# Briefing Paper for Surrey Heartlands Integrated Care System (ICS) Area Prescribing Committee (APC)

*Surrey Downs, Guildford & Waverley, North West Surrey, East Surrey Place & associated partner organisations*

## NICE Technology Appraisals: Local implementation

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| **NICE TA Guidance name and number** | Romosozumab for treating severe osteoporosis<br>Technology appraisal guidance 791 | | |
| **Available at** | https://www.nice.org.uk/guidance/ta791 | | |
| **Date of issue** | 25 May 2022 | **Implementation deadline** | 25 August 2022 |

| **Medicine details[1]** | |
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| **Name, brand name and manufacturer** | Romosozumab (Evenity®)<br>UCB |
| **Mode of action** | Romosozumab is a humanized IgG2 monoclonal antibody produced using recombinant DNA technology in Chinese hamster ovary (CHO) cells.<br><br>Romosozumab inhibits sclerostin, a regulatory factor in bone metabolism. Sclerostin both inhibits bone formation and promotes bone resorption.<br><br>Romosozumab therefore has a dual effect: it prevents inhibition of bone formation and it inhibits osteoclast activity and bone resorption.<br><br>Both effects from the same therapy have not been seen in other osteoporosis treatments to date. |
| **Licensed indication** | Treatment of severe osteoporosis in postmenopausal women at high risk of fracture |
| **Formulation** | Evenity® 105 mg solution for injection in pre-filled pen |
| **Usual dosage and contraindications** | Usual dosage<br>The recommended dose is 210 mg romosozumab (administered as two subcutaneous injections of 105 mg each) once monthly *for 12 months.*<br><br>Patients should be adequately supplemented with calcium and vitamin D before and during treatment.<br><br>Patients treated with Evenity® should be given the package leaflet and the patient alert card.<br><br>Following completion of romosozumab therapy, *transition to antiresorptive therapy is recommended* in order to extend the benefit achieved with romosozumab beyond 12 months.<br><br>Contraindications<br>• Hypersensitivity to the active substance(s) or to any of the excipients<br>• Hypocalcaemia |

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| | • History of myocardial infarction or stroke<br><br>Special warnings and precautions for use:<br><br><u>Myocardial infarction and stroke</u><br>In randomised controlled studies, an increase in serious cardiovascular events (myocardial infarction and stroke) has been observed in romosozumab treated patients compared to controls.<br><br>*Romosozumab is contraindicated in patients with previous myocardial infarction or stroke.*<br><br>When determining whether to use romosozumab for an individual patient, consideration should be given to her fracture risk over the next year and her cardiovascular risk based on risk factors (e.g. established cardiovascular disease, hypertension, hyperlipidaemia, diabetes mellitus, smoking, severe renal impairment, age). romosozumab should only be used if the prescriber and patient agree that the benefit outweighs the risk. If a patient experiences a myocardial infarction or stroke during therapy, treatment with romosozumab should be discontinued.<br><br><u>Hypocalcaemia</u><br>Transient hypocalcaemia has been observed in patients receiving romosozumab.<br><br>Hypocalcaemia should be corrected prior to initiating therapy with romosozumab and patients should be monitored for signs and symptoms of hypocalcaemia. If any patient presents with suspected symptoms of hypocalcaemia during treatment, calcium levels should be measured. Patients should be adequately supplemented with calcium and vitamin D.<br><br>Patients with severe renal impairment (estimated glomerular filtration rate [eGFR] 15 to 29 ml/min/1.73 m2) or receiving dialysis are at greater risk of developing hypocalcaemia and the safety data for these patients is limited. Calcium levels should be monitored in these patients. |
| **Comparison with NICE TA use[2]** | <u>Imminent fracture risk</u><br>The company proposes that romosozumab would only be used when there is an *imminent fracture risk*. It defines this as when a person has severe osteoporosis and has had a *major osteoporotic fracture within 24 months*. A major osteoporotic fracture was defined as a clinical spine, hip, forearm or humerus fracture.<br><br>This is narrower than the marketing authorisation.<br><br><u>Equalities consideration</u><br><br>The NICE TA states:<br><br>'*There are no equalities issues relevant to the recommendations.*<br><br>*3.22 The patient experts explained that although romosozumab has a marketing authorisation for women after menopause, this should not prevent using romosozumab for men, because the benefits of treatment are likely to be similar. The committee noted that there* |

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| | *may be some people who have been through the menopause but do not identify as a woman. The committee concluded that romosozumab will be considered within its marketing authorisation but that the recommendation need not specify sex. The company noted that osteoporosis is more common in women than men, and people of low socioeconomic status have increased fracture risk, higher mortality after fracture, longer hospital stays and greater risk of re-admission. However, issues related to differences in prevalence or incidence of a disease cannot be addressed in a technology appraisal. In response to consultation, a consultee highlighted that rare types of osteoporosis had not been considered. However, the committee did not consider this an equality issue that could be resolved by this appraisal. The committee concluded that no other equality issues raised were relevant since romosozumab is recommended.'*<br><br>The use in people after menopause is broader than the marketing authorisation.<br><br>*This is the current dose considered by NICE as part of this NICE evaluation. Subsequent changes in the license following NICE publication will need to be considered by the Area Prescribing Committee and* ***will not be routinely funded*** *by local commissioners.* |

| **Disease and potential patient group** | |
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| **Brief description of disease[2]** | Osteoporosis is a progressive skeletal disorder. It is characterised by low bone mass and deterioration of the structure of bone tissue leading to an increase in bone fragility and risk of fracture.<br><br>Osteoporosis is defined by a T-score of −2.5 standard deviations (SD) or below on dual-energy X-ray absorptiometry (DXA) scanning. The T-score relates to the measurement of bone mineral density (BMD) using central (hip and/or spine) DXA scanning, and is expressed as the number of standard deviations (SD) from peak BMD.<br><br>Osteoporosis occurs most commonly in postmenopausal women, men over 50 years, and in patients taking long-term oral corticosteroids (glucocorticoids). Other risk factors for osteoporosis include increasing age, vitamin D deficiency and low calcium intake, lack of physical activity, low body mass index (BMI), cigarette smoking, excess alcohol intake, parental history of hip fractures, a previous fracture at a site characteristic of osteoporotic fractures, and early menopause.<br><br>Some diseases are also known to be associated with osteoporosis such as rheumatoid arthritis and diabetes. Certain medications may also increase the risk of fracture in some patients, through mechanisms such as induction of liver enzymes which interfere with vitamin D metabolism.<br><br>The patient experts explained that osteoporosis affects all aspects of daily life, including walking, eating and breathing. People with the disease often have difficulty doing day-to-day tasks. Fractures can be painful and have a substantial effect on a person's independence and are also associated with increased mortality.<br><br>Because of this, people with osteoporosis live in fear of having another fracture. The patient experts explained how the physical |

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| | changes from osteoporosis, such as loss of height or a stooped posture, can cause feelings of shame.<br><br>The clinical experts explained that it is important to build bone strength and prevent fragility fractures, particularly in people at the highest risk of fracture. The committee concluded that severe osteoporosis can have a substantial effect on quality of life, and that this would be improved by preventing fragility fractures. |
| **Potential patient numbers per 100,000**[3,4] | 22/100,000 |

## SUMMARY

**Guidance**[2]

1.1 Romosozumab is recommended as an option for treating severe osteoporosis in people after menopause who are at high risk of fracture, only if:

- they have had a major osteoporotic fracture (spine, hip, forearm or humerus fracture) within 24 months (so are at imminent risk of another fracture) and
- the company provides romosozumab according to the commercial arrangement.

1.2 This recommendation is not intended to affect treatment with romosozumab that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

**Why the committee made these recommendations**

Current treatments for people with severe osteoporosis after menopause include bisphosphonates, such as alendronic acid, and other types of medicines, such as denosumab or teriparatide. The company proposes that romosozumab would only be used when there is an imminent fracture risk. It defines this as when a person has severe osteoporosis and has had a major osteoporotic fracture within 24 months. This is narrower than the marketing authorisation.

Clinical trial evidence suggests that romosozumab followed by alendronic acid is more effective at reducing the risk of fractures than alendronic acid alone. Comparing romosozumab indirectly with other bisphosphonates and other medicines for this condition suggests that romosozumab is likely to be at least as effective at reducing the risk of fractures in people with osteoporosis after menopause. But the extent of the benefit is uncertain because of differences between the trial populations in the indirect comparisons. The most likely cost-effectiveness estimates for romosozumab followed by alendronic acid, compared with alendronic acid alone, are within what NICE normally considers an acceptable use of NHS resources. So, romosozumab is recommended.

Please note:
Romosozumab is a unique osteoporosis therapy that stimulates bone formation and decreases bone resorption. Most people at high risk of fracture have bisphosphonates as their first treatment but these do not provide optimal fracture risk reduction within 12 months, instead reaching optimal reduction by 36 months, therefore romosozumab will meet a high unmet need for people who are at high risk of fracture.

There is an unmet need for people with very high fracture risk for whom current drugs are not suitable, or for those at particularly high risk of vertebral or hip fractures.

**Cost implications* [2,3,4]**

**Cost:**
The price for romosozumab is £427.75 for 2 pre-filled pens administered subcutaneously as a single monthly dose (BNF online, accessed October 2021). The company has a commercial arrangement. This makes romosozumab available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

**Annual or monthly cost per patient:**

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| Monthly cost | £427.75 |
| Annual cost | £5,133 |

Please note: The length of treatment is 1 year only, followed by antiresorptive therapy.

**Has dose escalation been considered as part of the NICE costing template?**
No.

**Costing information per CCG:**

**1. NICE resource impact statement***

The eligible population is defined as the prevalent and the incident population, where prevalence is defined as *how common* a disease or condition is within a population, either at a point in time or over a given period of time (it includes new and existing cases) and incidence is the number of *new cases* of a disease among a certain group of people during a specific period of time.

The resource impact template states that for Surrey Heartlands CCG, that the eligible population for treatment with romosozumab Year 1 (prevalent + incident population) is 467 and the eligible population for treatment with romosozumab Year 2-5 (incident population) is 233 – see appendix 1.

Table 1: Estimated number of people in Surrey Heartlands CCG receiving treatment with romosozumab each year 2022/23

| | 2022/23 | 2023/24 | 2024/25 | 2025/2026 | 2026/27 |
|---|---|---|---|---|---|
| Uptake % | 10 | 20 | 30 | 40 | 50 |
| People receiving treatment with romosozumab (prevalent population) | 23 | 0 | 0 | 0 | 0 |
| People receiving treatment with romosozumab (incident population) | 23 | 46 | 69 | 92 | 115 |
| **Total number of people receiving treatment with romosozumab** | **46** | **46** | **69** | **92** | **115** |

## 2. NICE resource impact template

Table 2: The change in total drugs cost (future practice, year 5) is £485,709 (drugs and administration) for NHS Surrey Heartlands CCG (does not include savings from changes in fracture activity).

| | Change in drug costs £ | | | | |
|---|---|---|---|---|---|
| | **Year 1** | **Year 2** | **Year 3** | **Year 4** | **Year 5** |
| **Surrey Heartlands CCG** | £191,000 | £192,000 | £289,000 | £386,000 | £486,000 |
| **£ per 100,000 population** | £18,204 | £18,300 | £27,546 | £36,791 | £46,322 |

**NICE funding requirements are based on Quality Adjusted Life Years (QALY) threshold. If there is evidence that the incremental cost rises above this threshold in the future, the APC may reconsider the commissioning status.*

**Availability of PAS and details (if appropriate):**
Yes - the PAS price will be given to trusts which would reduce the cost price stated above.

The PAS price only applies to trusts and primary care services would not be able to prescribe and supply at this reduced price, in line with the NICE TA.

**Availability of homecare service (if appropriate):**
Yes

**Alternative treatments and cost per patient per year**

**Other NICE recommended products: postmenopausal osteoporosis**

| NICE TA | Title | Date | Technology and dosage | Cost per patient per year* |
|---|---|---|---|---|
| TA464 | Bisphosphonates for treating osteoporosis | August 2017 Updated July 2019 | Alendronic acid tablet 10mg daily, alternatively 70mg once a week | £10 |
| | | | Ibandronic acid tablet 150mg monthly | £24.70 |
| | | | Risedronate sodium tablet 5mg daily, alternatively 35 mg once weekly. | £245.44 |
| | | | Zoledronic acid infusion 5mg once as a single dose | £102 + £96 admin cost |
| TA161 | Raloxifene and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women | October 2008 Updated Feb 2018 | Teriparatide 20 micrograms daily for maximum duration of treatment 24 month (prefilled devices for injection) | £2,980 PAS price available |
| | | | Raloxifene tablet 60mg once daily | £51.22 |
| TA204 | Denosumab for the prevention of osteoporotic fractures in postmenopausal women | October 2010 | Denosumab 60 mg every 6 months, injection | £366 - £439 + £192 admin cost |

*BNF costs accessed 6.6.22

**Options not reviewed by NICE but used in standard practice: postmenopausal osteoporosis**

| Technology and dosage | Indication | Cost per patient per year* |
|---|---|---|
| Strontium ranelate 2 g once daily, dose to be taken in water and at bedtime. | Severe osteoporosis in men and postmenopausal women at increased risk of fractures [when other treatments are contra-indicated or not tolerated] (initiated by a specialist) | £1,948.83 |
| Tibolone 2.5 mg daily | Osteoporosis prophylaxis in women at high risk of fractures when other prophylaxis contra-indicated or not tolerated | £69.68 |

*****BNF costs accessed 6.6.22

**Impact to patients**

- An additional treatment option would be valued by patients.
- This medicine is available under a homecare service so will be delivered directly to the patient.

**Impact to primary care prescribers**

- This is a National Tariff excluded high-cost drug and is commissioned by integrated care systems (ICS) / clinical commissioning groups (CCGs) for use in secondary care. There should be no prescribing in primary care.
- Primary care prescribers should be aware that their patient is receiving this medicine and ensure that this is recorded in the patient's notes in order to be alert to potential side-effects and interactions with other medicines prescribed in primary care. This will also ensure that GP records, which are accessed by other healthcare providers, are a true and accurate reflection of the patient's medication.

**Impact to secondary care**

- Providers are NHS hospital trusts.
- The initiation, administration and on-going treatment is managed by secondary care.
- Homecare arrangements will be managed by the trust.
- This medicine is available on homecare and as a subcutaneous injection so once the patient is confident in self-administering, will only require appointments for review and/or monitoring.
- An additional treatment option would be valued by clinicians.

**Impact to commissioners**

- The technology is commissioned by ICS/CCGs and they are required to comply with the recommendations in a NICE TA within 3 months of its date of publication.
- Potential savings for out-patient appointments as this medicine is available on homecare.

**Implementation**

- NICE TA implementation must be within 90 days of publication.
- Blueteq forms to be developed.
- Trusts to follow internal governance procedures to add to their formulary and initiate homecare.
- Review osteoporosis pathway to determine the place of romosozumab.
- Agree responsibility for the initiation of antiresorptive therapy after 12 months treatment with romosozumab.

**Recommendation to APC**

**National Tariff excluded high-cost drug:** Yes

**Recommended traffic light status:** RED

**Additional comments:**

**1. Definition of severity**

There is no definition of severe osteoporosis in the NICE TA. The National Osteoporosis Guideline Group (NOGG) and Royal Osteoporosis Society (ROS) issued a Consensus Advisory Statement on 30th May 2022 on the use of romosozumab following the 2022 NICE Appraisal. This is available at: NOGG-ROS-Romosozumab-statement-May-2022.pdf and also attached.

The consensus statement suggest that referral for, and consideration of treatment with romosozumab, is prioritised as follows:

*'in postmenopausal women who have had a MOF within 24 months, with any one of the following:*

- *a BMD T-Score ≤-3.5 (at the hip or spine), or*
- *a BMD T-score ≤-2.5 (at the hip or spine) and either*
  - *o vertebral fractures (either a vertebral fracture within 24 months or a history of ≥2 osteoporotic vertebral fractures), or*
  - *o very high fracture risk (e.g., as quantified by FRAX).'*

Following the approved duration of treatment with romosozumab (12 months), treatment with alendronate, zoledronate or denosumab should be initiated without delay.

This criteria are different to the ARCH trial which was the main source of clinical-effectiveness evidence for romosozumab, which used T-scores of -2.5 or less or -2.0 or less. As the definition of osteoporosis is a T-score of -2.5 or less, this would include patients with all degrees of severity.

The NOGG/ROS consensus statement has been discussed nationally and regionally, and while approaches will be made to NICE by PrescQIPP, https://www.prescqipp.info/ , to clarify the definition of severe osteoporosis, the adoption of the NOGG/ROS criteria would be a pragmatic and consistent approach, and is proposed across Kent, Surrey and Sussex.

A small change is also proposed which is to change the term in the NOGG/ROS statement from 'postmenopausal women' to 'people after menopause'.

**2. Transition to antiresorptive therapy.**

Romosozumab is licensed for use for 12 months. Following completion of romosozumab therapy, transition to antiresorptive therapy is recommended in order to extend the benefit achieved with romosozumab beyond 12 months.

There needs to be agreement as to whether the primary or secondary care physician is responsible for this.

**References:**


1 Specification of Product Characteristics. emc. Available at: https://www.medicines.org.uk/emc/product/10956 Accessed <30.5.22>

2 NICE Technology Appraisal Guidance: Romosozumab for treating severe osteoporosis. Technology appraisal guidance. Published: 25 May 2022. Available at: https://www.nice.org.uk/guidance/ta791 Accessed <30.5.22>

3 NICE Resource impact report: Romosozumab for treating severe osteoporosis (TA791). Published May. Available at: https://www.nice.org.uk/guidance/ta791/resources Accessed <30.5.22>

4 NICE Resource impact template: Romosozumab for treating severe osteoporosis (TA791). Published May. Available at: Romosozumab for treating severe osteoporosis (TA791). Published May. Available at: https://www.nice.org.uk/guidance/ta791/resources Accessed <30.5.22>


Declaration of interest:

| | Name | Role | Date | Declaration of interests (please give details below) |
|---|---|---|---|---|
| **Prepared by** | Tejinder Bahra | Lead Commissioning Pharmacist | 1.6.22 | None |
| **Reviewed by:** | | | | |

Explanation of declaration of interest:
None.

Version control sheet:

| Version | Date | Author | Status | Comment |
|---|---|---|---|---|
| 1 | 6.6.22 | Tejinder Bahra | Draft | Out for consultation |
| 2 | 5.7.22 | Tejinder Bahra | Final | Out for clinical comment |

**Appendix 1: Number of people eligible for treatment in England and Surrey Heartlands CCG population**

| Population | Proportion of previous row (%) | England | Surrey Heartlands CCG |
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| Total population | | 56,286,961 | 1,049,170 |
| Number of postmenopausal people (50 years and older)[1] | 19.62% | 11,043,600 | 205,850 |
| People after menopause with osteoporosis (Defined as BMD T-score ≤-2.5)[2] | 21.80% | 2,407,500 | 44,875 |
| People after menopause with osteoporosis who have had a major osteoporotic fracture in the last 13-24 months[3] | 3.3% | 78,800 | 1,469 |
| People after menopause with severe osteoporosis who have had a major osteoporotic fracture in the last 13-24 months and are at high risk of fracture[3] | 17.5% | 13,790 | 257 |
| **People after menopause with severe osteoporosis who have had a major osteoporotic fracture in the last 13-24 months at high risk of fracture with no history of MI or stroke (prevalent population)** | **91%** | **12,520** | **233** |
| People after menopause with osteoporosis who have had a major osteoporotic fracture in the last 12 months[3] | 3.3% | 78,800 | 1,469 |
| People after menopause with severe osteoporosis who have had a major osteoporotic fracture in the last 12 months and are at high risk of fracture[3] | 17.5% | 13,790 | 257 |
| **People after menopause with severe osteoporosis who have had a major osteoporotic fracture in the last 12 months at high risk of fracture with no history of MI or stroke (incident population)[4]** | **91%** | **12,521** | **233** |
| **Eligible population for treatment with romosozumab Year 1 (prevalent + incident) population** | | **25,043** | **466** |
| **Eligible population for treatment with romosozumab Year 2-5 (incident) population** | | **12,521** | **233** |

1 Office for National Statistics
2 Fragility fractures in Europe: burden, management and opportunities
3 Clinical expert opinion
4 The cardiovascular risk factors and incidence of cardiovascular events in postmenopausal women at high risk of fracture

Comments received:

| Clinician | Comment | Response |
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| Laura Attipoe<br>Rheumatology Consultant<br>Kingston Hospital | Hi - thanks for this<br>Just wanted to clarify regarding clinician prescribing of this drug - would we be free to prescribe it as long as NICE recommendations are met? | Hi Laura<br>CCGs have 90 days to implement the guidance from NICE and so once this guidance has been to the APC the Blueteq forms will be enabled and you will be good to go. We would advise not initiating treatment until the implementation has taken place. Tejinder is way ahead of the 90 day implementation deadline and so hopefully by mid-July the Blueteq forms will be enabled (post APC) and patient initiation can start.<br><br>Best Wishes<br>Clare |
| | | Ah ok, thanks for keeping us updated |
| Dr Rod Hughes<br>Rheumatology Consultant<br>ASPH | Hi Clare<br><br>3 questions spring to mind<br><br>Would be great if the severe OP could be defined by T and Z score as it is with teriperatide so we know what threshold needs to be passed<br><br>Do they need to have been on another anti resorptive first?<br><br>Can they progress to romo if they have already received teriperatide?<br><br>regards<br><br>Rod | |
| Sian Griffith<br>Consultant Rheumatologist | Dear Clare<br>Divya has explained. | Hi Dr Griffiths<br>The traffic light RED status recommendation means that |

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| Rheumatology Clinical Lead and Trust Lead for Osteoporosis<br>Surrey and Sussex Healthcare NHS Trust | I am happy with proposed status | romosozumab should only be prescribed in secondary care through specialist Rheumatology Teams. Hope that helps clarify |
| Georgina Randall<br>Senior Pharmacy Technician – Pharmaceutical Commissioning | Comment 1:<br><br>Hi Tejinder,<br>Please can this info below from the TA (section 3.22) be reflected either in the main paper or the front cover as EQIA related……thanks.<br><br>"The patient experts explained that although romosozumab has a marketing authorisation for women after menopause, this should not prevent using romosozumab for men, because the benefits of treatment are likely to be similar. The committee noted that there may be some people who have been through the menopause but do not identify as a woman. The committee concluded that romosozumab will be considered within its marketing authorisation but that the recommendation need not specify sex. The company noted that osteoporosis is more common in women than men, and people of low socioeconomic status have increased fracture risk, higher mortality after fracture, longer hospital stays and greater risk of re-admission. However, issues related to differences in prevalence or incidence of a disease cannot be addressed in a technology appraisal. In response to consultation, a consultee highlighted that rare types of osteoporosis had not been considered. However, the committee did not consider this an equality issue that could be resolved by this appraisal. The committee concluded that no other equality issues raised were relevant since romosozumab is recommended." | Thanks George – included in the paper as requested. |

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| | This came to me whilst I was checking the TA for Blueteq form purposes…..the rare types bit might be applicable to IFR/commissioning stance??<br>George | |
| | Comment 2:<br><br>Also, would it just be rheum people prescribing this?<br>Is there a place for this being suggested as part of a post-surgical fracture package of care in some fragile patients?? i.e. orthopods actively identifying patients who would/should be using….because they have just recently fx'd? Or perhaps these patients get fast-tracked to a rheum specialist/pharmacist prescriber? | |
| Dr Cai Neville MD FRCP<br>Consultant Rheumatologist<br>Clinical Lead for Rheumatology<br>College Tutor for Medicine<br>Royal Surrey County Hospital | I can't see that 'severe' osteoporosis is defined anywhere - the trial used T score of -2.5, which is not severe.<br><br>Are we going to define severity? | |
| Sian Griffith<br>Consultant Rheumatologist<br>Rheumatology Clinical Lead and Trust Lead for Osteoporosis<br>Surrey and Sussex Healthcare NHS Trust | | Dear All,<br><br>That is the difficult part, but the bit where we may have local discretion. We need to try and reserve for those patients at highest risk of further fracture so recent/ recurrent fragility fracture of vertebrae/ pelvis/ femur/ humerus (within 2 years) plus above threshold for treatment NOGG???? It is really hard because if we tighten definition too much we can't treat the ones who need it most (recurrent fractures). However we don't want patients with t score -2.5, wrist fracture who have never had a bisphosphonate to be asking for it….<br><br>We can have a line about benefit of treatment must outweigh risk of cardiovascular side effects as judged by treating |

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| | | clinician….<br>Recent significant fragility fracture in last two years, or recurrent fracture despite treatment….<br>Low BMD t score < -2.5 and/ or NOGG treatment/ imminent risk of fracture??<br><br>What does everyone think? |
| Dr Ritu Malaiya<br>MSc FRCP<br>Consultant Rheumatologist<br>Epsom & St Helier University Hospitals NHS Trust<br>BSR Council Regional Chair - London South<br>NEIAA Regional Champion - London | May I introduce Dr Mehdi Mirzazadeh (cc'd) into the discussion - he is our osteoporosis lead. | |
| Carina Joanes<br>Lead Commissioning Pharmacist – Guildford & Waverley ICP | | Thank you for all the comments so far,<br><br><u>Definition:</u><br>NICE has been quite specific about what they consider severe osteoporosis:<br><br>Romosozumab is recommended as an option for treating severe osteoporosis in people after menopause who are at high risk of fracture, only if:<br>• they have had a major osteoporotic fracture (spine, hip, forearm or humerus fracture) within 24 months (so are at imminent risk of another fracture)<br><br>There is quite a comprehensive discussion of how they came to this conclusion, see section 3:<br>https://www.nice.org.uk/guidance/ta791/resources/romosozumab-for-treating-severe-osteoporosis-pdf-82611612263365 |

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| | | In section 3.6, it includes the definitions for the t-score in the trials:<br>People were randomised to have either romosozumab or alendronic acid for 12 months, followed by open-label oral alendronic acid for at least another 12 months in both arms.<br>ARCH included ambulatory women after menopause aged 55 to 90 if they met at least 1 of the following criteria:<br>• A T-score of -2.5 or less at the total hip or femoral neck and either 1 or more moderate or severe vertebral fractures, or 2 or more mild vertebral fractures<br>• A T-score of -2.0 or less at the total hip or femoral neck and either 2 or more moderate or severe vertebral fractures, or a fracture of the proximal femur 3 to 24 months before randomisation.<br><br>Would this definition work?<br><br><u>Place in therapy:</u><br><br>The evidence for romosozumab indicates that after 1 year of treatment, the best outcomes include maintenance with alendronic acid.<br>For teriparatide, it is also important to follow up treatment with the return to the best tolerated treatment so far, as it is a one off therapy,<br>I therefore recommend that we update the pathway.<br><br>In the ARCH trial, only 10% of patients had other treatments before initiating the romosozumab (or alendronic acid in the control arm) however this is unlikely to be the place in therapy for now as the trials showed an increase in serious cardiovascular events (myocardial infarction and stroke), and we are familiar to the fact that new adverse effects emerge when new medicines are used in |

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| | | the wider population after trials, and therefore the benefits need to outweigh the risks. The number of patients who were followed up towards the 5-years after initiation were very small in the trials, so it is not possible yet to know the long-term benefits.<br><br>I wonder if you've had the opportunity to see the SIGN guidelines which already include the Romosozumab: https://www.sign.ac.uk/media/1813/sign-142-qrg-v3.pdf, it has an excellent flow chart which could be used as a starting point.<br>The full guideline is on the following link:<br>https://www.sign.ac.uk/media/1812/sign-142-osteoporosis-v3.pdf<br><br>It seems to me, that romosozumab has a similar mode of action to denosumab in that they both prevent bone resorption, I wonder whether we will end up requiring life-long treatment to maintain the benefit – the information given to NICE suggests that a one year treatment followed by alendronic acid will provide a 5 year benefit, with a signal that the effect may wane over time.<br><br>Romosozumab<br>https://go.drugbank.com/drugs/DB11866<br><br>Denosumab:<br>https://go.drugbank.com/drugs/DB06643 |
| Dr Cai Neville MD FRCP<br>Consultant Rheumatologist<br>Clinical Lead for Rheumatology<br>College Tutor for Medicine<br>Royal Surrey County Hospital | | A T score of -2.5 is the definition of osteoporosis. It is not 'severe' osteoporosis (whatever that is).<br>A combination of a low trauma fracture plus T score of -2.5 is a huge proportion of the elderly population. Pretty much anyone over the age of 75 who has a low trauma fracture.<br>A T score of -2.0 is osteopenia.<br><br>There is also a grey area for patients who have had multiple spinal |

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| | | fractures but a relatively normal hip DEXA.<br><br>I second Sian's suggestion that we discuss and come to an agreement about what we consider 'severe' to be, and then update our pathway. |
| Mehdi Mirzazadeh, BA,MD, MSc, MRCP, FRCPath<br>Consultant in Metabolic Medicine and Chemical Pathology<br>Honorary Senior Lecturer St George's University of London<br>Director of South West Thames Newborn Screening Laboratory<br>Clinical Lead for Metabolic Bone Diseases<br>Epsom and St Helier University Hospitals NHS Trust | | Thanks for copying me in Ritu!<br><br>NOGG has published a statement on it (attached), which might be useful for more clarification.<br>@JOHNS, Clare (NHS SURREY HEARTLANDS CCG), would you please send me a copy of the document!<br><br>Best wishes<br><br>Mehdi |
| | Hi Bahra,<br><br>Please see my comments as below:<br><br>1. I have sent NOGG statement to the group before, and I think it clarifies the eligibility a lot better.<br>2. Red status would be a problem in Epsom, as our Rheumatology services are already under a lot of pressure and providing more nursing time for initiation and follow up would be difficult without additional staff and appropriate funding. I think we can probably start Romo in the hospital , but would be ideal if GPs can continue. | Dear Dr Mirzazadeh,<br><br>I hope you are well.<br><br>Firstly, please accept my apologies in the delay in replying to you, as I have been on annual leave and I was waiting for some guidance from national organisations.<br><br>Thank you so much for your participation in this discussion and your very helpful insights and information, in particular the NOGG/ROS statement. |

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| | 3. The estimated number of patients referred to osteoporosis in rheumatology services in Epsom ans St Helier who will be eligible per year , based on the current referral pattern and NICE criteria, would be around 75-100 patients in the trust, but this will probably increase after the CCG approves the funding.<br>1. As stated in the guideline, establishing the history of a low impact fracture in the last two years is not always possible, so some patients were excluded on that basis from my estimated number.<br>2. DEXA scans are not calibrated for age > 80 , but the eligibility criteria is T score based. This may increase the number of bone density scans requested and needs to be discussed with radiologists. It should be clarified in our approach if we accept the DEXA for age > 80 for consideration of Romo<br>3. It should be made clear for primary care colleagues that Romo is contraindicated in pts with previous MI/Stroke, so they should not be referred for treatment.<br>4. Majority of patients with recent fractures are seen by FLS or primary care colleagues, but not in rheumatology; so there will be a need for estimation of the numbers that may be eligible from those services, too .<br>Best wishes<br><br>Mehdi | The approach we are pursuing in Surrey (and also across Kent and Sussex) is to propose the NOGG/ROS consensus statement as a definition of severity. This seems a pragmatic and consistent approach and we will be asking clinicians in our area if they agree with this.<br><br>Surrey Heartlands ICS is not the lead commissioner for ESHUT (this is SWL CCG) so I have copied in my colleagues from SWL, Brigitte and Vinty, as this long discussion chain will be useful to them in considering their commissioning stance.<br><br>Thanks again for your help – it is much appreciated. |

Second consultation:

| Question | Clinician response | Clinician response | Clinician response | Clinician response |
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| | Dr Rod Hughes<br>Consultant Rheumatologist<br>Ashford and St Peter's Hospitals NHS Foundation Trust. | Helen Marlow<br>Lead Primary Care Pharmacist and NICE Medicines and Prescribing Associate<br>Surrey Downs ICP | Dr Rebecca Rogers<br>GP Sunbury-on-Thames<br>GP Prescribing Lead for North West Surrey, NHS Surrey Heartlands Clinical Commissioning Group<br>GP Appraiser NHS England (South, South East) | Sarah Watkin<br>Associate Director of Pharmacy<br>Surrey Heartlands Integrated Care System NHS Surrey Heartlands |
| Acknowledge that as there is currently no definition for severe osteoporosis in the NICE TA, and therefore to accept the definition as per the NOGG/ROS consensus statement.<br><br>This is the same approach across Kent, Surrey and Sussex and potentially much wider. | Agree | Agree to use this definition – there is some suggestion of definition within the evidence on NICE website, but not clear so NOGG/ROS consensus seems reasonable | I've reviewed the paper, and agree with question 1 regarding the definition. I do have a query about the use of a "very high FRAX" as that may be interpreted differently by individuals. A referral pathway with guidance for what levels of FRAX would be useful moving forwards. | I accept but how do we word the 'extra' criteria over and above NICE. We could agree as per NICE and reference that the NCOG has advised that severe is…… |
| Agree to change the wording in the NOGG/ROS from 'postmenopausal women' to 'people after menopause' to be more inclusive and in line with NICE TA791. | Agree | Yes | Agree | I accept change in wording to people after menopause |
| Agree on who is responsible for starting anti-resorptive therapy | Think this has to be a secondary care initiation otherwise might lead to | These patients are under secondary care and so the specialist should either start | It would be really helpful if the selection of antiresorptive was advised | In relation to who starts the anti-resorptive tx I think it is important that patients are |

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| after 12 months treatment with romosozumab – primary or secondary care. | overuse | anti-resorptive therapy or recommend to GP to initiate the anti-resorptive therapy, as the GP won't necessarily know /be expected to know the remosozumab course is finished and that anti-resorptive therapy is needed | by secondary care. I am mindful that the trigger to this may not be clear, as the patient won't need to see the specialist for the administration of injections. My preference would however be a directive from secondary care. | not lost to follow up and are only treated for 12 months so I have two points to make on this one;<br>a) As this is a PbRe medicine the Provider should be responsible for stopping it at 12m and then reviewing for the most appropriate anti-resorptive agent which then gets started as per our usual traffic light status for those drugs<br>b) Do Trusts have systems in place to ensure and assure that treatment will be limited to 12 months? |