Asthma Treatment & the “SMART” Regimen

The SMART regimen (or Symbicort Maintenance And Reliever Therapy) has been approved recently by Health Canada. Symbicort is a combination of budesonide, a corticosteroid and formoterol, a long-acting beta agonist. Symbicort was formerly approved only for maintenance treatment of asthma where combination therapy was appropriate. The monograph stated that Symbicort should not be used as a rescue medication for acute asthma symptoms. The new SMART indication allows Symbicort to be used as maintenance therapy and for the relief of acute asthma symptoms. The Canadian Asthma Consensus Guidelines (last updated in 2003) do not recognize this new indication; however “the 2006 Global Initiative for Asthma (GINA) guidelines do incorporate SMART therapy and suggest formoterol / budesonide can protect from severe exacerbations and may be used for both maintenance and reliever therapy”.

Patients who are adequately controlled with occasional use of a short-acting beta agonist (e.g. Ventolin-salbutamol) and children under 12 should not use SMART therapy. The maintenance dosing for SMART therapy is one or two inhalations twice daily or two inhalations once daily. If reliever therapy is needed one inhalation may be taken. If relief is not obtained in a few minutes up to 6 additional doses may be taken to a maximum of 8 inhalations of Symbicort per day. If another reliever medication is used (e.g. salbutamol) no more than 4 inhalations of Symbicort per day should be used. The SMART dosing guidelines are for the Symbicort 100 Turbuhaler (budesonide 100 mcg/ formoterol 6 mcg) and the Symbicort 200 Turbuhaler (budesonide 200 mcg / formoterol 6 mcg).

Reported adverse effects with the SMART regimen include tremors or palpitations which usually resolve after a few days. The need for increased use of rescue medication may indicate worsening asthma requiring reassessment. It is important for patients using the SMART regimen to continue to use Symbicort regularly as maintenance therapy in addition to rescue medication as needed.

Domperidone & Risk of Heart Rhythm Effects

“Domperidone is indicated for the symptomatic management of upper gastrointestinal motility disorders associated with chronic and subacute gastritis and diabetic gastroparesis”. Health Canada has reported heart rate and rhythm disturbances suspected to be associated with domperidone. Adverse reactions include arrhythmia, atrial fibrillation, ventricular tachycardia, bradycardia, palpitations, prolongation of the QTc interval and Torsades de Pointes. Although the product monograph for domperidone warns of arrhythmia, QTc prolongation & Torsades de Pointes are not included to date.

Patients reporting adverse effects tended to have complex medical histories and multiple medications making it difficult to definitively establish domperidone as the cause. Health Canada is continuing to monitor the situation. In the meantime, clinicians should be aware of the possible association of heart rate and rhythm disorders with domperidone. Females, advanced age, bradycardia, pre-existing cardiac disease and electrolyte disturbances are factors which may be associated with an increased risk of QTc prolongation. Other drug related factors include the concomitant use of one or more drugs known to increase the risk of QTc prolongation. Administration of drugs sharing the same metabolic pathway as domperidone (cytochrome P450 3A4) may result in higher blood levels of domperidone (which may lead to adverse effects). Examples of such drugs include macrolide antibiotics, HIV protease inhibitors, selective serotonin reuptake inhibitors and grapefruit juice.

Amiodarone-Simvastatin Interaction ...

The coadministration of amiodarone and simvastatin (Zocor) may result in higher blood levels and simvastatin toxicity. Both drugs share a common metabolic pathway (the enzyme CYP 3A4). Patients have reported symptoms of rhabdomyolysis (weakness, muscle pain and dark urine). The concurrent administration of these drugs should be avoided. Alternatives include pravastatin (Pravachol) and rosuvastatin (Crestor). The metabolism of lovastatin (Mevacor), fluvastatin (Lescol) and to a lesser extent, atorvastatin (Lipitor) may be inhibited by amiodarone.
Factive 320 mg tablets
gemifloxacin (Abbott Canada)
(not currently a benefit of ODB)

Factive is a third generation quinolone antibiotic (as is Levaquin–levofloxacin) indicated in adults for the treatment of acute bacterial exacerbations of chronic bronchitis caused by Streptococcus pneumoniae, Haemophilus influenzae, Haemophilus parainfluenzae or Moraxella catarrhalis. To reduce the development of drug-resistant bacteria Factive should only be used to treat infections caused by susceptible bacteria.

Contraindications: Factive is contraindicated in patients with:

- a history of hypersensitivity to the product or to other fluoroquinolones
- a history of prolongation of the QTc interval or patients at risk of QTc prolongation (e.g. electrolyte disorders, patients receiving Class 1A antiarrhythmics-quinidine, procainamide or Class III antiarrhythmics-amiodarone, sotalol). QTc prolongation may be associated with higher doses; therefore the recommended dose should not be exceeded (particularly in patients with renal or hepatic impairment). Concurrent administration with other drugs known to prolong the QTc interval has not been studied with Factive, therefore caution is recommended.

The safety of Factive in pregnancy or lactation has not been established.

Precautions: Caution is recommended in patients with central nervous system (CNS) disorders (e.g. epilepsy) or in patients predisposed to convulsions. Although reports of CNS effects are rare in clinical trials with Factive, convulsions, increased intracranial pressure and toxic psychosis have been reported with other fluoroquinolones. As with other drugs in this class there is a risk of rupture of a tendon (especially in patients taking concomitant corticosteroids). Pseudomembranous colitis is a risk. Although Factive has a low potential for photosensitivity reactions, unnecessary exposure to the sun or artificial ultraviolet rays (e.g. sunlamps) should be avoided.

Drug Interactions:

- Ferrous sulfate, aluminum or magnesium containing antacids, zinc supplements and preparations containing these cations reduce the systemic availability of Factive. These products should not be taken less than 3 hours before or 2 hours after Factive.
- The coadministration of sucralfate significantly reduces the absorption of Factive therefore Factive should be administered at least 2 hours before sucralfate.
- Drugs which prolong the QTc interval (e.g. erythromycin, antipsychotics, tricyclics, etc.) have not been studied with Factive. Caution is recommended with concurrent administration.
- Factive may increase the INR in patients taking warfarin. Monitoring is recommended.

Adverse Effects: The most commonly reported adverse effects include: diarrhea, rash, nausea, headache, abdominal pain, vomiting, dizziness and taste disturbances. In clinical trials rash occurred in about 2.8% of patients 8 to 10 days following initiation of therapy. Rash was more common in females under 40 years of age, in postmenopausal women taking hormone replacement therapy and in patients on a longer course of therapy (i.e. more than 7 days). If rash develops Factive should be discontinued.

Dose & Administration: The recommended dose for the treatment of acute bacterial exacerbation of chronic bronchitis is 320 mg once daily for 5 days. Renally compromised patients with a creatinine clearance of <40 ml/min and patients on hemodialysis should receive a dose of 160 mg once daily. The tablets may be taken without regard to meals with plenty of fluids and swallowed whole.

Availability & Storage: Factive is supplied (in 5 tablet blisters) as a white to off-white oval, scored, film-coated tablet with “GE320” debossed on both sides. The tablets should be stored from 15° to 30°C protected from light.

Please refer to the product monograph for complete information

The new Meds Check Medication Review Program, an initiative funded by the MOH & LTC provides the opportunity for ODB recipients, in the community and in retirement homes, who are on 3 or more chronic medications, to have a thorough medication review by their pharmacist. For more information contact your closest Medical Pharmacy.