

PIPELINE

New Treatment for Chronic Hepatitis B Approved The Food and Drug Administration (FDA) has approved Baraclude™ (entecavir) tablets and oral solution for the treatment of chronic hepatitis B virus infection in adults with evidence of acute viral replication and either evidence of persistent elevations in serum aminotransferases (ALT or AST) or histologically active disease.^{1,2} Liver function should be monitored during and after Baraclude therapy.^{1,2} Reports of severe acute exacerbations of hepatitis B have been seen in patients who discontinue Baraclude therapy.^{1,2} Bristol-Myers Squibb Company, the manufacturer of Baraclude, has agreed to conduct a post-marketing study to assess the risks of cancers and liver-related complications with Baraclude therapy.²

Recent New Drug Application (NDA) Approvals^{3*}

Drug Name	Indication(s)	Drug Class	Approval Date	Route of Administration	Comments
Asmanex® Twisthaler® 220 mcg (mometasone furoate inhalation powder); Manufactured by Schering-Plough	First-line maintenance treatment of asthma as preventive therapy in patients 12 years of age and older	Corticosteroid	03/31/2005	Inhalation	The product is anticipated to be available in 4Q 2005.
Baraclude™ (entecavir); Manufactured by Bristol-Myers Squibb	Treatment of chronic hepatitis B infection in adults with evidence of active viral replication and either evidence of persistent elevations in serum aminotransferases (ALT or AST) or histologically active disease	Nucleoside analogue	03/29/2005	Oral Tablets, oral solution	This product is now available.
Xibrom™ (bromfenac ophthalmic solution) 0.09%; Manufactured by ISTA Pharmaceuticals	Treatment of ocular inflammation following cataract surgery	Non-steroidal anti-inflammatory drug (NSAID)	03/28/2005	Topical Twice daily	The product is expected to launch in the 2Q 2005.
Boniva® (ibandronate sodium) 150 mg Tablets; Manufactured by Roche/GlaxoSmithKline	Treatment of postmenopausal osteoporosis	Bisphosphonate	03/25/2005	Oral Tablets; Once-monthly dosing regimen	New formulation of an already approved product. The product is expected in launch in April 2005.
Nexium® I.V. (esomeprazole sodium) for injection; Manufactured by AstraZeneca	Short-term treatment of gastroesophageal reflux disease (GERD) in patients with a history of erosive esophagitis who are unable to take capsules	Proton pump inhibitor (PPI)	04/01/2005	Injection-IV Once-daily	Treatment duration should not exceed 10 days and does not require an in-line filter.

Recent NDA Submissions^{3*}

Drug Name	Indication(s)	Drug Class	Submission Date	Route of Administration	Comments
Enhance SC™ (hyaluronidase); Manufactured by Halozyme Therapeutics	Use as a “spreading agent” to enhance the drug delivery of local anesthesia, contrast agents, and for subcutaneous fluid replacement (hypodermoclysis)	Recombinant human hyaluronidase	03/28/2005	Injection - subcutaneous	
Vivitrex® (naltrexone long-acting injection); Manufactured by Alkermes	Treatment of alcohol dependence	Narcotic antagonist	04/01/2005	Injection-intramuscular Once-monthly	
Nuvigil™ (armodafinil) Tablets [C-IV]; Manufactured by Cephalon	To improve wakefulness in patients suffering from excessive sleepiness associated with narcolepsy, shift work sleep disorder (SWSD), and obstructive sleep apnea/hypopnea syndrome (OSA/HS)	Anti-narcoleptic	03/31/2005	Oral Tablets	Single-isomer formulation of modafinil, the active ingredient in Provigil
Lubiprostone; Manufactured by Sucampo Pharmaceuticals/Takeda Pharmaceuticals	Treatment of chronic idiopathic constipation (CIC) and associated symptoms in adults	Chloride channel activator	03/31/2005	Oral	

Recent Product Launches^{3*}

Drug Name	Indication(s)	Drug Class	Launch Date	Route of Administration	Comments
Zanaflex® capsules (tizanidine hydrochloride); Manufactured by Acorda Therapeutics/Elan	Short-acting drug for the management of spasticity	Alpha-2 adrenergic agonist	04/04/2005	Oral Capsules available in 2 mg, 4 mg and 6 mg strengths	Tizanidine tablets are available generically in 2 mg and 4 mg strengths.
Trelstar® Depot 3.75 mg and Trelstar® LA 11.25 mg (triptorelin pamoate for injectable suspension); Manufactured by Watson Pharmaceuticals	Palliative treatment of advanced prostate cancer when orchiectomy or estrogen administration are either not indicated or are unacceptable to the patient	Synthetic luteinizing hormone-releasing hormone (LHRH) agonist	04/04/2005	Injection-intramuscular Trelstar Depot is administered once a month; Trelstar LA is administered once every three months	
Lunesta™ (eszopiclone); Manufactured by Sepracor	Treatment of insomnia	GABA (gamma-aminobutyric acid) receptor agonist	04/04/2005	Oral Tablets	Product is classified as a Schedule IV controlled substance.

First Generic Approvals/Launches^{3*}

Generic Drug Name	Reference Brand	Dosage Form/Strength(s)	Approval Date	Launch Date
dicyclomine hydrochloride	Bentyl®	Syrup, 10 mg/5 mL	03/24/2005	To be determined
cyclosporine	Neoral®	Capsules, 50 mg	03/25/2005	03/25/2005
quinapril hydrochloride and hydrochlorothiazide	Accuretic®	Tablets, 10 mg/12.5 mg, 20 mg/12.5 mg, 20 mg/25 mg	03/28/2005	To be determined

* Adapted from RxPipeline Services, for more information contact: pipeline@caremark.com

DRUG SAFETY

Reminyl® (galantamine) Labeling Changes On April 1, 2005, the FDA issued a MedWatch Alert to notify healthcare professionals of changes to the *Precautions* section of the Reminyl prescribing information.⁴ The labeling changes reflected the addition of information from two randomized, two-year, placebo-controlled trials in patients with mild cognitive impairment.⁴ Thirteen patients on Reminyl therapy (n=1,026) and one patient on placebo (n=1,022) died.⁴ The reported deaths were due to a variety of causes that could be anticipated in an elderly population.⁴ About half of the Reminyl deaths appeared to result from various vascular causes.⁴ Reminyl is approved for the treatment of mild-to-moderate dementia of the Alzheimer's type.⁵

FDA Announces a Series of Changes to the Non-Steroidal Anti-inflammatory (NSAID) Drug Class⁶ On April 7, 2005, the FDA announced changes around the marketing of prescription and over-the-counter (OTC) NSAIDs, including those that are COX-2 selective. The FDA is asking manufacturers of all prescription NSAIDs to revise their labels to include a boxed warning highlighting the potential for increased risk of cardiovascular events and gastrointestinal bleeding associated with their use. Manufacturers of all prescription NSAIDs will be asked to revise their labeling to include a boxed warning, as well as provide a *Medication Guide* for patients addressing these concerns. The FDA is requesting that manufacturers of OTC NSAIDs include more specific information about the potential for increased risk of cardiovascular and gastrointestinal events, as well as additional information that may assist patients in the safe use of these drugs. The changes requested in the FDA Public Health Advisory do not apply to aspirin.

In addition, the FDA has asked Pfizer, Inc. to voluntarily withdraw Bextra® (valdecoxib) from the market due to its unfavorable overall risk versus benefit profile. The FDA has also requested that Pfizer, Inc. include a boxed warning in their Celebrex® (celecoxib) label. Pending further discussions with the agency, Pfizer, Inc. has agreed to suspend sales and marketing of Bextra in the United States and to work with the FDA on the boxed warning for Celebrex.

HEALTHCARE NEWS

FDA Releases Final Chlorofluorocarbon (CFC) Ruling for Metered Dose Inhalers⁷ On March 31, 2005, the FDA announced that after December 31, 2008, albuterol metered-dose inhalers (MDIs) employing CFC propellants must no longer be produced, marketed, or sold in the United States. CFC-containing MDIs for asthma and chronic obstructive pulmonary disease were previously exempt from a general ban of CFC production and importation.

NEW/UPDATED NATIONAL CLINICAL GUIDELINES

American College of Physicians (ACP) Releases Obesity Guidelines⁸ The ACP issued guidelines for the pharmacologic and surgical management of obesity in primary care. This clinical guideline is available in the April 5,

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2005 issue of *Annals of Internal Medicine*. The ACP recommends that clinicians counsel all obese patients (Body Mass Index ≥ 30 kg/m²) regarding lifestyle and behavioral changes, including diet and exercise, as a means of promoting sustained weight loss. When diet and exercise alone fail to assist the patient in reaching these goals, available drugs for the treatment of obesity should be considered. This guideline provides recommendations on pharmacologic and surgical treatments of obesity based on a review of the evidence.

References

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