Alendronate, etidronate, risedronate, raloxifene, strontium ranelate and teriparatide for the primary/ secondary prevention of osteoporotic fragility fractures in postmenopausal women (TA 160/ TA161) – post Judicial Review

Date: July 2009

Project Specification Form	
Appraisal title	**Alendronate, etidronate, risedronate, raloxifene, strontium ranelate and teriparatide for the primary/ secondary prevention of osteoporotic fragility fractures in postmenopausal women (TA 160/ TA161)**
Synopsis of the technical issue	These appraisals were initiated in August 2002 with a single scope for both primary and secondary prevention and included bisphosphonates (licensed at that time), raloxifene, teriparatide. In February 2004, the appraisal was split into separate appraisals for primary and secondary prevention (the latter issued as TA87). For primary prevention, additional work to incorporate the identification costs of women at high risk of fracture, the inclusion of epidemiological data pertaining to the unpublished WHO algorithm and work exploring various scenarios/ assumptions resulting from consultation on the first Appraisal Consultation Document and discussions with the Guideline Development Group. These additional analyses extended the timelines of the appraisal of primary prevention to coincide with the appraisal of strontium ranelate (for both primary and secondary prevention, referred to NICE in June 2004) and the need to consider an update of TA87. In June 2005, the Institute decided to align its work on osteoporosis and develop one technology appraisal on primary prevention and one on secondary prevention (the update on TA87), including all respective drugs referred. ACDs for both appraisals were first issued in September 2005. Following consultation, further sensitivity analyses were carried out, new analyses were required following price reductions for generic alendronate and discussions were held with the Guideline Development Group to facilitate an alignment of approaches. Early in 2007 FADs were issued for the initiation of treatment with alendronate only. Following an appeal, the appraisal was referred back to the Committee to also include guidance for women who cannot take alendronate. New FADs were issued for appeal early in 2008. These FADs recommended alendronate as first line treatment for women at high risk of fracture as defined by age, bone mineral density and other risk factors. The other drugs, being more expensive,

	were recommended for women who cannot take alendronate at ages and bone mineral density values at which they become cost effective. An appeal was received from Servier, who manufactures strontium ranelate, and heard in September 2008. The Appeal Panel dismissed the appeal on all points. Servier applied for a judicial review. The points raised were similar to the points raised in the appeal in 2008. The court hearing was held in January 2009. Three points were argued in the judicial review. The High Court ruled in favour of NICE on 2 of the 3 grounds: there was no discrimination and the correct approach to subgroup analyses was used. The third point was that NICE was unfair because consultees and commentators, including Servier, could not access the economic model, because it contained third party confidential information. The High Court asked us to continue to negotiate permission to release this information. Since then NICE has been able to reach agreement on the release of the economic model for consultation with the data owner, Professor John Kanis. The Judge requested that consultees and commentators will have an opportunity to comment on the model and has specified that an Offer to Disclose the model should be open to consultees and commentators for 28 days. This period ended on 7 May 2009 The model was released on the basis that C&Cs agree to the following conditions for its use: • *"You shall first have signed a written undertaking to Professor Kanis in the form attached to this letter as Appendix A (or in the case where the signatory is an individual, in the form attached to this letter as Appendix B). An original copy of the signed undertaking must be returned to NICE before the model will be released. The number of individuals named in the schedule to each Undertaking in Appendix A as being individuals to whom you are permitted to disclose the Model shall not exceed three, and these names will be provided to Professor Kanis.* • *This economic model enclosed and its contents are confidential and are protected by intellectual property rights, which are owned by the School of Health and Related Research, University of Sheffield. It cannot be used for any other purpose than to inform your understanding of the appraisal. Accordingly, neither the model nor its contents should be divulged to anyone other than those individuals within your organisation who need to see to them to enable you to prepare your response. Those to whom you do show the documents must be advised they are bound by the terms of the Confidentiality Acknowledgement and Undertaking Form that has already been signed and returned to the Institute by your organisation in June 2008.*

	• *You may not make copies of the file and you must delete the file from your records when the appraisal process, and any possible appeal, are complete. You must confirm to us in writing that you have done so. You may not publish it in whole or part, or use it to inform the development of other economic models.* • *The model must not be re-run for purposes other than informing comment on it."* The Judge specified the consultation period to be 8 weeks. The Decision Support Unit will be commissioned to review responses to the model consultation and report on its findings to the Appraisal Committee. Only comments on the economic model will be considered, not comments on input parameters into the model, or comments made on aspects of the model that had previously been described in Assessment Reports or other consultation documents. This report will be sent out for a 4 week consultation period. The Appraisal Committee will then be asked to consider the comments from consultees and commentators on the model, the review of the Decision Support Unit and the comments received on the report from the Decision Support Unit. The Appraisal Committee will then advise on the impact that these comments may have on the existing Guidance TA160 and 161, and issue new FADs.
Question(s) to be answered by DSU	➢ Provide an expert view on whether the comments received on the executable model provide a justifiable challenge to the model used for the formulation of the guidance. ➢ Have individual comments on the model been made with enough justification, supporting information, and details of the implementation in the model for them to be replicated? ➢ Has the impact of the individual comments on the model on the cost effectiveness results of the economic model been established correctly?
How will DSU address these questions?	o Study the documentation that describes the original ScHARR model and the technical reports that describe the additional analyses explored by NICE. o Liaise with the technical team at NICE on details of the workings of the economic model. o Review the responses from consultees on the release of the executable model. o Assess the impact on cost effectiveness (subject to feasibility within time lines) of the comments on the model that are considered acceptable by meeting the following criteria: o Relate to the economic model o Do not relate to model inputs, assumptions or other modelling approaches that were previously known

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Documentation to be provided	• The full evaluation report for the appraisal. • The executable economic models shared with consultees. • Relevant documentation related to the judicial review; particularly the court of appeal ruling.