

Combination analgesics

The annual spend on combination analgesics across England, Wales and Scotland is approximately £104 million [NHSBSA (Nov22-Jan23) and Public Health Scotland (Oct-Dec 22)]. This bulletin reviews the use of combination analgesic preparations and recommendations for self care where appropriate. Combinations of paracetamol and tramadol are not considered in this bulletin. Please refer to [PrescQIPP Bulletin 208: Paracetamol and tramadol combination products](#).

Recommendations

- Combination analgesics should not be a first-line treatment choice. The use of single-ingredient analgesics is preferred to allow for independent titration of each drug.
- When assessing pain, determine whether there is a need for a non-opioid and an opioid analgesic to be taken simultaneously. Ensure that an adequate dose of each analgesic is used.
- Be aware that the advantages of lower doses of codeine 8mg or 15mg have not been substantiated. The low dose of the opioid may be enough to cause opioid side-effects (in particular, constipation) and can complicate the treatment of overdose, yet may not provide significant additional relief from pain.
- Combination analgesics (except those with low-dose opioids, e.g. co-codamol 8mg/500mg, co-dydramol 10mg/500mg) may be considered for those with stable chronic pain and for people taking a lot of tablets to reduce the number of tablets taken.
- Do not initiate co-proxamol for any new patient.
- Review all patients still being prescribed co-proxamol to assess their pain management and switch them to an alternative pain management regime (either drug or non-drug treatment) for safety concerns, particularly toxicity in overdose.
- Non-pharmacological measures and/or paracetamol or non-steroidal anti-inflammatory drugs (NSAIDs) are preferred options for mild secondary chronic pain, for example in endometriosis, headaches, irritable bowel syndrome, low back pain and sciatica, neuropathic pain, osteoarthritis (OA), rheumatoid arthritis and spondyloarthritis.
- Be aware that headaches, period pain, mild fever and back pain can be treated at home with over the counter (OTC) pain relief and lifestyle changes; note that quantities for purchase may be restricted e.g. to a three day supply. Refer to the [PrescQIPP bulletin: Self care – Over the counter items](#).

Introduction

It is recognised that chronic pain is complex, with challenges for assessment and management.¹⁻³ Combination analgesic preparations contain a simple analgesic, for example paracetamol with an opioid or NSAID in one single preparation.⁴

The formulation, licensed indication, and which medicines are included in combination analgesics are tabulated in Table 1.

Table 1: Combination analgesics⁴

Combination	Formulations	Licensed Indication	Paracetamol	Codeine	Aspirin	Dihydrocodeine	Dextropropoxyphene	Ibuprofen
Co-codamol 8mg/500mg	Tablets, capsules, effervescent tablets	Moderate pain	500mg	8mg				
Co-codamol 12.8mg/500mg	Tablets	Moderate pain	500mg	12.8mg				
Co-codamol 15mg/500mg	Tablets, capsules, effervescent tablets	Moderate pain	500mg	15mg				
Co-codamol 30mg/500mg	Tablets, capsules, caplets, effervescent tablets, oral solution	Moderate to severe pain	500mg	30mg				
Co-dydramol	Tablets	Mild to moderate pain 10mg/500mg Severe pain 20mg/500mg, 30mg/500mg	500mg 500mg 500mg			10mg 20mg 30mg		
Co-proxamol	Tablets	Unlicensed use for pain relief only for patients who find it difficult to change, because alternatives are not effective or suitable.	325mg				32.5mg	
Paracetamol and ibuprofen	Tablets	Temporary relief of mild to moderate pain which has not been relieved by ibuprofen or paracetamol individually such as migraine, headache, backache, period pain, dental pain, rheumatic and muscular pain, cold and flu symptoms, sore throat and fever. ⁵	500mg					200mg
Codeine and ibuprofen	Tablets	Short term treatment of acute moderate pain in patients over 12 years of age which is not considered to be relieved by other analgesics (e.g. paracetamol, ibuprofen or aspirin) alone, such as: rheumatic and muscular pain, backache, neuralgia, migraine, headache, dental pain, dysmenorrhoea. ⁶		12.8mg				200mg

Individual responses to analgesia vary considerably, both in terms of efficacy and side-effects; even with the same chronic pain syndrome, the underlying pain mechanisms may differ between individuals. This provides challenges with assessment and management in routine clinical practice. National guidance does advise that if an individual either fails to tolerate, or has an inadequate response to a drug, then it is worthwhile considering a different agent from the same class.¹⁻⁴ There is also increasing evidence that variations in drug responses are linked to genetic factors (e.g. opioids).² When assessing pain, it is necessary to weigh up carefully whether there is a need for a non-opioid and an opioid analgesic to be taken simultaneously. An adequate dose of each analgesic should be used.⁴

Combination analgesics reduce the scope for effective titration of the individual components in the management of pain of varying intensity.⁴ They should be avoided as a first-line treatment choice.⁷ The BNF states that compound analgesic preparations containing paracetamol or aspirin with a low dose of an opioid analgesic (e.g. 8mg of codeine per combination tablet) are commonly used, but the advantages have not been substantiated. The low dose of the opioid may be enough to cause opioid side-effects (in particular, constipation) and can complicate the treatment of overdose yet may not provide significant additional relief of pain.⁴

A full dose of the opioid component (e.g. 60mg codeine in compound analgesic preparations effectively augments the analgesic activity but is associated with the full range of opioid side-effects (including nausea, vomiting, severe constipation, drowsiness, respiratory depression, and risk of dependence on long-term administration). The elderly, are particularly susceptible to opioid side-effects and should receive lower doses.⁴ Further resources for patients and healthcare professionals to support prescribing of opioid medicines for pain are available from [Opioids Aware](#). Fixed dose combination analgesics (except those with low-dose opioids), may be considered for those with stable chronic pain and for people taking a lot of tablets (to reduce the number of tablets taken).⁷ The BNF classifies co-codamol and co-dydramol as less suitable for prescribing.⁴

Caffeine is often included, in small doses, in analgesic preparations. It is claimed that the addition of caffeine may enhance the analgesic effect, but the alerting effect, mild habit-forming effect and possible provocation of headache may not always be desirable. Moreover, in excessive dosage or on withdrawal, caffeine may itself induce headache.⁴

Many combination analgesics (with low dose opioids) are available OTC for people to self-care (e.g. for minor conditions associated with pain, headache, migraine, period pain or back ache).⁸

Evidence

Systematic reviews report a synergistic analgesic effect and better safety profile of combined analgesics; this is associated with no increase in adverse effects due to the initial lower doses of individual analgesics.^{9,10,11} However, a Cochrane review about the analgesic efficacy of single dose oral analgesics adds that information about analgesics with inadequate data or where trial results are unreliable due to susceptibility to publication bias, should inform clinician and patient choice.¹²

Codeine combination preparations

Codeine or 3-methylmorphine is a mild opioid with analgesic and antitussive effect. Its analgesic activity is mostly due to activity as a pro-drug and around 10% is converted to morphine by the cytochrome P450 enzyme CYP2D6. Poor metabolisers, with one or two non-functional alleles are present in 7–10% of the white population and may have decreased metabolism of codeine to morphine, and lower possibility for the analgesic effect in comparison to normal (extensive metabolisers). Ultrarapid metabolism is considered to occur in 1–7% of the white population, whereas the incidence is 5–10% and 3% for Southern and Northern Europeans, respectively. As a result, in patients with more than two copies of the CYP2D6 functional allele, there is increased formation of morphine and a higher potential for experiencing adverse effects (such as sleepiness, confusion, and shallow breathing), even at recommended doses of codeine.¹⁰

Doses of codeine in combinations with other drugs vary significantly, from 8mg up to 60mg; although

of note is that the vast majority of studies investigated the effects of higher dose codeine ($\geq 30\text{mg}$) combinations.¹⁰

Sixteen placebo-controlled studies that involved 3378 subjects suffering from acute pain were analysed for the efficacy of low-dose codeine ($\leq 30\text{mg}$) combination products. Twelve of them found low-dose codeine combinations more efficient in relieving pain than the assigned comparator. According to 20 randomised clinical trials which included at least one dose of codeine (from 30mg to 240mg daily), the vast majority of reported side-effects were mild or moderate in severity. There was no indication in the available sources which clearly linked low doses of codeine to substance use disorder in non-dependent subjects.¹⁰

A systematic review and meta-analysis of ten RCTs demonstrated that there is low to moderate level evidence that combination analgesic products containing low-dose codeine provide small to moderate pain relief for acute and chronic pain conditions in the immediate short term with limited trial data on use beyond 24 hours. Further research examining regular use of these medicines is needed with more emphasis on measuring potential harmful effects.¹¹

Co-proxamol

Co-proxamol tablets (dextropropoxyphene 32.5mg, a weak opioid in combination with paracetamol 325mg) are no longer licensed because of safety concerns, particularly toxicity in overdose.^{4,13} Co-proxamol was withdrawn from the UK market by the end of 2007, after an initial phased withdrawal over two years.¹⁴ US clinical data from 2010 showed that dextropropoxyphene results in prolongation of P-R and Q-T intervals, and widened QRS complexes, even at normal therapeutic doses.¹⁴ The risk of death after co-proxamol overdose is 2.3 times that for tricyclic antidepressants and 28.1 times that for paracetamol.¹⁵ It is estimated that the withdrawal of co-proxamol from the UK has saved around 300 to 400 lives each year from self-poisoning, around a fifth of which were accidental.¹⁴ Refer to [Questions and answers on the withdrawal of the marketing authorisations for medicines containing dextropropoxyphene](#).

The available evidence suggests that the combination of dextropropoxyphene and paracetamol is no more effective than paracetamol on its own, or ibuprofen for short term pain. For long term pain there is no evidence that the combination of dextropropoxyphene and paracetamol is more effective than alternative pain killers. From a safety perspective, dextropropoxyphene has a narrow therapeutic index meaning that the dose needed to treat the patient and the dose that could harm the patient is small. Many cases of fatal overdose were accidental. It is important that patients receive adequate pain relief and it is necessary for people currently taking dextropropoxyphene containing medicines be transferred to alternative treatments.¹⁶ Be aware that the frail elderly are more susceptible to the side-effects of opioids.⁴

All use of co-proxamol in the UK is now on an unlicensed basis and should only be prescribed for mild to moderate pain in existing patients who find it difficult to change because alternatives are not effective or suitable.⁴ Whilst the demand for co-proxamol has decreased, the medicine costs have increased [NHSBSA Nov 22-Jan23]. The price increase is due to co-proxamol now only being available as a "special" product which is included in Part VIID Drug Tariff Special Order products. It costs £217.26 for 100 tablets.¹³ This does not represent good value for money for the NHS compared to alternative analgesics. If the clinician does decide to continue prescribing of co-proxamol, the GMC guidance around prescribing unlicensed medicines should be followed.¹⁷

Co-proxamol is an item which NHS England recommends should not routinely be prescribed in primary care, as it is poor value for money and has limited clinical value with safer treatment alternatives available. Updated guidance is expected soon. The current guidance advises the former Clinical Commissioning Groups (CCGs):¹⁸

- That prescribers in primary care should not initiate co-proxamol for any new patient.
- To support prescribers in deprescribing co-proxamol in all patients and, where appropriate, ensure the availability of relevant services to facilitate this change.

Alternatives to co-proxamol

Review all patients still being prescribed co-proxamol with a view to assess their pain management and switch them to an alternative pain management regime (either drug or non-drug treatment) for safety concerns, particularly toxicity in overdose. Some alternatives to support deprescribing co-proxamol include:

- Review whether analgesia is still needed for the original painful condition in discussion with the individual. If no longer needed for the original condition, deprescribe. Follow usual pain pathways for any new painful condition identified.
- Ensure that patients have a wider pain management strategy in place that includes non-pharmacological measures.

If an analgesic is still needed, consider:

- A change to paracetamol 500mg tablets or capsules at a dose of 1g four times a day. The paracetamol dosing should be adjusted appropriately in patients weighing less than 50 kg, or with other risk factors for hepatotoxicity such as acute malnutrition, or for those taking medicines that may affect liver function.⁴
- If regular dosing paracetamol on its own is ineffective, the addition of codeine phosphate using a 'when required' dose might be beneficial. For codeine phosphate, the BNF recommends a dose of 30-60mg every four hours, when necessary, to a maximum of 240mg daily for mild to moderate pain. This dose will need to be reduced in patients with hepatic or renal impairment. A full dose of codeine (e.g. 60mg) will cause severe constipation and a laxative should be co-prescribed if taken regularly long term.⁴
- Another compound analgesic, if safe and appropriate to do so e.g. co-codamol 30mg/500mg tablets or co-dydramol 10mg/500mg tablets.

Ibuprofen and Paracetamol

The National Institute for Health and Care Excellence (NICE) guidance for OA advises to not routinely offer paracetamol or weak opioids unless:

- They are only used infrequently for short-term pain relief and
- All other pharmacological treatments are contraindicated, not tolerated or ineffective.¹⁹ Refer to table 2, summary of relevant NICE recommendations, for further details.

A Cochrane review assessed the efficacy of single-dose paracetamol plus ibuprofen in a variety of dose combinations after wisdom tooth removal. The authors concluded that paracetamol/ibuprofen combinations provide better analgesia than the same dose of either drug alone, with fewer patients on the combination requiring rescue analgesia or experiencing an adverse event.²⁰

The All Wales Medicines Strategy Group advises that the combination of paracetamol 1000mg to 4000mg daily plus ibuprofen 400mg has been shown to be significantly superior to paracetamol alone in patients with hip or knee OA but is associated with a higher risk of gastrointestinal bleeding.³

National Guidance

The NICE Clinical Knowledge Summaries (CKS) on analgesia - mild-to-moderate pain recommends avoiding combination analgesics as first-line treatment. The CKS recommends to:

- Prescribe single-constituent analgesics to allow independent titration of each drug, taking into account local prescribing guidelines.
- Be aware that fixed-dose combination analgesics containing low doses of opioids (such as codeine 8mg plus paracetamol 500mg or dihydrocodeine 10mg plus paracetamol 500mg) are no more effective than paracetamol alone and can cause opioid adverse effects such as constipation.
- Consider fixed-dose combination analgesics (except those with low-doses of opioids) for people with chronic, stable pain and for people taking a lot of tablets (to reduce the number of tablets taken).⁷

Table 2 provides a summary of relevant NICE guideline recommendations on pharmacological, non-pharmacological and 'do not do' recommendations.

Table 2: Summary of relevant NICE recommendations

Low back pain and sciatica [NG59] ²¹			
Do not do recommendations	Non-pharmacological options	First choice medications	Alternative options
<p>Do not offer paracetamol alone for managing low back pain.</p> <p>Do not routinely offer opioids for managing acute low back pain.</p> <p>Do not offer opioids for managing chronic low back pain.</p> <p>Do not offer opioids for managing chronic sciatica.</p>	<p>Provide information on the nature of low back pain and sciatica and encouragement to continue with normal activities.</p> <p>Consider a group exercise programme (biomechanical, aerobic, mind–body or a combination of approaches) within the NHS for people with a specific episode or flare-up of low back pain with or without sciatica. Take people's specific needs, preferences and capabilities into account when choosing the type of exercise.</p> <p>Consider manual therapy (spinal manipulation, mobilisation or soft tissue techniques such as massage) for managing low back pain with or without sciatica, but only as part of a treatment package including exercise, with or without psychological therapy.</p> <p>Consider a combined physical and psychological programme, incorporating a cognitive behavioural approach (preferably in a group context that takes into account a person's specific needs and capabilities), for people with persistent low back pain or sciatica: when they have significant psychosocial obstacles to recovery (for example, avoiding normal activities based on inappropriate beliefs about their condition) or when previous treatments have not been effective.</p>	<p>Consider oral NSAIDs for managing low back pain, taking into account potential differences in gastrointestinal, liver and cardio-renal toxicity, and the person's risk factors, including age.</p> <p>When prescribing oral NSAIDs for low back pain, consider appropriate clinical assessment, ongoing monitoring of risk factors, and the use of gastroprotective treatment.</p> <p>Prescribe oral NSAIDs for low back pain at the lowest effective dose for the shortest possible period of time.</p> <p>Be aware of the risk of harms and limited evidence of benefit from the use of NSAIDs in sciatica. If prescribing NSAIDs for sciatica, the same considerations apply as for low back pain.</p>	<p>Consider weak opioids (with or without paracetamol) for managing acute low back pain only if an NSAID is contraindicated, not tolerated or has been ineffective.</p>

Osteoarthritis [NG226] ¹⁹			
Do not do recommendations	Non-pharmacological options	First choice medications	Alternative options
<p>Do not routinely offer paracetamol or weak opioids unless:</p> <ul style="list-style-type: none"> • They are only used infrequently for short-term pain relief and • All other pharmacological treatments are contraindicated, not tolerated or ineffective. <p>Do not offer strong opioids to people to manage OA.</p> <p>Do not routinely offer insoles, braces, tape, splints or supports.</p> <p>Do not offer transcutaneous electrical nerve stimulation (TENS).</p>	<p>Explain to people with OA how it is diagnosed, managed and the core treatments, along with information and support.</p> <p>Activity and exercise (e.g. local muscle strengthening, general aerobic fitness).</p> <p>Interventions to achieve weight loss if the person is overweight or obese.</p> <p>Consider walking aids for people with lower limb OA.</p> <p>Only offer insoles, braces, tape, splints or supports to people with OA if there is joint instability or abnormal biomechanical loading and therapeutic exercise is ineffective or unsuitable without the use of an aid or device and the addition is likely to improve movement and function.</p> <p>Only consider manual therapy (such as manipulation, mobilisation or soft tissue techniques):</p> <ul style="list-style-type: none"> • For people with hip or knee OA and • Alongside therapeutic exercise. 	<p>Offer a topical NSAID to people with knee OA.</p> <p>Consider a topical NSAID for people with OA that affects other joints.</p> <p>If topical medicines are ineffective or unsuitable, consider an oral NSAID for people with OA and take account of:</p> <ul style="list-style-type: none"> • Potential gastrointestinal, renal, liver and cardiovascular toxicity • Any risk factors the person may have, including age, pregnancy, current medication and comorbidities. <p>Offer a gastroprotective treatment (such as a proton pump inhibitor) for people with OA while they are taking an NSAID.</p>	<p>If oral or topical NSAIDs are insufficient for pain relief, not tolerated or ineffective, then the use of paracetamol or weak opioid analgesics should be considered for infrequent, short term pain relief. Risks and benefits should be considered, particularly in older people.</p> <p>Intra-articular corticosteroid injections should be considered when other pharmacological treatments are ineffective or unsuitable, or to support therapeutic exercise. It must be explained that these only provide short term relief (two to ten weeks).</p>

Headaches [CG150] ²²			
Do not do recommendation	Non-pharmacological options	First choice medications	Alternative options
Tension headache Do not offer opioids for the acute treatment of tension-type headache.		Aspirin (not if under 16), paracetamol or an NSAID	
Migraine Do not offer an ergot or an opioid for the acute treatment of migraine.		Offer combination therapy with an oral triptan and an NSAID, or an oral triptan and paracetamol, for the acute treatment of migraine, taking into account the person's preference, comorbidities and risk of adverse events.	For people who prefer to take only one drug, consider monotherapy with an oral triptan, NSAID, aspirin (900mg) or paracetamol for the acute treatment of migraine, taking into account the person's preference, comorbidities and risk of adverse events. For people in whom oral preparations (or nasal preparations in young people aged 12 to 17 years) for the acute treatment of migraine are ineffective or not tolerated: Consider a non-oral preparation of metoclopramide or prochlorperazine and If non-oral metoclopramide or prochlorperazine is used, consider adding a non-oral NSAID or triptan if they have not been tried.
Cluster headache Do not offer paracetamol, NSAIDs, opioids, ergots or oral triptans for the acute treatment of cluster headache.		Oxygen and/or a subcutaneous or nasal triptan	
Medication overuse headache	Advise people to stop taking all overused acute headache medications (including combination analgesics) for at least one month and to stop abruptly rather than gradually.		

England

NHS England has published guidance on 35 conditions for which over the counter items which should not routinely be prescribed in primary care. The guidance highlights products that are regarded as low priority for funding, poor value for money or for which there are safer alternatives. Self-care for minor illnesses is recommended as the first stage of treatment. It is envisaged that in most cases (unless specified), these minor conditions will clear up with appropriate self-care. If symptoms are not improving or responding to treatment, then patients should be encouraged to seek further advice.²³

The guidance states that patients should be encouraged to self-care for minor conditions associated with pain, headache, migraine, period pain or back pain.²³ A list of OTC preparations can be found in Table 3.

Also refer to the [PrescQIPP bulletin on Self care and over the counter items: A quick reference guide](#).⁸

Scotland

The Scottish Intercollegiate Guidance Network (SIGN) 136 on the management of chronic pain makes no specific recommendations on combination analgesics prescribed as a single product. However, paracetamol either alone or in combination with an NSAID is recommended in the management of pain in people with hip or knee OA in addition to non-pharmacological treatments.²

Wales

The All Wales Medicines Strategy Group advises on the combination of ibuprofen and paracetamol; stating that the combination of paracetamol 1000mg to 4000mg daily plus ibuprofen 400mg has been shown to be significantly superior to paracetamol alone in patients with hip or knee OA but is associated with a higher risk of gastrointestinal bleeding.³

Good practice: combination analgesics

- The use of single-ingredient analgesics is preferred to allow for independent titration of each drug.⁷ Refer to [PrescQIPP Bulletin 284 Chronic pain attachment 1](#) for up titration of opioids, non-opioids or NSAIDs.²⁴
- Trial treatment with opioids if extra pain relief is needed.^{2,3,24}
- If treatment goals are not met (e.g. at least 30% improvement in pain or other pre-agreed objective), or there is no clear evidence of response, stop treatment.²⁵
- Use of combination analgesics (except those with low-doses of opioids) should be limited to people with chronic, stable pain and for people taking multiple tablets (to reduce the number of tablets taken and aid adherence).⁷
- Recommend appropriate use of low dose opioids (OTC analgesics) for self-care for pain, headaches, migraine, period pain or back pain.⁸ Also, refer to Table 3 for OTC low dose preparations.
- Issue combination analgesics on acute prescriptions to ensure there are agreed regular reviews for continued use.
- Use [shared decision-making](#) with the person²⁶ to review the efficacy of all analgesics after an initial trial at the optimum dose, usually after two weeks, using the narrative clinical history, and a visual analogue scale or numerical scores. e.g. [Pain Assessment and Documentation tool \(PADT\)](#) or [British Pain Society \(BPS\) pain scales](#).²⁴
- The person and prescriber should agree readily assessable outcomes with combination analgesics, e.g. reduction in pain intensity and ability to achieve specific functional improvement/improvement in sleep or mood.

- Discuss potential harms of opioid therapy if the combination analgesics prescribed contains an opioid.²⁴ Attachment 2 may be used to discuss these with the patient.
- Refer to the Live Well with Pain leaflets [Take the 'temperature' of your opioid painkillers](#) and [The Great Opioid Side Effect Lottery](#) to highlight the adverse effects that opioids can cause.
- Treat the underlying cause of pain where possible.⁷
- Be aware that treatment of moderate or severe depression (where present) may reduce pain.²
- Consider early referral to specialist pain management services, where pain is severe, not responding adequately to management, or for specific specialist assessment and/or treatments.²
- Offer non-pharmacological and pharmacological options. For chronic pain encourage physical exercise, consider manual therapy including physiotherapy, acupuncture, acceptance and commitment therapy (ACT) or cognitive behavioural therapy (CBT).²⁴ Further information on self-management of chronic pain can be found in attachment 3.

Refer also to the following bulletins which include guidance on chronic pain opioid initiation, withdrawal and stopping therapy:

- Bulletin 218 Reducing opioid prescribing in chronic pain <https://www.prescqipp.info/our-resources/bulletins/bulletin-218-reducing-opioid-prescribing-in-chronic-pain>
- Bulletin 284 Chronic pain <https://www.prescqipp.info/our-resources/bulletins/bulletin-284-chronic-pain/>
- Bulletin 208 Paracetamol and tramadol preparations <https://www.prescqipp.info/our-resources/bulletins/bulletin-208-paracetamol-and-tramadol-combination-products/>

Costs and Savings

Table 3 provides information on example OTC brands, pack sizes, costs, cost per 28 days at maximum dose and the dosage in adults for codeine, dihydrocodeine and paracetamol as single ingredient drugs and combination analgesic presentations.¹³

Table 3: Cost of analgesic combinations¹³

Drug	Quantity	Cost ^{13,27}	Cost/28 days at maximum dose ¹³	Dosage in adults ⁴	OTC Brand available/ex-amples
Codeine 8mg + Paracetamol 500mg					
Co-codamol 8mg/500mg tablets	30	£1.11	£8.29	8mg/500mg to 16mg/1000mg every four to six hours as required; maximum 64mg/4000mg per day	Migravele Yellow® tablets
	100	£3.70			
Co-codamol 8mg/500mg capsules	32	£8.89	£62.23		Not available
	100	£27.78			
Co-codamol 8mg/500mg effervescent tablets	32	£2.93	£20.52		
	100	£9.16			
Codeine 12.8mg + Paracetamol 500mg					
Co-codamol 12.8mg/500mg tablets	20	£4.20	£40.02 - £47.04	12.8mg/500mg to 25.6/1000mg every four to six hours as required; maximum 102.4mg/4000mg per day	Solpadeine Max® tablets
	30	£5.36			

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Drug	Quantity	Cost ^{13,27}	Cost/28 days at maximum dose ¹³	Dosage in adults ⁴	OTC Brand available/ex-amples
Codeine 15mg + Paracetamol 500mg					
Co-codamol 15mg/500mg capsules	100	£7.25	£16.24	15mg/500mg to 30mg/1000mg every four to six hours as required; maximum 120mg/4000mg per day	Not available
Co-codamol 15mg/500mg tablets	100	£2.81	£6.29		
Co-codamol 15mg/500mg effervescent tablets sugar free	100	£8.25 - £13.00	£18.48 - £29.12		
Codeine 30mg + Paracetamol 500mg					
Co-codamol 30mg/500mg capsules	100	£3.97	£8.96	30/500mg to 60/1000mg every four to six hours as required; maximum 240/4000mg per day	Not available
Co-codamol 30mg/500mg effervescent tablets	32	£3.04	£21.28		Not available
	100	£9.50			
Co-codamol 30mg/500mg tablets	30	£1.21	£9.03		Not available
	100	£4.03			
Co-codamol 30mg/500mg/5ml solution sugar free	150ml	£11.99	£89.53	Not available	
Dihydrocodeine 10mg + Paracetamol 500mg					
Co-dydramol 10mg/500mg tablets	30	£2.72	£20.31	10/500mg to 20/1000mg every four to six hours as required; maximum 80/4000mg per day	Paramol® tablets 7.46mg/500mg
	100	£9.07			
Dihydrocodeine 20mg + Paracetamol 500mg					
Co-dydramol 20mg/500mg tablets	56	£5.87	£22.26 - £23.48	20/500mg to 40/1000mg every four to six hours as required; maximum 160/4000mg per day	Not available
	112	£11.13			
Dihydrocodeine 30mg + Paracetamol 500mg					
Co-dydramol 30mg/500mg tablets	56	£6.82	£27.28	30/500 to 60/1000mg every four to six hours as required; maximum 240/4000mg per day	Not available
Ibuprofen 200mg + Codeine 12.8mg					
Ibuprofen and codeine 200mg/12.8mg tablets	24	£5.49	£35.65 - £38.43	12.8mg/200mg to 25.6mg/400mg every four to six hours as required; maximum six tablets in 24 hours ⁶	Nurofen® Plus tablets
	32	£6.79			
Paracetamol 500mg + Ibuprofen 200mg					
Paracetamol + ibuprofen 500mg/200mg tablets	12	£2.58	£36.12	500mg/200mg to1000/400mg tablets up to three times a day; no more than six tablets in 24 hours ⁵	Nuromol® Dual Action Pain Relief

Charts 1 and 2 Illustrates the cost of combination analgesics, paracetamol, ibuprofen and codeine per 28 days at maximum licensed dose in England, Wales, Northern Ireland and Scotland.^{4,13,28}

324. Combination pain relief 2.0

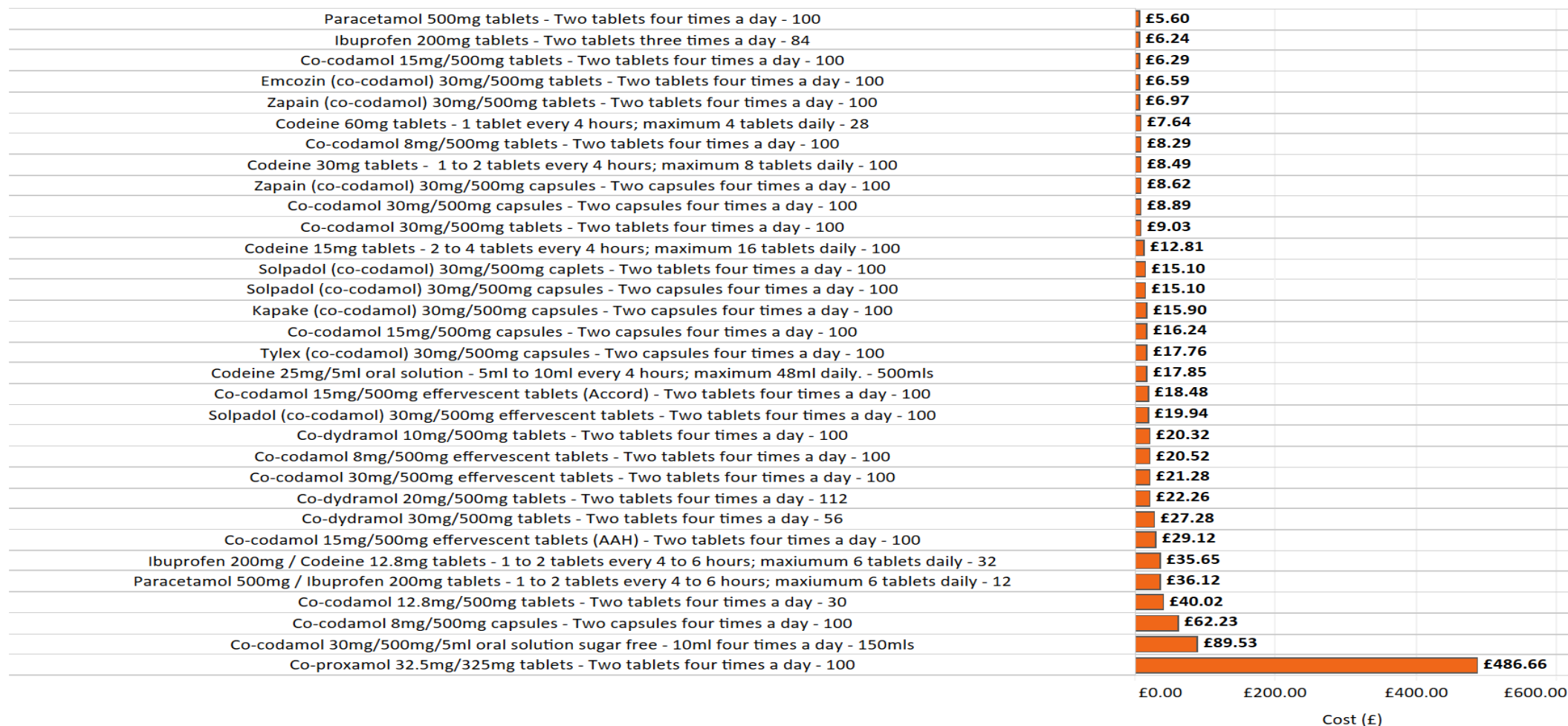
Chart 1: Cost per 28 days at maximum licensed dose of combination analgesic, England, Wales & Northern Ireland^{4,13,27}



Select Area Required:
CNS- Combination analgesics

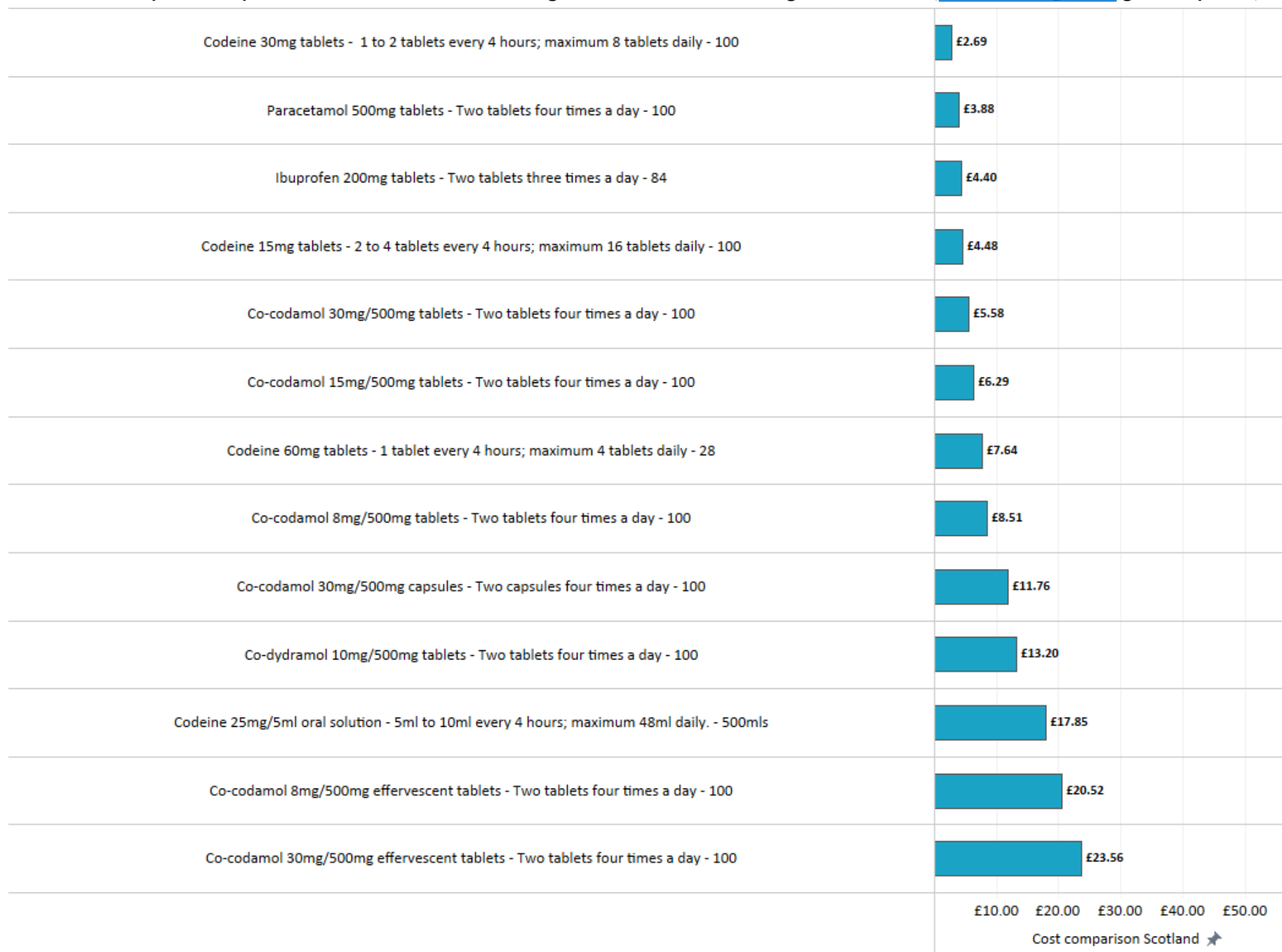
Select Country:
England, Wales & Northern Ireland

CNS- Combination analgesics - Cost per 28 days



324. Combination pain relief 2.0

Chart 2: Cost per 28 days at maximum licensed dose of generic combination analgesic, Scotland ([Scottish Drug Tariff](#) generic prices)^{4,13,28}



Savings

Potential savings can be achieved through:

- Reducing combination analgesic prescribing.
- Switching co-codamol capsules (8mg/500mg, 15mg/500mg, 30mg/500mg) to tablets.
- Limiting co-codamol effervescent tablets prescribing to patients with swallowing difficulties only.
- Deprescribing co-proxamol tablets.
- Reducing the prescribing of combination analgesics which are available to purchase OTC in packs of 32 or less (refer to table 3).

Table 4 provides data on potential savings on combination analgesic prescribing across England, Wales and Scotland.

Table 4: Combination analgesics potential annual savings for England, Wales and Scotland and per 100,000 population [NHSBSA (Nov 22-Jan 23) and Public Health Scotland (Oct-Dec 22)]

Combination analgesic saving	England savings	Wales savings	Scotland savings	Annual savings per 100,000
10% reduction in prescribing of combination analgesics (not included below)	£5,950,525	£645,002	£1,359,099	£11,139
80% switch co-codamol (8mg/500mg, 15mg/500mg, 30mg/500mg) capsules to tablets	£6,380,779	£670,527	£963,773	£11,223
25% switch of co-codamol effervescent tablets to co-codamol plain tablets	£4,710,531	£293,367	£579,833	£7,819
50% reduction in co-proxamol tablets	£786,904	£13,061	Data not available	£1,120
Total	£17,828,739	£1,621,957	£2,902,705	£31,301

Summary

Combination analgesics should not be a first-line treatment choice as the use of single-ingredient analgesics is preferred to allow for independent titration of each drug. Combination analgesics (except those with low-dose opioids, e.g. co-codamol 8mg/500mg, co-dydramol 10mg/500mg) may be considered for those with stable chronic pain and for people taking a lot of tablets to reduce the number of tablets taken. Regular review, short term use and [shared decision-making](#)²⁶ must form part of the prescribing process.

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Additional PrescQIPP resources

Briefing	https://www.prescqipp.info/our-resources/bulletins/bulletin-324-combination-analgesics/
Implementation tools	
Data pack	https://data.prescqipp.info/?pdata.u/#/views/B324_Prescribingofcombination-analgesics/FrontPage?iid=1

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