failure acute, tubulointerstitial nephritis); skin and subcutaneous tissue disorders (dermatitis exfoliative, erythema multiforme, photosensitivity reaction, pruritus, Stevens-Johnson syndrome, toxic epidermal necrolysis, urticaria); vascular disorders (hypotension, vasculitis).

* Hearing impairment (including hearing loss, deafness and/or tinnitus) has been reported in some patients receiving azithromycin. Many of these have been associated with prolonged use of high doses in investigational studies. In those cases where follow up information was available, the majority of these events were reversible.

See the Zmax SR product monograph for complete information on adverse reactions.

ADMINISTRATION

Absorption: The Zmax SR microspheres encapsulate the active drug and prevent dissolution and absorption of azithromycin in the low pH of the stomach; in the higher pH of the small intestine the microspheres dissolve and the drug is absorbed in the small intestine.

Administration of Zmax SR with food may increase absorption of azithromycin compared to the recommended mode of administration (empty stomach). Coadministration of an antacid with Zmax SR does not affect absorption.

Hepatic Impairment: No dosage adjustment for Zmax SR is recommended for patients with mild-to-moderate hepatic impairment, based on studies with immediate-release formulations. Nonetheless, since the liver is the principal route of elimination for azithromycin, the use of Zmax SR should be undertaken with caution in patients with impaired hepatic function (see **ACTION AND CLINICAL PHARMACOLOGY, Special Populations and Conditions, Hepatic Insufficiency** sections of the product monograph).

Renal Impairment: No dosage adjustment for Zmax SR is recommended for patients with GFR 10-80 mL/min. Zmax SR should be used cautiously in patients with GFR <10 mL/min. No studies have been conducted in patients requiring hemodialysis (see **WARNINGS AND PRECAUTIONS, Renal Impairment**, and **ACTION AND CLINICAL PHARMACOLOGY, Special Populations and Conditions, Renal Insufficiency** sections of the product monograph).

Vomiting after Dosing

In the event that a patient vomits within 5 minutes of administration of Zmax SR, the healthcare provider should consider additional antibacterial treatment since there would be minimal absorption of azithromycin. Since insufficient data exist on absorption of Zmax SR if a patient vomits between 5 and 60 minutes following administration, alternative therapy should be considered. Neither a second dose of Zmax SR nor alternative treatment is warranted if vomiting occurs ≥60 minutes following administration, in patients with normal gastric emptying. In patients with delayed gastric emptying, alternative therapy should be considered.

Administration

Instructions for Pharmacists: To reconstitute, add 60 mL water and replace cap. Shake bottle well before dispensing. Do not refrigerate. Reconstituted suspension should be consumed in a single dose and within 12 hours of reconstitution.

OVERDOSAGE

For management of a suspected drug overdose, contact your regional Poison Control Centre.

Ototoxicity and gastrointestinal adverse events may occur with an overdose of azithromycin SR.

Experience with azithromycin indicates adverse events experienced in higher than recommended doses are similar to those seen at normal doses. In the event of overdose, general symptomatic and supportive measures are indicated as required.

Based on Product Monograph dated July 14, 2010.

Product Monograph available upon request. Call 1-800-463-6001, visit www.pfizer.ca, or contact

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Member



A little spice keeps C. diff away

by Ed Susman

SAN ANTONIO | If that yummy meatball contains the common spice turmeric, people may be able to avoid nosocomial infections with increasingly hard-to-treat *Clostridium difficile*.

The magic ingredient in turmeric, curcumin, appeared to inhibit the growth of various strains of *C. difficile* in vitro, reported Dr. Rattan Patel, a microbiologist and gastroenterologist at Cedars Sinai Medical Center in Los Angeles.

"It's likely that daily use of turmeric in hospital settings, in food products such as curry or soup, can potentially decrease the incidence of *Clostridium difficile*-associated diarrhea,"

Dr. Patel suggested at the recent annual meeting of the American College of Gastroenterology meeting.

The use of turmeric as a protective agent against gastrointestinal disorders is not a new idea. Dr. Patel said indigenous people on the Indian subcontinent have been using turmeric for more than 2,000 years as a protective ingredient to ward off infection.

He noted more studies are needed to determine the mechanism of action and physiological effects of the spice.