NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Consideration of consultation responses on review proposal

Review of TA160, TA161 and TA204; Technologies for the primary and secondary prevention of osteoporotic fractures[1]

TA160 and TA161 were issued following judicial review in January 2011.

TA204 was issued in October 2010, and was scheduled to be considered for review alongside TA160 and TA161.

In August 2012 the clinical guideline on assessing the risk of fragility fractures in people with osteoporosis was published (CG146).

In July 2012 Guidance Executive agreed to reschedule the review proposal for the above technology appraisals to explore how treatment intervention thresholds from the technology appraisals can be aligned to the assessment of absolute fracture risk recommended in CG146, and to carry out a feasibility study through NICE's Decision Support Unit.

Background

At the GE meeting of 13 August 2013 it was agreed we would consult on the review plans for this guidance. A four week consultation has been conducted with consultees and commentators and the responses are presented below.

[1] Review of TA160; Alendronate, etidronate, risedronate, raloxifene and strontium ranelate for the primary prevention of osteoporotic fragility fractures in postmenopausal women, TA161; Alendronate, etidronate, risedronate, raloxifene, strontium ranelate and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women, and TA204; Denosumab for the prevention of osteoporotic fractures in postmenopausal women.

Proposal put to consultees:	To develop an implementation tool that allows the recommendations from TA160, 161 and 204 to be expressed in line with the recommendations for risk assessment in the short clinical guideline (CG146), without a full review of the evidence for bisphosphonates, raloxifene or teriparatide in post-menopausal women. To combine this with the recently referred appraisal of drugs for osteoporosis treatment in men. That we consult on this proposal, and hold an exploratory workshop to discuss responses received in consultation. This workshop will include stakeholders and other NICE guidance producing centres to explore the best way to support the development of the underpinning evidence base for the forthcoming NICE quality standard.
Rationale for selecting this proposal	In the previously published technology appraisal recommendations on osteoporosis treatments, intervention thresholds were defined using age, T-score and a number of risk factors, the latter being considered qualitatively. The clinical guideline on risk assessment (CG146) was published in August 2012 and recommends the use of absolute fracture risk for risk assessment, integrating all risk factors quantitatively. Therefore, it is desirable for NICE recommendations on treatment decisions to be aligned with the recommendations on risk assessment. The development of an approach that aligns the technology appraisals with CG146 would be more efficient than a full review of the appraisals, which would take a lot or resource and time to develop. Also, the various licence extensions for osteoporosis treatments, and the new clinical evidence and the majority of the safety data are not expected to lead to considerably different recommendations. The first line treatment recommended in the technology appraisals, alendronate, is now available at an extremely low annual treatment cost. For these reasons, a full update of the guidance is not considered a good use of NICE resources. The Department of Health has referred a multiple technology appraisal of drugs for the treatment of osteoporosis in men to NICE with the remit 'to appraise the clinical and cost effectiveness of alendronate, denosumab, risedronate, strontium ranelate, teriparatide and zoledronic acid within their licensed indications for the prevention of osteoporotic fractures in men'. The marketing authorisations for treatment in men are based on bridging studies. Such studies are considered sufficient for granting a marketing authorisation with the indication "treatment of osteoporosis in men at increased risk of fracture" provided that: the duration of the study is at least one year; the dosage is

	justified, and the manufacturer justifies that the cut-off of BMD, age and any other risk factor chosen for the inclusion of men in the pivotal study will generate a fracture risk of a similar magnitude compared with postmenopausal women that were recruited in the studies used to obtain the indication for treatment of postmenopausal osteoporosis in women , and the magnitude of the changes in BMD versus placebo is similar to that observed in postmenopausal osteoporotic women treated with the same compound and is proportional to the decreased incidence of fractures in treated women. Therefore, efficacy data for fracture outcomes in men is not available for all treatments. It has also been suggested that the risk of hip and vertebral fracture is similar in men and women for any given BMD. It is therefore likely that the assessment of cost effectiveness of treatments for osteoporosis in men will largely be based on studies in postmenopausal women. Consideration of the clinical and cost effectiveness of these technologies in men at the same time as considering an approach to align the technology appraisals with CG146, without a full review of the evidence for the previously appraised technologies in post-menopausal women, would allow for an efficient use of technology appraisal resources, and is likely to result in better and comprehensive guidance to the NHS.

GE is asked to consider an updated proposal in the light of the comments received from consultees and commentators, and discussed at the stakeholder workshop. It is asked to agree on the final course of action for the review.

Recommendation post consultation and stakeholder workshop:	• To carry out an MTA on all relevant bisphosphonates for treatment in women and men, and schedule this into the work programme as soon as possible • To carry out an MTA on non-bisphosphonates for treatment in women and men when the MTA on bisphonsphonates is concluded • An interim translation tool is not considered appropriate **Rationale** At the stakeholder workshop on 3 December 2013, participants discussed the appropriateness of the review proposal and explored the best approach to updating existing NICE technology appraisal guidance on treatments for osteoporosis. Participants included clinicians, manufacturer representatives, patient group

	representatives and NHS commissioners. During the stakeholder workshop, clinical specialists and patient representatives stated that current NICE technology appraisal guidance for the prevention of osteoporotic fragility fractures needed to be updated to include new technologies, changes in therapeutic indications and prices, new clinical evidence and that new guidance should reflect recent changes to current UK clinical practice. The original proposal to create an interim translation tool was not favoured by the workshop participants because 1. Of the lack of clear methodologies and processes to do this 2. Of the uncertainty how this could create guidance for treatment in men in an appropriate way 3. It would not be able to include new prices and other bisphosphonates for which guidance is needed 4. It would not address one of the main problems in clinical practice: the need for updated guidance on bisphosphonate treatments for people who cannot tolerate or comply with alendronate treatment. Attendees expressed the need for clear and usable guidance in the NHS for treatments for the prevention of osteoporotic fragility fractures in both men and women. The following approach addresses the issues raised in comments received during consultation on the review proposal and during the stakeholder workshop: **It is proposed that NICE appraises** • **all relevant bisphosphonates licensed for the prevention of osteoporotic fragility fractures in women and men as an MTA, and that this should be given priority in scheduling.** This MTA will develop the framework for the link between absolute fracture risk and intervention thresholds based on cost effectiveness. It is likely that it will not need to include full systematic reviews of the evidence for risedronate and alendronate. • **all non-bisphosphonate licensed for the prevention of osteoporotic fragility fractures in women and men as an MTA which will be scheduled to begin when the MTA on bisphosphonates has published its final appraisal determination.** This split into 2 MTAs is considered the most efficient approach to address the urgency of updated guidance

	on bisphosphonates. A large MTA with all respective drugs would need to run to double timelines, and would take considerably longer to develop than an MTA for bisphosphonates only. The proposed approach would result in: • technology appraisal guidance to be aligned with existing clinical guidelines • guidance for treatments of osteoporosis in men • updated guidance including changes in costs, clinical evidence and recent changes in UK clinical practice • guidance on the use of zoledronate and ibandronate in osteoporosis

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Medicines and Healthcare products Regulatory Agency		You should know that European Medicines Agency has started a review of medicines containing strontium ranelate. The link to this review is below: http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/referrals/Protelos_and_Osseor/human_referral_prac_000025.jsp&mid=WC0b01ac05805c516f The results of this review of the risk and benefits of the drug may have a bearing on NICE recommendations. NICE technology appraisal guidance TA160 currently recommends (paragraph 1.3) strontium ranelate for postmenopausal women who cannot take a bisphosphonate and are at a high risk of	Comment noted. NICE is aware of the conclusions from the safety review for strontium ranelate further restricting the use of strontium ranelate to patients who cannot be treated with other medicines approved for osteoporosis. In addition these patients should continue to be evaluated regularly by their doctor and treatment should be stopped if patients develop heart or circulatory problems, such as uncontrolled high blood pressure or angina. As recommended in a previous review, patients who have a history of certain heart or circulatory problems, such as stroke and heart attack, must not

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		fractures as determined by their T-score, age and other risk factors for fracture.	use the medicine NICE will add this information on the website for TA160 and 161.
Merck Sharp & Dohme	Agree	"MSD believes the review of TA160, 161 and 204 should proceed in order to align the use of absolute fracture risk (FRAX® or QFracture) recommended in the clinical guideline (CG146) with the technology appraisals, which currently base risk of fracture on patient characteristics such as age, T-score and a number of risk factors. In addition, with the DoH referring an MTA of drugs for the treatment of osteoporosis in men to NICE, MSD agrees that aligning the above technology appraisals for osteoporosis in post-menopausal women with CG146 is a good use of NICE resources, which in combination would result in comprehensive guidance to the NHS. Concerning on-going research, odanacatib is being developed by MSD for the treatment of osteoporosis and is currently in phase III trials. The indications and timelines associated with this product can be found in PharmaScan."	Comment noted. No action required. Comment noted. New technologies routinely go through the NICE single technology appraisal process. However, if the licensing date coincides with the appropriate technology appraisal review, it may be included in a multiple technology appraisal.
Royal College of Nursing	No comment	There are no comments to submit at this time on behalf of the Royal College of Nursing to inform on the review proposal of the above appraisal.	-

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National Osteoporosis Society	Disagree	The National Osteoporosis Society welcomes the news that NICE are to progress the guidance available for the management of people at high risk of fracture. We are pleased to see NICE considering methods based on fracture risk assessment, which the National Osteoporosis Society has been encouraging NICE to adopt for a number of years. We are in agreement with NICE that it is appropriate, in fact necessary, for this guidance to be updated. However we are concerned with the recommendation of the Guidance Executive proposal: *To develop an implementation tool that allows the recommendations from TA160, 161 and 204 to be expressed in line with the recommendations for risk assessment in the short clinical guideline (CG146), without a full review of the evidence for bisphosphonates, raloxifene or teriparatide in post-menopausal women.* *To combine this with the recently referred appraisal of drugs for osteoporosis treatment in men.* **We urge NICE to undertake a full review of the guidance.** We appreciate that undertaking a full review would have significant resource implications and	Comment noted. No action required. Comment noted. Following consultation and the stakeholder workshop NICE has agreed to conduct an update of existing guidance, taking into account currently licensed technologies, the recommendations in NICE clinical guideline 146, changes in pricing and changes in clinical management of people at risk for osteoporotic fragility fractures, by conducting an MTA of bisphosphonates and a subsequent MTA on non-bisphosphonates.

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		potentially result in a longer time interval between CG146 and the technology appraisals being aligned; but we feel anything less would be a disservice to patients and clinicians. Since the development of TA160 and 161, there have been fundamental changes in clinical practice with respect to managing patients at high risk of fracture. It is imperative that a comprehensive review of the technology appraisals encompasses all contemporary treatments and recognises significant changes in drug costs, incorporating costs associated with adverse drug reactions, adherence to drug schedules and the recent significant changes in clinical practice, particularly for those patients taking drugs longer term. The recent changes in monitoring using recurrent risk assessments are deemed essential for patient safety and clinical quality; these changes also have health resource implications that have not been considered to date. The review must: • provide clinically relevant and seamless guidance that individualises care of patients at high risk of fracture, incorporates the principles of CG146 and is substantiated by reworked TAs for all available drug treatments. • recognise that the two risk assessment tools,	

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		FRAX and QFracture recommended with equal merit in CG146, give different absolute risks at an individual level. • include men, post-menopausal women and those at risk of glucocorticoid-induced osteoporosis • include zoledronate as an established treatment for patients at high fracture risk • take into consideration changes to the cost of risedronate and imminent price changes for ibandronate and zoledronate • take into account changes in clinical practice, with related changes in the utilisation of health care resources: • active reviewing of treatment after 5 years of therapy (http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON120213). The review must not: • make a distinction between primary and secondary fracture prevention: • Prior fracture is inherently a component of fracture risk assessment and will thus be reflected in the output.	

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		• The European Medicines Agency no longer make this distinction, nor is it made in the approved indications for treatment • provide recommendations that leave patients and clinicians in a position where, if unable to take first line treatment, they are only able to access further treatment if their condition deteriorates. This is currently the case and is unworkable in clinical practice. The implication on p7 of the Guidance Executive proposal threatens to yield a similar recommendation *i.e. if one drug cannot be used for reasons of intolerance or contraindication, another may not be recommended at the same level of fracture risk.* Many clinical management issues (e.g. younger women, cancer induced osteoporosis) exist beyond the review of the technology appraisals that require guidance, and we would like to seek assurance that a clinical guideline will be developed in the future.	
Primary Care Rheumatology Society	Disagree	The Primary Care Rheumatology Society feels that a review of the above Technology Appraisals is necessary because: 1) The complexity of TA160 and TA161 make them unworkable in general practice.	Comments noted. Following consultation and the stakeholder workshop NICE has agreed to conduct an update of existing guidance, taking into account currently licensed technologies, the recommendations in NICE clinical

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		2) The different treatment thresholds for different interventions for women who are intolerant of alendronate is unethical. It puts an intolerable strain on the doctor / patient relationship when a GP has to refuse treatment for a patient because they have not achieved the necessary threshold for an alternative drug despite having been previously treated with alendronate. 3) Has the cost-effectiveness thresholds for treatment been updated to include the massive reductions in the price of bisphosphonates such as alendronate and bisphosphonate? 4) The evolving role of practical fracture risk assessment tools such as FRAX and Q Fracture to assess 10 year fracture probability is incompatible with the guidance in the above TAs. The QOF rheumatoid arthritis indicators for 2013/14 include an annual osteoporosis assessment using a fracture risk assessment tool and therefore GPs are using these tools on a regular basis. 5) New guidance that NICE needs to consider is the "Diagnosis and management of osteoporosis in postmenopausal women and older men in the UK: National Osteoporosis Guideline Group (NOGG) Update 2013" by J.E.	guideline 146, changes in pricing and changes in clinical management of people at risk for osteoporotic fragility fractures, by conducting an MTA of bisphosphonates and a subsequent MTA on non-bisphosphonates.

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		Compston, Claire Bowring, Alun Cooper, Cyrus Cooper, Cyril Davies, Roger M Francis, John A Kanis, David Marsh, Eugene V McCloskey, David M Reid and Peter Selby. This update includes new advice on the management of glucocorticoid-induced osteoporosis, the role of calcium and vitamin D therapy and the benefits and risks of long-term bisphosphonate therapy.	
Arthritis and Musculoskeletal Alliance	Disagree	ARMA fully support the comments from the National Osteoporosis Society.	Comment noted. Following consultation and the stakeholder workshop NICE has agreed to conduct an update of existing guidance, taking into account currently licensed technologies, the recommendations in NICE clinical guideline 146, changes in pricing and changes in clinical management of people at risk for osteoporotic fragility fractures, by conducting an MTA of bisphosphonates and a subsequent MTA on non-bisphosphonates.
Lilly	Agree (with caveat)	We broadly welcome any proposals which will make the TA160, 161 and 204 simpler and easier to apply in clinical practice, and where the recommendations for treatments for severe osteoporosis will not be disadvantaged and remain	Comment noted. Following consultation and the stakeholder workshop NICE has agreed to conduct an update of existing guidance taking into account currently licensed technologies, the

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		available for suitable patients. However, we believe the practical implementation of the proposed changes to the guidance needs to be explored further. The use of FRAX to calculate the absolute risk of fracture is suitable for the initial identification of patients and guiding the selection of initial treatment, but unfortunately FRAX's fracture risk measurement is unable to assess the treatment effect or treatment response, and hence, unable to guide subsequent treatment decisions. The new guidance will therefore need to clearly define 'unsatisfactory response' to treatment (NICE TA161, section 1.8) under the proposed approach, and will likely require the continued use of a T-score measurement and the monitoring of additional fragility fractures. We would also like bring to NICE's attention that the use of the FRAX tool may underestimate the absolute fracture risk in patients with more than one fragility fracture and these patients may therefore not receive the appropriate treatment. In addition, the FRAX tool is not routinely used for patients at high risk of fracture (especially in secondary care) as these patients are easily identified clinically and will be considered eligible for treatment in any case.	recommendations in NICE clinical guideline 146, changes in pricing and changes in clinical management of people at risk for osteoporotic fragility fractures, by completing an MTA of bisphosphonates and a subsequent MTA on non-bisphosphonates.

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		As the process and methods for this proposal is different to NICE's normal approach, NICE should ensure that any recommendations produced using this approach do not place treatments at a disadvantaged position compared to the original guidance. NICE has announced that it will carry out a multiple technology appraisal of alendronate, denosumab, risedronate, strontium ranelate, teriparatide and zoledronic acid within their licensed indications for the prevention of osteoporotic fractures in men. Due to the lack of data for osteoporosis in men, the main evidence will be based on evidence from female data. We are wondering whether a full MTA is justified given the resources required. Lilly's on-going research or new evidence coming out in the next few years that is relevant to the review can be found in appendix 1. **Appendix 1 – Ongoing Lilly sponsored studies** **MOVE trial (GHDK, Phase 4) NCT00887354:** Osteoporotic Patients with Recent Pertrochanteric Fracture Comparison of the Effects of Teriparatide with those of Risedronate on Lumbar Spine BMD in Patients with Low Bone Mass and a Recent Pertrochanteric Hip Fracture	

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		• Primary
		  ○ Change in lumbar spine BMD (18 month)
		• Secondary
		  ○ Patient-reported outcomes
		  • Pain
		  • SF-36 Health Survey
		  ○ Performance-based measure
		  • Timed up-and-go test
		• Exploratory
		  • Radiographic assessments of fracture healing
		  • Incidence of nonunion and mechanical failure of the implant
		  • Recovery of the ability to walk post-fracture
		GHDW- VERO study NCT01709110:
		Teriparatide and Risedronate in the Treatment of Patients with Severe Postmenopausal Osteoporosis: Comparative Effects on Vertebral Fractures
		• Primary Objective	

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		○ To evaluate if teriparatide 20 µg subcutaneously once daily is superior in reducing the incidence of new vertebral fractures during 24 months of therapy, when compared with risedronate 35 mg orally once weekly, in postmenopausal women with prevalent vertebral fragility fractures. ○ The incidence of new vertebral fractures will be assessed by quantitative vertebral morphometry measurements (QM) with qualitative visual semiquantitative grading (SQ) confirmation. • Secondary objectives: Reducing incidence of : ○ pooled new and worsening vertebral fractures ○ pooled clincal fractures ○ non vertebral fragility fractures **ExFOS: Extended Forsteo® Observational Study** A European, prospective observational study to evaluate fracture outcomes, back-pain, health-	

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		related quality of life, safety and compliance in patients with osteoporosis treated with Forsteo® for a maximum of 24 month with a follow up of at least 18 month • Patient population: Patients prescribed Forsteo • Primary Objective: ○ To determine the change over time in the incidence of clinical vertebral and non-vertebral fragility fractures in patients treated with Forsteo® for a maximum of 24 months, with a post-treatment follow-up of at least 18 month. • Secondary Objectives: Back pain, HRQL measured with EQ5D, Compliance.	
Amgen	Agree (with caveat)	We provide our comments here in anticipation of more detailed discussion at the Exploratory Workshop, scheduled for 4 October 2013. In summary, at this time, Amgen are supportive in principle of the review proposal. However, we note, the proposal provides limited detail of the process the Institute would use to conduct the review. It is also unclear but implied that the proposal may lead	Comment noted. Following consultation and the stakeholder workshop NICE has agreed to conduct an update of existing guidance taking into account currently licensed technologies, the recommendations in NICE clinical guideline 146, changes in pricing and changes in clinical management of

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		to a simplification of the existing technology appraisal recommendations with the potential for important differences between the patient populations recommended for specific medicines being “lost in translation” from the current risk factor combinations (age, T-score, prior facture and number of independent clinical risk factors for fracture) to absolute fracture risk. If this is the case and this simplification leads to a blurring of the specific recommendations for each technology currently included in TA160, 161 and 204, we may not be able to support the proposal. We summarise below those comments we consider a priority for discussion at the Exploratory Workshop. We also provide some additional comments for consideration. **Priority topics for discussion at the Exploratory Workshop**: 1. The review proposal suggests this appraisal would replace the currently referred multiple technology appraisal for the prevention of osteoporotic fractures in men [ID 558]. If this is the case, the methods and process to evaluate and incorporate evidence for this indication should be provided in detail at the Workshop. 2. The Institute should confirm which technology appraisal process would be followed for this	people at risk for osteoporotic fragility fractures, by completing an MTA of bisphosphonates and a subsequent MTA on non-bisphosphonates.

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		proposal and if any deviations are anticipated from the relevant current published process guide. 3. The review proposal (page 6) notes, "*However, a pragmatic way forward may be to use minimum fracture risk levels at which treatment can be recommended for the interventions included in the technology appraisals. Such approach would require the acceptance of some simplifying assumptions and decision rules, but would be a more efficient way of aligning the current NICE technology appraisal recommendations with the Clinical Guideline recommendations.*" It is essential the Institute provide clarity at the Exploratory Workshop as to the simplifying assumptions and decision rules that might be required. It will not be acceptable to initiate this review and then for these assumptions and decision rules to evolve during the appraisal process. As the Institute have commissioned analysis from the Decision Support Unit to support this proposal, the Institute should now be in a position to clearly present the anticipated outcomes of the proposal and any simplifying assumptions and decision rules it believes will be necessary. It will be completely unacceptable if the review proposal leads to a simplification of the existing	

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		Technology Appraisal recommendations, which fails to pick up the different recommendations for medications other than oral bisphosphonates. The existing recommendations, particularly in secondary prevention, provide different recommendations for strontium ranelate, raloxifene, denosumab and teriparatide. With denosumab recommended in a broader patient population than strontium ranelate, raloxifene, and teriparatide, and strontium ranelate and raloxifene are recommended in a broader patient population than teriparatide. These differences are evident in the recommendations from TA204 (Section 1 Guidance) where there are no restrictions on the use of denosumab based on age, T-score and number of independent clinical risk factors for fracture in secondary prevention, while such restrictions are in place for strontium ranelate, raloxifene, and teriparatide in TA161. The Appraisal Committee provide their rationale for this broader recommendation for denosumab in Sections 4.24 & 4.25 of the TA204 guidance where they acknowledge that denosumab is both cost-effective compared both to strontium ranelate and raloxifene in the age, T-score and independent risk factor sub-	

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		groups in which these medicines are recommended in TA161 and cost-effective compared with no treatment in those age, T-score and independent risk factor sub-groups in whom strontium ranelate and raloxifene are not recommended in TA161. In order to reflect the different clinical and cost-effectiveness of these medicines as considered by the appraisal committees of TA160/161/204, these differential recommendations for each medicine must be maintained within any updated recommendations resulting from the proposed review. Failure to do so could result in the Institute issuing guidance that leads to inefficient use of NHS resources. **Additional comments**: 1. Appendix 2, page 17 & page 19 Table 1; "*Denosumab (Prolia; Amgen) has received an extension to the UK marketing authorisation to include bone loss associated with hormone ablation in men with prostate cancer at increased risk of fractures, and the treatment of osteoporosis in men. The list price has not changed: £183 for a 1 ml pre-filled syringe, 60 mg per ml solution (annual cost £366)*". Please note this is incorrect, the indication bone loss associated with hormone ablation in men with	

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		prostate cancer at increased risk of fractures was approved as part of the initial marketing authorisation for denosumab and was not the result of an extension to the marketing authorisation. 2. Appendix 2, page 22; "*The manufacturer of denosumab does not anticipate any further extensions to the marketing authorisation for denosumab in this patient population. However, denosumab has received a license extension for male osteoporosis and is currently suspended as the manufacturer has informed NICE that they will not provide an evidence submission for the appraisal*." Please note this is incorrect, a license extension for denosumab in male osteoporosis is currently under consideration by the European Medicines Agency and therefore a license extension has not yet been granted. Please also note, Amgen has not confirmed a submission would not be provided for an appraisal of male osteoporosis. This would depend on the decision problem set and the availability of appropriate evidence to support an appraisal. Amgen understands an STA of denosumab in this indication was not referred by the DH, but rather it has been superseded by the referral of the multiple technology appraisal for the prevention of	

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		osteoporotic fractures in men [ID 558]. 3. The recommendation (page 3) does not include denosumab within the list of therapies to be considered, although TA204 is specifically mentioned earlier in the same text. Figure 2, page 44 "*Cost and volume of denosumab prescribed in primary care, and in hospitals that has been dispensed in the community in England*". Note, this chart appears to incorrectly imply a significant uptake of denosumab following the publication of TA204. The axes of the chart need to be adjusted as otherwise the reader may be misled about uptake of denosumab compared with other medicines following publication of the technology appraisal.	

No response received from:

Manufacturers/sponsors	General
• AAH Pharmaceuticals (alendronate, etidronate, risedronate) • Accord Healthcare (alendronate) • Actavis UK (risedronate) • Alliance Healthcare (alendronate, etidronate, risedronate) • Almus Pharmaceuticals (alendronate) • Apotex UK (alendronate • Arrow Generics (alendronate)	• Allied Health Professionals Federation • Board of Community Health Councils in Wales • British National Formulary • Care Quality Commission • Commissioning Support Appraisals Service • Department of Health, Social Services and Public Safety for Northern Ireland

• Aspire Pharma (risedronate) • Bluefish Pharmaceuticals (risedronate) • Consilient Health (alendronate) • Daiichi Sankyo UK (raloxifene) • Doncaster Pharmaceuticals (alendronate) • Dr Reddy's Laboratories (risedronate) • Fannin (alendronate)Focus Pharmaceuticals (alendronate) • Kent Pharmaceuticals (alendronate) • Mawdsley-Brooks & Co Ltd (alendronate) • Mylan UK (alendronate, etidronate, risedronate) Ranbaxy (risedronate) • Servier Laboratories (strontium ranelate) • Sigma Pharmaceuticals (alendronate, risedronate) • Teva UK (alendronate, risedronate) • Warner Chilcott UK (etidronate, risedronate, risedronate with calcium and calciferol) • Wockhardt Pharmaceuticals (alendronate) • Zentiva (alendronate, risedronate) <u>Patient/carer groups</u> • Action on Pain • Afiya Trust • Arthritis Care • BackCare • Black Health Agency • Disability Rights UK • Equalities National Council • Independent Age • Leonard Cheshire Disability • Muslim Council of Britain	• Healthcare Improvement Scotland • National Association of Primary Care • National Pharmacy Association • NHS Alliance • NHS Commercial Medicines Unit • NHS Confederation • Scottish Medicines Consortium <u>Comparator manufacturer(s)</u> • AAH Pharmaceuticals (calcitriol) • Doncaster Pharmaceuticals (calcitriol) • Novartis Pharmaceuticals(calcitonin) • Nycomed UK (parathyroid hormone) • Roche Products (calcitriol, ibandronic acid) • Sigma Pharmaceuticals (calcitriol) • Teva UK (calcitriol) <u>Relevant research groups</u> • Bone Research Society • Chronic Pain Policy Coalition (CPPC) • Cochrane Metabolic & Endocrine Disorders Group • Cochrane Musculoskeletal Group • Health Research Authority • Institute for Ageing and Health • MRC Clinical Trials Unit • National Institute for Health Research • Research Institute for the Care of Older People <u>Assessment Group</u> • Assessment Group tbc

• Muslim Health Network • Pain Concern • Pain Relief Foundation • Pain UK • South Asian Health Foundation • Specialised Healthcare Alliance • Women's Health Concern <u>Professional groups</u> • British Association for Services to the Elderly • British Geriatrics Society • British Health Professionals in Rheumatology • British Institute of Musculoskeletal Medicine • British Institute of Radiology • British Menopause Society • British Orthopaedic Association • British Pain Society • British Society for Rheumatology • British Society of Rehabilitation Medicine • Physiotherapy Pain Association • Royal College of General Practitioners • Royal College of Pathologists • Royal College of Physicians • Royal College of Radiologists • Royal Pharmaceutical Society • Royal Society of Medicine • Society and the College of Radiographers • Society for Endocrinology • United Kingdom Clinical Pharmacy Association	• National Institute for Health Research Health Technology Assessment Programme <u>Associated Guideline Groups</u> • National Clinical Guideline Centre • National Collaborating Centre for Women and Children's Health • National Osteoporosis Guideline Group <u>Associated Public Health Groups</u> • Public Health England • Public Health Wales NHS Trust

Others • Department of Health • NHS Barnet CCG • NHS England • NHS Milton Keynes CCG • Welsh Government	

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