Innovation Observatory

NHS National Institute for Health Research

HEALTH TECHNOLOGY BRIEFING
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Tanezumab for moderate to severe chronic pain associated with osteoarthritis and chronic low back pain

NIHRIO ID	17200	**NICE ID**	9757
Developer/Company	Pfizer Ltd, Eli Lilly & Co	**UKPS ID**	644897

Licensing and market availability plans	Currently in phase III clinical trials

SUMMARY

Tanezumab is in clinical development for the treatment of moderate to severe chronic pain associated with osteoarthritis and chronic low back pain. Pain is an unpleasant sensory experience associated with damage to body tissues due to an injury, physical pressure, or inflammation of some part of the body. Chronic pain is persistent or recurrent and lasts for longer than 12 weeks. Moderate pain interferes significantly with daily living activities, and severe pain is disabling and causes an inability to perform daily living activities. Effective long-term treatment options for managing moderate to severe chronic pain are limited. Currently available pain medicines like opioids and analgesics may increase the risks of addiction, gastrointestinal, cardiovascular and renal problems.

Tanezumab is a type of monoclonal antibody, which works by selectively targeting, binding to and inhibiting nerve growth factor (NGF). NGF levels increase in the body as a result of injury, inflammation or in chronic pain states. By inhibiting NGF, tanezumab may help to keep pain signals produced by muscles, skin and organs from reaching the spinal cord and brain. Tanezumab has a novel mechanism that acts in a different manner than opioids and other analgesics, including nonsteroidal anti-inflammatory drugs, and may offer an alternative treatment option for managing chronic pain.

PROPOSED INDICATION

Moderate to severe chronic pain in adult patients associated with osteoarthritis (OA) and nociceptive chronic low back pain (CLBP), where treatment is inadequate or inappropriate with other analgesics.[a]

TECHNOLOGY

DESCRIPTION

Tanezumab (PF-04383119, RN624) is a humanized monoclonal antibody directed against nerve growth factor (NGF), a modulator of nociceptor function, with potential analgesic activity. Tanezumab binds to NGF and prevents NGF binding to its high affinity, membrane-bound, catalytic receptor tropomyosin-related kinase A (TrkA), which is present on sympathetic and sensory neurons; reduced stimulation of TrkA by NGF inhibits the pain-transmission activities of these neurons. NGF, a neurotrophin, is critical to the growth and maintenance of sympathetic and sensory neurons. In addition, NGF may induce mast cells to release inflammatory proteins and may induce the upregulation of substance P and other pain-related peptides in sympathetic and sensory neurons. Upon neurotrophin binding, TrkA phosphorylates itself and members of the MAPK pathway, mediating the multiple neuronal effects of NGF.[1]

Tanezumab is currently in development for the treatment of moderate to severe chronic pain in adult patients associated with OA and CLBP. In the phase III clinical trials of subjects with OA of the hip or knee (NCT02697773, NCT02709486, NCT02528188, NCT02674386), tanezumab is administered as a subcutaneous (SC) injection of 2.5mg or 5mg at 8-weekly intervals over periods of up to 80 weeks.[2-5] In the phase III clinical trial of subjects with CLBP (TANGO; NCT02528253), tanezumab is administered as a SC injection of 5mg or 10mg at 8-weekly intervals over a period of 56 weeks.[6]

INNOVATION AND/OR ADVANTAGES

Tanezumab has a novel mechanism that acts in a different manner than currently available pain medicines, in a treatment area where no significant transformative medicines have been licensed in recent years.[7-9] Being a monoclonal antibody, tanezumab does not cross the blood brain barrier.[10] As a non-opioid compound and based on its mechanism of action, tanezumab has no evidence of addiction. [11,12]

In previous clinical trials in OA, tanezumab demonstrated significant improvement compared to placebo, naproxen or oxycodone treatment in the WOMAC Pain subscale as well as the WOMAC Physical Function subscale and the Patient's Global Assessment of pain.[13-15]

In previous CLBP clinical trials, tanezumab provided significant improvement across the Low Back Pain Intensity (LBPI) score, Roland Morris Disability Questionnaire (RMDQ), and Patient Global Assessment of Low Back Pain compared to both placebo and naproxen treatment.[16,17]

[a] Information provided by Pfizer Ltd

DEVELOPMENT STATUS AND/OR REGULATORY DESIGNATIONS

Tanezumab does not currently have Marketing Authorisation in the EU/UK for any indication.

Tanezumab is in phase III clinical development for cancer pain.[18]

Tanezumab has a Fast Track designation by the US FDA for the treatment of chronic pain in patients with OA and CLBP in June 2017.

PATIENT GROUP

DISEASE BACKGROUND

The definition of pain provided by the International Association for the Study of Pain (IASP) is 'an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage'.[19] Pain can be categorized according to different dimensions, including by its pathophysiological mechanism (nociceptive or neuropathic pain), duration (chronic or acute) and severity (e.g. mild, moderate or severe).

Neuropathic pain arises from an abnormality in processing sensations by the central nervous system (as in phantom limb pain) or in the peripheral nervous system (as in neuropathy).[20] In contrast, nociceptive pain originates with an injury involving nociceptors, which are pain receptors found primarily in the skin or joints (somatic sources) or the walls of organs (visceral sources). Nociceptors are activated by inflammatory mediators released in response to tissue damage or trauma.[21] Injuries causing nociceptive pain may be mechanical (as with a traumatic injury), thermal (as with a burn), or chemical (as with poisoning).

Chronic pain has been recognised as pain that persists past normal healing time when associated with injury, and usually pain is regarded as chronic when it lasts or recurs for more than 3 – 6 months.[22] Pain severity can be assessed using different types of instrument to assess pain-related interference with activities (disability) and the intensity of pain. However, functional progress should be assessed in parallel to pain on movement.[23]

Patients suffering from chronic pain have poorer quality of life compared to general population and patients with limiting illnesses. It restricts their physical activity, compromising their ability to work, playing with their children, enjoying a good relationship with their spouses, performing routine tasks, and enjoy a good night's sleep.[24]

OA is a chronic, progressive musculoskeletal condition that results in structural changes in the joint and can cause pain, swelling, and stiffness.[25] CLBP is characterized by pain and muscle tension or stiffness[26] although it is not possible to identify a specific nociceptive cause and is termed 'non-specific'; only a small proportion have a clearly defined pathological cause of their pain.[27]

CLINICAL NEED AND BURDEN OF DISEASE

There is broad consensus on the substantial healthcare and economic burden of chronic pain in the UK, although recent research is limited on the different pain modalities. A study of the global burden of disease in England from 1990 to 2013 established that the leading cause of disability-adjusted life years in 2013 was low back and neck pain.[28]

Data from a systematic review published in 2016 indicated that the prevalence of chronic pain, derived from 7 studies, ranged from 35.0% to 51.3% (pooled estimate 43.5%, 95% CIs 38.4% to 48.6%). The prevalence of moderate-severely disabling chronic pain (Von Korff grades III/IV), based on 4 studies, ranged from 10.4% to 14.3%. 12 studies stratified chronic pain prevalence by age group, demonstrating a trend towards increasing prevalence with increasing age from 14.3% in 18–25 years old, to 62% in the over 75 age group, although the prevalence of chronic pain in young people (18–39 years old) may be as high as 30%.[29]

Chronic pain was more common in female than male participants, across all measured phenotypes.[29] Chronic pain affects between one-third and one-half of the UK population, corresponding to just under 28 million adults, based on data from the best available published studies. This figure is likely to increase further in line with an ageing population.[b]

Specifically to OA, in 2013 an estimated 8.75 million people aged 45 years and over (33%) in the UK sought treatment for OA - 60% female, 40% male.[30] Nearly three quarters of people with OA report some form of constant pain, with one in eight describing their pain as often unbearable.[31]

Specifically to back pain, it is estimated that back pain affects around one third of the UK adult population at some point each year.[32,33] Between one in four and one in seven young people have long–term low back pain.[34,35] Arthritis Research UK's musculoskeletal calculator estimates 9.11 million (16.9%) people in England have back pain, 5.5 million of whom have severe back pain.[36]

The economic burden of chronic pain conditions is considerable. The estimated cost to the NHS for low back pain in 2008 was £2.1 billion, and indirect costs including loss of productivity as £10.7 billion.[37] For OA the estimated cost to the NHS in 2008 was £5.2 billion[38] and an estimated £3.2 billion in lost production.[39]

PATIENT TREATMENT PATHWAY

TREATMENT PATHWAY

The patient pathway is dependent on the associated pain model diagnosis. For both OA and CLBP, a holistic approach to assessment and management should be employed.[40,41] The person's function, quality of life, occupation, mood, relationships and leisure activities should be considered and a plan should be developed with the person (and their family members or carers as appropriate) for managing their condition. Comorbidities that compound the effect of OA or CLBP should be considered when formulating the management plan.

Current pharmacotherapies for chronic pain such as pain due to OA and CLBP are limited and clinical guidelines focus on holistic care including psychotherapy physical therapy, pharmacotherapy and/or surgical interventions.[40,41] The risks and benefits of treatment options should be discussed with the person, taking into account comorbidities and the physician should ensure that the information provided can be understood. Self-management strategies should be agreed with the patient and

[b] Information supplied by Pfizer Ltd

positive behavioural changes, such as exercise, weight loss, use of suitable footwear and pacing should be appropriately targeted.[42, 15]

About 40% of patients have inadequate management of their chronic pain.[43] In the National Pain Audit approximately 30% of patients only received moderate pain relief from their pain treatments, with around 55% receiving little to no relief, despite receiving concomitantly multiple non-pharmacological and pharmacological treatments.[44]

CURRENT TREATMENT OPTIONS

Effective pharmacotherapeutic options for managing chronic pain are limited. Current pharmacological interventions are recommended in most guidelines are for the shortest possible period of time or have limited evidence when used long term.[40,41,45,46] The risk-benefit profile of available pharmacologic treatment, such as addiction, gastrointestinal, cardiovascular and renal concerns, especially for long-term use, may be inadequate in certain patients.[47]

Paracetamol, NSAIDs, topical NSAIDs and capsaicin, intraarticular steroids and opioids are all used for OA, but national and international recommendations generally state these should be used at the lowest effective dose for the shortest possible time owing to tolerance and known side effects. Opioids should only be considered if other treatments are insufficient for pain relief and risks and benefits should be considered, particularly in older people.[40,41]

PLACE OF TECHNOLOGY

If licensed, tanezumab will offer an additional treatment option for adult patients with moderate to severe chronic pain associated with OA and nociceptive CLBP, where treatment is inadequate or inappropriate with other analgesics.

CLINICAL TRIAL INFORMATION

Trial	**NCT02697773, EudraCT-2013-002222-23; tanezumab vs placebo; phase III**
Sponsor	Pfizer Ltd, Eli Lilly & Co
Status	Published in abstract
Source of Information	Abstract,[48] trial registry[3]
Location	EU (not UK), USA, Canada
Design	Randomised, placebo-controlled
Participants	n=698; aged ≥ 18 yrs; OA of the knee or hip, documented history that subject tried acetaminophen, NSAIDS and either tramadol or opioids, and had insufficient pain relief or cannot take/tolerate; based on American College of Rheumatology criteria with x-ray confirmation and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) ≥5
Schedule	Randomised 1:1:1 to SC tanezumab 2.5 mg on day 1 and 2.5mg at wk 8; SC tanezumab 2.5 mg on day 1 and 5 mg at wk 8; SC placebo on day 1 and at wk 8
Follow-up	Active treatment for 16 wks, follow-up for 24 wks

Primary Outcomes	Change from baseline to wk 16 in: WOMAC Pain, WOMAC Physical Function, Patient's Global Assessment of OA (PGA-OA)
Secondary Outcomes	Key secondary endpoint:[c] Proportion of patients with ≥ 50% improvement in WOMAC Pain from baseline to Week 16 Safety Endpoints:[c] Adverse events (AEs) Joint safety – Adjudicated joint safety events and total joint replacements Neurologic safety – Outcomes of neurological exams and consultations • Standardized neurologic exams at all visits; Neuropathy Impairment Score, orthostatic BP
Key Results	The study met all three co-primary efficacy endpoints using the step-down testing procedure, demonstrating that among patients with moderate-to-severe OA pain of the knee or hip, both dosing regimens of tanezumab were associated with a statistically significant improvement in pain, physical function and the patients' overall assessment of their OA, compared to placebo.[48]
Adverse effects (AEs)	The most common AEs (≥3% in any treatment group and more frequent in each tanezumab treatment group than in the placebo treatment group) were nasopharyngitis, pain in extremity, and paresthesia. The incidence of serious AEs or withdrawals due to AEs was similar between treatment groups. Adjudicated rapidly progressive OA occurred in 1.3% of tanezumab-treated subjects during the 40-week study.[48]
Expected reporting date	Study completion date reported as Jan 2019

Trial	NCT02709486,**EudraCT-2013-004508-21**; **tanezumab versus placebo; phase III**
Sponsor	Pfizer Ltd, Eli Lilly & Co
Status	Complete but unpublished
Source of Information	Trial registry[2]
Location	EU (incl UK) and Japan
Design	Randomised, placebo-controlled
Participants	n=849; aged ≥ 18 yrs; OA of the hip or knee; a history of insufficient pain relief from acetaminophen and history that subject tried, NSAIDS and either tramadol or opioids, and had insufficient pain relief or cannot take/tolerate; WOMAC Pain subscale score ≥ 5
Schedule	Randomised to SC tanezumab 2.5mg; or SC tanezumab 5mg; or SC placebo; each administered at 8-wk intervals over 24 wks
Follow-up	Active treatment for 24 wks, safety follow-up for 24 wks.
Primary Outcomes	Change from baseline to wk 16 in: • WOMAC Pain, WOMAC Physical Function, Patient's Global Assessment of OA (PGA-OA)
Secondary Outcomes	wks 1, 2, 3, 4, 6, 8, 10, 12, 16, 20, 24, 28 and 32:

[c] Data on file from the study protocol and draft report.

	- Average pain score in the index knee or hip change from baseline wks 2, 4, 8, 12, 16 and 32: - WOMAC pain subscale change from baseline - WOMAC physical function subscale change from baseline - Patient's global assessment of osteoarthritis (5 point Likert scale) change from baseline - OMERACT OARSI responder index wks 2, 4, 8, 12, 16, 24 and 32 - Treatment response: reduction in the WOMAC pain subscale of 30%, 50%, 70% and 90% - Treatment response: reduction in the WOMAC physical function subscale of 30%, 50%, 70% and 90% - Treatment response: improvement of ≥2 points in patient's global assessment of osteoarthritis - WOMAC stiffness subscale change from baseline - WOMAC average score change from baseline - WOMAC pain subscale item: pain when walking on a flat surface, change from baseline - WOMAC pain subscale Item: pain when going up or down stairs, change from baseline wks 2, 4, 8, 12, 16, 24 and 32 - Usage of rescue medication (incidence and number of days of use) wks 2, 4, 8, 12, 16 and 24: - Usage of rescue medication (amount taken) wks 2, 4, 8, 12, 16, 24, 32 and 48: - Orthostatic (supine / standing) blood pressure assessments - Physical examination of all major joints - Heart rate in beats per minute - Blood pressure in mmHg - Neurologic exam (neuropathy impairment score) wks 8, 16 and 24: - Work productivity and activity impairment questionnaire for osteoarthritis (WPAI:OA) impairment scores change from baseline - EQ 5D-5L health state utility and five Items (mobility; self-care; usual activities; pain/discomfort; anxiety/depression) change from baseline wks 8, 16, 24, 32 and 48: - Anti-tanezumab antibody assessments wks 16 and 24: - Cumulative distribution of percent change from baseline in the WOMAC pain subscale score - Cumulative distribution of percent change from baseline in the WOMAC physical function subscale score - Patient reported treatment impact assessment-modified (mPRTI) wks 16 and 32:

	- Clinical chemistry testing - Hematology testing wk 24: - Incidence of discontinuation due to lack of efficacy - Survey of autonomic symptom scores - Time to discontinuation due to lack of efficacy - General examination including cardiovascular, respiratory, abdominal and skin systems wks 24 and 48: - Electrocardiogram Baseline and wks 32 and 48: - Health care resource utilisation wk 48: - Incidence of subjects with adverse events - Incidence of individual adjudication outcomes - Incidence of all cause total joint replacements
Key Results	Not reported
Adverse effects (AEs)	Not reported
Expected reporting date	Study completion date reported as Nov 2018

Trial	**NCT02528188, EudraCT-2012-003721-22 ; tanezumab versus NSAID; phase III**
Sponsor	Pfizer Ltd, Eli Lilly & Co
Status	Ongoing
Source of Information	Trial registry[4]
Location	EU, USA and other countries
Design	Randomised, active-controlled
Participants	n=3,078; aged ≥ 18 yrs; OA of the hip or knee; receiving stable dose regimen of oral NSAID at screening, a history of insufficient pain relief from, inability to tolerate or contraindication to acetaminophen and either tramadol or opioids; WOMAC Pain subscale score ≥ 5
Schedule	Randomised to SC placebo every 8 wks plus oral NSAID (naproxen 500 mg, celecoxib 100 mg or diclofenac 75 mg) twice daily; SC tanezumab 2.5mg every 8 wks plus oral placebo for NSAID twice daily; SC tanezumab 5mg every 8 wks plus oral placebo for NSAID twice daily
Follow-up	Active treatment up to 56 wks, safety follow-up for 24 wks.
Primary Outcomes	wk 80: Incidence of a predefined composite endpoint as specified in protocol wk 16: Change from Baseline in WOMAC Pain Subscale Score Change from Baseline in WOMAC Physical Function Subscale Score Change from Baseline in Patient's Global Assessment of Osteoarthritis
Secondary Outcomes	wk 80: - Incidence of individual adjudication outcomes as specified in protocol

	- Incidence of all cause total joint replacements - Incidence of Subjects with Adverse Events wks 56 and 80: - Change from Baseline in Minimum Joint Space Width of the index knee - Change from Baseline in Minimum Joint Space Width of the index hip - Incidence of subjects with progression of osteoarthritis in the index knee and/or hip according to Bland and Altman method - Change from Baseline 12-lead Electrocardiogram wks 2, 4, 8, 24, 32, 40, 48, 56 and 64: - WOMAC Pain subscale change from Baseline - WOMAC Physical Function subscale change from Baseline - Patient's Global Assessment of Osteoarthritis change from Baseline - OMERACT OARSI responder index - Treatment Response: Reduction in the WOMAC Pain subscale of 30%, 50%, 70% and 90% - Treatment Response: Reduction in the WOMAC Physical Function subscale of 30%, 50%, 70% and 90% - Treatment Response: Improvement of 2 points in Patient's Global Assessment of Osteoarthritis - WOMAC Stiffness subscale change from Baseline - WOMAC Average change from Baseline - WOMAC Pain Subscale Item: Pain When Walking on a Flat Surface, change from Baseline - WOMAC Pain Subscale Item: Pain When Going Up or Down Stairs, change from Baseline - Incidence of Rescue Medication Use - Orthostatic (supine/standing) blood pressure - Number of Days of Rescue Medication Use Baseline, wks 2, 4, 8, 16, 34, 32, 40, 48, 56, 64 and 80: - Change from Baseline Sitting Heart Rate - Change from Baseline Sitting Blood Pressure - Neurologic examinations Baseline, wks 8, 16, 32, 48, 56 and 80: - Anti tanezumab antibody levels - Lower Extremity Activity Scale: change from Baseline Baseline and wks 16, 24, 56 and 64: - Work Productivity and Activity Impairment Questionnaire for Osteoarthritis (WPAI:OA) impairment scores change - EuroQol 5 Dimension (EQ 5D 5L) dimensions and overall health utility score wks 16, 24, and 56: - Cumulative distribution of percent change from Baseline in the WOMAC Pain subscale score - Cumulative distribution of percent change from Baseline in the WOMAC Physical Function subscale score wks 16 and 56: - Change from Baseline in average daily minutes of physical activity - Change from Baseline in average daily physical activity counts - Change from Baseline in average daily minutes of moderate to vigorous physical activity - Change from Baseline in average daily minutes of bouted (sustained) moderate to vigorous physical activity - Change from Baseline in average daily step count

	- Patient Reported Treatment Impact Assessment Modified (mPRTI) - Treatment Satisfaction Questionnaire Medicine v.II (TSQM v.II) satisfaction with effectiveness, side effects and convenience, and overall satisfaction wks 1, 2, 3, 4, 6, 8, 10, 12, 16, 20, 24, 32, 40, 48, 56 and 64: - Average pain score in the index joint change from Baseline Wk 56: - Incidence and Time to discontinuation due to Lack of Efficacy wk 56: - Incidence of Physical Examination Findings Baseline, wks 16 and 64 : - Incidence of Subjects with Clinical Laboratory Test Abnormalities Screening and wks 24, 56 and 80: - Survey of Autonomic Symptom scores wks 2, 4, 8 and 16: - Amount of Rescue Medication Taken Baseline and wks 64, and 80: - Health Care Resource Utilization
Key Results	N/A
Adverse effects (AEs)	-
Expected reporting date	Study completion date estimated as February 2019

Trial	**TANGO, NCT02528253, EudraCT-2012-005495-34; tanezumab vs placebo and tramadol PR; phase III**
Sponsor	Pfizer Ltd, Eli Lilly & Co
Status	Ongoing
Source of Information	Trial registry[6]
Location	5 EU countries (not UK), USA, Canada, Japan, and South Korea
Design	Randomised, placebo-controlled and active-controlled
Participants	n=1,816; aged ≥ 18 yrs; CLBP ≥3 mths in duration; Quebec Task Force in Spinal Disorders class 1 or 2, with documented history of previous inadequate treatment response to at least 3 different categories of agents commonly used and generally considered effective for the treatment of CLBP.
Schedule	Randomised to placebo SC injection every 8 wks for 2 injections followed by tanezumab 5mg injection every 8 wks for 5 injections; placebo SC injection every 8 wks for 2 injections, followed by tanezumab 10mg SC injection for 5 injections; tanezumab 5mg SC injection seven times at 8 wk intervals (56 wks); tanezumab 10mg SC injection seven times at 8 wk intervals (56 wks); tramadol PR oral
Follow-up	Active treatment for 56 wks, follow-up for24 wks
Primary Outcomes	Change from baseline in daily average LBPI score (tanezumab vs placebo)[Time frame: wk 16]

Secondary Outcomes	wks 2, 4, 8, 12 and 16: - Usage of rescue medication wks 2, 4, 8, 16, 24, 32, 40, 48, 56, and 64: - Patient's global assessment of low back pain (not wk 56) - Change from baseline in the Brief Pain Inventory short form - CLBP Responder Index (not wk 64) wks 2, 4, 8, 12, 16, 24, 32, 40, 48, 56 and 64: - Change from baseline in daily average LBPI score (not wk 16) - Pain intensity response wks 2, 4, 8, 16, 24, 32, 40, 48, 56, 64 and 80: - Change from baseline to wks 2, 4, 8, 16 (for tanezumab vs tramadol) 24, 32, 40, 48, 56, 64 and 80 in RMDQ total score - RMDQ response wks 8, 16, 24, 40, 56, and 64: - Euro Quality of Life Health State Profile (EQ 5D 5L) wk 16: - Change from baseline to wk 16 in the RMDQ for tanezumab vs placebo Change from baseline in the daily average LBPI score wks 16 and 56: - Treatment satisfaction questionnaire for medication - Patient reported treatment impact assessment modified wks 16, 24 and 56: - Cumulative distribution of % change from baseline in RMDQ score - Cumulative distribution of % change in from baseline in average LBPI score • Work Productivity and Activity Impairment Questionnaire: Low Back Pain [Time frame: wks 16, 56, or 64] • Discontinuation due to lack of efficacy [Time frame: up to wk 56] • Health care resource utilization [Time frame: baseline, wks 64 and 80]
Key Results	-
Adverse effects (AEs)	-
Expected reporting date	Study completion date reported as Jan 2019

ESTIMATED COST

The cost of tanezumab is not yet known.

ADDITIONAL INFORMATION

RELEVANT GUIDANCE

NICE GUIDANCE

- NICE clinical guideline. Neuropathic pain in adults: pharmacological management in non-specialist settings (CG173). Updated April 2018
- NICE clinical guideline. Osteoarthritis: care and management (CG177). February 2014
- NICE guideline in development. Chronic pain: assessment and management (GID-NG10069). Publication expected August 2020
- NICE guidelines. Low back pain and sciatica in over 16s: assessment and management (NC59). November 2016
- NICE quality standard in development. Pain management (young people and adults) (GID-QS10093). Publication date TBC
- NICE quality standard. Low back pain and sciatica in over 16s (QS155). July 2017
- NICE quality standard. Osteoarthritis (QS87). June 2015
- NICE interventional procedure guidance. Lateral interbody fusion in the lumbar spine for low back pain (IPG574). February 2017
- NICE interventional procedure guidance. Percutaneous coblation of the intervertebral disc for low back pain and sciatica (IPG543). January 2016
- NICE interventional procedures guidance. Peripheral nerve-field stimulation for chronic low back pain (IPG451). March 2013
- NICE interventional procedures guidance. Deep brain stimulation for refractory chronic pain syndromes (excluding headache) (IPG382). March 2011

NHS ENGLAND (POLICY/COMMISSIONING) GUIDANCE

- NHS England. 2013 NHS Standard Contract for Specialised Pain. D08/S/a

OTHER GUIDANCE

- Scottish Intercollegiate Guidelines Network. Management of chronic pain.[49]

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