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BEXTRA (valdecoxib) film-coated tablets &
DYNASTAT (parecoxib sodium)
powder/powder and solvent for solution for injection

IMPORTANT SAFETY INFORMATION
CARDIOVASCULAR RISKS IN CORONARY BYPASS GRAFT (CABG) SURGERY AND SERIOUS SKIN REACTIONS

21 December 2004

Dear Healthcare Professional:

Pfizer wishes to draw your attention to new safety information on cardiovascular and serious skin adverse events in relation to the use of parecoxib sodium[1] (Dynastat) and valdecoxib (Bextra).

Dynastat was introduced for i.v. use in the European Union (EU) in March 2002 and is indicated for the short-term treatment of postoperative pain. Bextra was introduced for oral use in the European Union (EU) in April 2003 and is indicated for symptomatic relief of the signs and symptoms of osteoarthritis and rheumatoid arthritis and for primary dysmenorrhoea.

NEW CONTRAINDICATION FOLLOWING CABG SURGERY
Both Dynastat and Bextra are **CONTRAINDICATED** for the treatment of post-operative pain following CABG surgery and should not be used in this setting.

Dynastat (parecoxib sodium) and Bextra (valdecoxib) were evaluated for the treatment of pain following coronary artery bypass graft (CABG) surgery.

The first CABG study evaluated the safety of parecoxib sodium/valdecoxib 40 mg BID given for up to 14 days in 462 patients (311 on parecoxib sodium/valdecoxib and 151 on placebo).

The second CABG surgery study evaluated parecoxib sodium (40mg then 20mg bid) /valdecoxib 20 mg bid or placebo/valdecoxib 20 mg bid or placebo/placebo for up to 10 days in 1671 patients (544 receiving parecoxib/valdecoxib, 544 placebo/valdecoxib and 548 placebo/placebo).

Both CABG studies showed a higher rate of serious cardiovascular thromboembolic events (e.g. myocardial infarction, cerebrovascular accident) in the parecoxib sodium/valdecoxib treatment arm compared to the group of patients receiving placebo. This was not observed in a general surgery setting.

We are planning further studies to assess the long-term CV safety of Bextra in patients who require chronic treatment for arthritis with a COX-2 inhibitor.

[1] Parecoxib sodium is the prodrug of valdecoxib.

The Product Information for Dynastat and Bextra has now been revised accordingly (See attached).

UPDATED PRODUCT INFORMATION REGARDING SERIOUS SKIN REACTIONS

- Serious skin reactions, some of them fatal, including erythema multiforme, exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, have been reported through post-marketing surveillance in patients receiving valdecoxib.
- The reported rate of serious skin events appears to be greater for valdecoxib as compared to other COX-2 selective inhibitors.
- Patients appear to be at highest risk for these events early in the course of therapy; the onset of the event occurring in the majority of cases within the first 2 weeks of treatment.
- Patients without a history of sulphonamide allergy may also be at risk for serious skin reactions.
- Parecoxib sodium and valdecoxib should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Pfizer has sought to modify the Dynastat and Bextra SPCs at this time to include the above warnings.

Pfizer is fully committed to monitoring the safety of Dynastat and Bextra and will continue to provide you with any important updated information in order to help ensure that the product is labelled and used appropriately.

Please see the revised Product Information for Dynastat and Bextra enclosed with this letter.

If you have any questions concerning this important safety information, please contact Pfizer Ltd. Medical Information at 1800 633363.

Yours Sincerely,

John Farrell.

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Dr John Farrell,
Medical Director