LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Activase Pharmaceuticals Limited Marketing Authorisations (licences) for the medicinal products Ranitidine 150 mg and 300 mg Tablets (PL 28444/0102-3) on 09 January 2013. These medicines are only available on prescription from your doctor.

Ranitidine Tablets are used to treat:
- ulcers in the stomach or first part of the small intestine (duodenum)
- problems caused by acid in the food passage (reflux oesophagitis)
- Zollinger-Ellison syndrome, and ulcers caused by serious illnesses.

For children (aged 3 to 18 years), Ranitidine Tablets are used to treat:
- ulcers in the stomach or first part of the small intestine (duodenum)
- treat and prevent problems caused by acid in the food
- pipe (oesophagus) or too much acid in the stomach.

The active ingredient, ranitidine hydrochloride, belongs to a group of medicines called H₂-antagonists’. They reduce the amount of acid in the stomach.

No new or unexpected safety concerns arose from these simple applications and it was, therefore, judged that the benefits of using Ranitidine 150 mg and 300 mg Tablets outweigh the risks; hence Marketing Authorisations have been granted.
SCIENTIFIC DISCUSSION

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INTRODUCTION

The MHRA granted Marketing Authorisations for the medicinal products Ranitidine 150 mg and 300 mg Tablets (PL 28444/0102-3) to Activase Pharmaceuticals Limited on 09 January 2013. The products are prescription-only medicines (POM). Ranitidine tablets are indicated for the following:

- the treatment of benign gastric ulcers and duodenal ulcers.
- Zollinger-Ellison Syndrome and for the treatment of reflux oesophagitis.
- the long-term treatment of duodenal and benign gastric ulcers to prevent their recurrence.
  long-term treatment in patients with a history of recurrent ulcers.

In children (3 to 18 years) Ranitidine Tablets are indicated for:

- short term treatment of peptic ulcer
- treatment of gastro-oesophageal reflux, including reflux oesophagitis and symptomatic relief of gastro-oesophageal reflux disease.

These applications were submitted as abridged applications according to Article 10c of Directive 2001/83/EC, as amended, cross-referring to Ranitidine 150 mg and 300 mg Tablets (PL 21880/0091-2), which were granted Marketing Authorisations to Medreich plc on 22 December 2010.

The active ingredient, ranitidine hydrochloride, is a specific rapidly acting histamine H₂-receptor antagonist. It exerts its action by inhibiting basal and stimulated secretion of gastric acid, reducing both the volume and the acid and pepsin content of the secretion.

No new data were submitted nor were they necessary for these simple applications, as the data are identical to those of the previously granted cross-reference products.
PHARMACEUTICAL ASSESSMENT

LICENCE NO: PL 28444/0102-3
PROPRIETARY NAME: Ranitidine 150 mg and 300 mg Tablets
ACTIVE(S): Ranitidine hydrochloride
COMPANY NAME: Activase Pharmaceuticals Limited
E.C. ARTICLE: Article 10c of Directive 2001/83/EC, as amended
LEGAL STATUS: POM

1. INTRODUCTION
These are abridged applications for Ranitidine 150 mg and 300 mg Tablets, submitted under Article 10c of Directive 2001/83/EC, as amended.

The applications cross-refer to Ranitidine 150 mg and 300 mg Tablets (PL 21880/0091-2), which were authorised to Medreich plc on 22 December 2010. The current applications are considered valid.

2. MARKETING AUTHORISATION APPLICATION FORM
2.1 Name(s)
The proposed names of the products are Ranitidine 150 mg and 300 mg Tablets. The products have been named in line with current requirements.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes
Each tablet contains 150 mg or 300 mg of the active ingredient, ranitidine hydrochloride. The tablets are for oral use and packaged in cold-form blister sheets (structure from outer to inner side: oriented polyamide/aluminium foil/hard polyvinylchloride [PVC] film with a backing of aluminium foil coated with heat seal lacquer) in the following pack sizes:-

(i) Blister sheets of five tablets each, in boxes of 5 tablets per carton.
(ii) Blister sheets of seven tablets each, in boxes of 7, 14, 28, 56, 98 and 112 tablets per carton.
(iii) Blister sheets of eight tablets each, in boxes of 8, 16, 24, 32, 40, 48, 56, 64, 72, 80, 88 and 96 tablets per carton.
(iv) Blister sheets of ten tablets each, in boxes of 10, 20, 30, 50, 60, 80, 100 and 120 tablets per carton.
(v) Blister sheets of fifteen tablets each, in boxes of 15, 30, 45, 60, 75, 90, 105 and 120 tablets per carton.
(vi) Blister sheets of thirty tablets each, in boxes of 30, 60, 90, 120 and 150 tablets per carton.

Not all pack sizes may be marketed.

The packaging, proposed shelf-life (3 years) and storage conditions (“Store in the original package.”) are consistent with the details registered for the cross-reference products.

2.3 Legal status
On approval, the products will be available as prescription-only medicines (POM).

2.4 Marketing Authorisation Holder/Contact Persons/Company
Activase Pharmaceuticals Limited, 11 Boumpoulinas, 3rd floor, P.C. 1060, Nicosia, Cyprus.

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The Qualified Person (QP) responsible for pharmacovigilance is stated and a satisfactory CV has been provided.

2.5 Manufacturers
The proposed manufacturing sites are consistent with those registered for the cross-reference products and evidence of Good Manufacturing Practice (GMP) compliance has been provided.

2.6 Qualitative and quantitative composition
The proposed compositions are consistent with the details registered for the cross-reference products.

2.7 Manufacturing process
The proposed manufacturing process is consistent with the details registered for the cross-reference products and the maximum batch size is stated.

2.8 Finished product/shelf-life specification
The proposed finished product specifications are in line with the details registered for the respective cross-reference products.

2.9 Drug substance specification
The proposed drug substance specification is consistent with the details registered for the cross-reference products.

2.10 TSE Compliance
None of the excipients contain materials of animal or human origin.

2.11 Bioequivalence
No bioequivalence data are required to support these simple abridged applications, as the proposed products are manufactured to the same formula and utilise the same processes as the reference products Ranitidine 150 mg and 300 mg Tablets (PL 21880/0091-2).

3. EXPERT REPORT
The applicant cross-refers to the data for Ranitidine 150 mg and 300 mg Tablets (PL 21880/0091-2), to which these applications are claimed to be identical. This is acceptable.

4. PRODUCT NAME & APPEARANCE
See 2.1 for details of the proposed product names. The appearances of the products are identical to the respective cross-reference products.

5. SUMMARIES OF PRODUCT CHARACTERISTICS (SmPCs)
The proposed Summaries of Product Characteristics are consistent with the details registered for the respective cross-reference products.
6. PATIENT INFORMATION LEAFLET (PIL) AND LABELLING

PIL
The patient information leaflet has been prepared in line with the details registered for the cross-reference products.

Milpharm Limited previously submitted satisfactory PIL user testing for the PIL for Ranitidine 150 mg and 300 mg Tablets (16369/0069-70), in accordance with Article 59 of Council Directive 2001/83/EC.

User testing of the package leaflet for Ranitidine 150 mg and 300 mg Tablets (PL 28444/0102-3) has been accepted based on the bridging report provided by the applicant making reference to the user-testing of the PIL for Ranitidine 150 mg and 300 mg Tablets (16369/0069-70), as the ‘parent PIL’.

Carton and blister
The proposed artwork is consistent with the artwork registered for the respective cross-reference products and complies with statutory requirements. In line with current legislation, the applicant has also included the names of the products in Braille on the outer packaging and has included sufficient space for a standard UK pharmacy dispensing label.

7. CONCLUSION
The data submitted with the applications are acceptable. The grant of Marketing Authorisations is recommended.
NON-CLINICAL ASSESSMENT

As these are abridged applications submitted under Article 10c of Directive 2001/83/EC, as amended, no new non-clinical data have been supplied and none are required.

The Marketing Authorisation Holder has provided adequate justification for not submitting an Environment Risk Assessment (ERA). As the applications are for identical versions of already authorised products, it is not expected that environmental exposure will increase following approval of the Marketing Authorisations for the proposed products.

The grant of Marketing Authorisations is recommended.
CLINICAL ASSESSMENT

As these are abridged applications submitted under Article 10c of Directive 2001/83/EC, as amended, no new clinical data have been supplied and none are required.

The Marketing Authorisation Holder has provided details of a suitable pharmacovigilance system that fulfils the requirements and provides adequate evidence that they have the services of a qualified person responsible for pharmacovigilance, and have the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

As the applications are for identical versions of already authorised reference products, for which safety concerns requiring additional risk minimisation have not been identified, a risk minimisation system is not considered necessary. The reference products have been in use for many years and the safety profile of the active ingredient is well-established.

The grant of Marketing Authorisations is recommended.
OVERALL CONCLUSION AND BENEFIT/RISK ASSESSMENT

QUALITY
The data for these applications are consistent with those previously assessed for the cross-reference products and as such have been judged to be satisfactory.

NON-CLINICAL
No new non-clinical data were submitted and none are required for applications of this type.

EFFICACY
These applications are identical to previously granted applications for Ranitidine 150 mg and 300 mg Tablets (PL 21880/0091-2).

SAFETY
No new safety data were supplied or required for these applications. Ranitidine hydrochloride has a well-established safety profile. No new or unexpected safety concerns arise from these applications.

PRODUCT LITERATURE
The SmPCs, PIL and labelling text are satisfactory, and consistent with those for the cross-reference products.

BENEFIT/RISK ASSESSMENT
The quality of the products is acceptable, and no new non-clinical or clinical safety concerns have been identified. The applicant’s products are identical to the cross-reference products. Extensive clinical experience with ranitidine hydrochloride is considered to have demonstrated the therapeutic value of the products. The benefit/risk balance is, therefore, considered to be positive.
RANITIDINE 150 MG TABLETS
RANITIDINE 300 MG TABLETS
PL 28444/0102-3

STEPS TAKEN FOR ASSESSMENT

1 The MHRA received the Marketing Authorisation applications on 02 November 2011.
2 Following standard checks and communication with the applicant the MHRA considered the applications valid on 07 December 2011.
3 Following assessment of the applications the MHRA requested further information relating to the dossier on 28 February 2012, 11 July 2012 and 04 October 2012.
4 The applicant responded to the MHRA’s request, providing further information on the 21 June 2012, 02 October 2012 and 25 October 2012.
5 The applications were granted on 09 January 2013.
In accordance with Directive 2010/84/EU, the Summaries of Product Characteristics (SmPCs) for products granted Marketing Authorisations at a national level are available on the MHRA website.
PATIENT INFORMATION LEAFLET

In accordance with Directive 2010/84/EU, the Patient Information Leaflets (PILs) for products granted Marketing Authorisations at a national level are available on the MHRA website.