Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

Minute

File No: none extant
Application No: n/a

Ms Klara Koelmeyer,
Application Entry & Support

RE: Fixed dose combination proposal – Servier Laboratories (Aust) Pty Ltd– PROTOS D strontium ranelate 2g / cholecalciferol (colecalciferol, Vitamin D3) 1000 IU sachets

I have received directly a proposal from Servier Laboratories to register a new fixed combination that will be submitted as a Category 1 application to begin with a PPF next month.

The proposed indications are:
"The proposed indication for the fixed dose combination product was mentioned in my email. The proposed indication will be: *"Treatment of osteoporosis in men and post-menopausal women at risk of vitamin D insufficiency. PROTOS D reduces the risk of fractures"*."

The stated benefits in terms of the adopted guideline at http://www.tga.gov.au/pdf/euguide/ewp024095enfin.pdf are:

"i)Treatment of osteoporosis to reduce the risk of fractures

ii) Correction of vitamin D deficiency
A study has been conducted to evaluate the efficacy of S 06911 (strontium ranelate 2 g + cholecalciferol 1000 IU fixed combination) on the correction of vitamin D insufficiency (i.e. to achieve a 25-OH vitamin D level superior to 50 nmol/L).

iii) Convenience/Compliance with regard to vitamin D intake.
Ensuring sufficient vitamin D intake is fundamental to all prevention and treatment programs for osteoporosis, and constitutes therefore the rationale to associate strontium ranelate and vitamin D3 in a fixed combination. The combination provides a convenient way to treat osteoporosis while simultaneously ensuring intake of the recommended amount of vitamin D.
Considering the need for vitamin D extrapolated from previous studies, the recommended daily doses in current guidelines and its high safety margin, a daily supplementation of 1000 IU of vitamin D was considered appropriate to correct the insufficiency in vitamin D commonly observed in the elderly osteoporotic population with no need for dose adaptation according to gender, age and population."

The first two of these are not specific to the fixed combination product but the third is a claim that would have to be subject to evaluation. The currently approved PI for PROTOS makes repeated reference to vitamin D but does not specify a dose. The specific dose would have to be subject to evaluation against earlier registration studies for PROTOS.

I have examined the proposal and it meets reasonable criteria for acceptance in principle and without prejudice. However, an area of weakness of the justification is the basis for the justification and for the chosen dose. It is desirable that this weakness be addressed in the application.

Servier Laboratories (Aust) Pty Ltd can be advised to proceed to lodge a Presubmission Planning Form.

Dr Neil Mitchell
Director, Prescription Medicines Evaluation Unit 5
Office of Medicines Authorisation
23rd May 2012