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Regulatory requirements for import and registration Lafutidine Tablet in India

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Abstract

Lafutidine is a histamine H_2 receptor antagonist, the gastro protective effect of which is related to its antisecretory activity and its ability to activate a sensory neuron-dependent mechanism of defense. The present study investigated whether intragastric administration of Lafutidine (10 and 30 mg/kg) modifies vagal afferent signalling, mucosal injury, intragastric acidity and gastric emptying after gastric acid challenge**.** The prepared tablets were evaluated in terms of their pre-compression parameters, physical characteristics etc. The optimized formulation was subjected to various kinetic release investigations and it has been observed that that the mechanism of drug releases was predominantly diffusion with a minor contribution from polymeric relaxation**.**

Key words: Intragastricacidity, Lafutidine, Rabeprazole, demand therapy, Heartburn

Introduction

Import and Registration:

Government of India, Ministry of Health and Family Welfare has published a Gazette Notification GSR no. 604 (E) dated 24.08.2001 amending the various provisions of the Drugs & Cosmetics Rules, thereby introducing a new provision for the registration of the manufacturing premises of foreign drug manufacturer and the individual drugs prior to their import into the country. The notification has also introduced few other provisions viz. enhanced import license fees, increased validity period of licence, deletion of exemption from requirement of import license for bulk drugs for actual users, requirement of minimum 60% of retained shelf life for imported drugs and provisions for import of small quantities of new drugs by Govt. hospitals for treatment of their own patients etc. Under the new dispensation, foreign manufacturers have to apply for registration certificate for their manufacturing premises and the individual drugs to be imported.

The applications can be made by authorized agents of foreign firms in India. The documents required for registration certificates have been clearly specified in the amendments. The validity of registration certificates will be 3 years from the date on which these are issued. A fee of 1500 USD is to be charged for the registration of overseas manufacturer's premises and fee of 1000 USD will be charged for every individual drug. The rules provide now for inspection of the premises of a foreign manufacturer by Indian Drug Authorities, whenever so required. In such cases, an additional fee of 5000 USD is to be charged. The rules also provided for payment of testing charges by registration holders. The foreign manufacturer or his authorized agent in India shall be liable to report any change in the manufacturing and testing process of a drug. The new registration and import licence scheme shall also cover diagnostic kits viz. HIV I & II, HBsAg, HCV and blood group reagents.

Import licence will be required for all types of drugs instead of existing import licence requirements for Schedule C & C (1) and Schedule X drugs only. Import licence in Form 10 would be granted after completing the registration of overseas manufacturers and their specific drugs to be imported. The import license for specific drugs will be valid for 3 years from the date on which these are granted. The import license fee has been kept Rs. 1000/- for a single drug and at the rate of Rs.100/- for additional drug. The fee of import licenses for test and analysis of a drug has been kept Rs. 100/- for a single drug and at the rate of Rs. 50/- for each additional drug. The exemption from import licences for the import of bulk drugs by the formulations for actual use under Schedule D has been deleted. A separate provision has been made to enable the Govt. hospitals to import small quantities of essential new drugs for the treatment of their owm patients. The fee for such import licences has been kept Rs. 100/- for a single drug and

the rate of Rs. 50/- for each additional drug.The notification will come into operation with effect from 1st January 2003. In order to enable a smooth change over the new import requirements, it is proposed that all manufacturers/importers who are to obtain registration certificates for drugs, and import licences in January 2003, should submit their applications for registration certificates on or before 31.3.2002 and import licence applications not later than 30.9.2002, thereby giving minimum lead time to process their applications. Existing import of drugs under Form 10 licences will continue up to 31.12.2002. Since the existing validity of Form 10 Licences extends up to the end of next calendar year, it will be stipulated in Form 10 Licences issued w.e.f. 1.1.2002 that validity of such licences will terminate automatically on 31.12.2002. The new scheme would take care of a long felt need for laying down import registration requirements similar to those adopted by various other countries. This compilation includes, Chapter III of the Drugs & Cosmetics Act, 1940; Part IV of the Drugs & Cosmetics Rules, 1945 amended up to 24th August 2001; related circulars issued to various agencies from time to time.

Methods

We studied the efficacy of two doses of Lafutidine (5 mg and 10 mg, each given orally twice daily), as compared with placebo, in preventing peptic ulcers in 285 patients without peptic ulcers who were receiving long-term NSAID therapy for rheumatoid arthritis (82 percent) or osteoarthritis (18 percent). The patients were evaluated clinically and by endoscopy at base line and after 4, 12, and 24 weeks of treatment. The evaluators were unaware of the treatment assignment. The primary end point was the cumulative incidence of gastric or duodenal ulceration at 24 weeks.

Contents- Lafutidine (Import & Mkt):

1. Application to import as a New Drug (Rule 122-A) for Clinical Trial purpose (CMC Data, 3 batches stability data
2. Specification, STP, BE Study protocol, ICF, CRF, EC approval
3. PI Undertaking as per SChedule Y
4. Import permission will be issued in Form 45 & Initiation of Clinical trial
5. Submission of Application for Registation Certificate (Form 41) alongwith Clinical Trial
6. Form 40, copy of Form 45, Copy of CT Permission, POA, Undertaking, Data as per Schedule D(I) & Schedule D(II)
7. Application for Form 10 (Form 8, Form 9, Form 41, Whole Sale License)

Results

The cumulative incidence of gastric ulcers was 20 percent in the placebo group, 13 percent in the group of patients receiving 5 mg of Lafutidine twice daily (P = 0.24 for the comparison with placebo), and 8 percent in the group receiving 10 mg of Lafutidine twice daily (P = 0.03 for the comparison with placebo). The proportion of patients in whom duodenal ulcers developed was significantly lower with both doses of lafutidine than with placebo (13 percent in the placebo group, 4 percent in the low-dose lafutidine group and 2 percent in the high-dose lafutidine group. Both doses of Lafutidine were well tolerated.

Conclusion

Lafutidine 10 mg produces a prompter rise in intragastric pH than rabeprazole 20 mg in fasting and postprandial *Helicobacter pylori*-negative male subjects. Lafutidine (INN) is a H_2 receptor antagonist and it belongs to therapeutic class of drugs used in acid peptic disorders. It is used to treat gastric ulcers, duodenal ulcers, and stomal ulcers, gastric mucosal lesions (erosion, haemorrhage, redness or oedema) associated with acute gastritis and acute exacerbation of chronic gastritis and as a preanaesthetic medication.

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