7 July 2003

000001
Dr Sam Sample
99 Sample Street
SAMPLETOWN NSW 0000

Dear Dr Sample

No. 22
Analgesics in musculoskeletal pain

It can be sometimes quite challenging balancing the need for adequate analgesia for patients in pain with the goal of using analgesic drugs safely without causing adverse effects.

Assess and document characteristics of pain

GPs are good at focusing on the individual before them. As pain is always subjective, pain assessment and analgesic control requires the patient's input. This individualised approach can help the patient understand what causes their pain and assist in monitoring the effectiveness of therapy.

Use paracetamol first: it is effective and has a good safety profile

Paracetamol is often given at insufficient doses, leading to perceptions that it is ineffective. However, when taken regularly *and* in appropriate doses, paracetamol is an effective analgesic for a wide range of painful conditions.

Consider the range of adverse effects and serious drug interactions with tramadol

While opioid adverse effects are familiar, the adverse effect and drug interaction profile of tramadol is perhaps less well-known to prescribers. It can cause common adverse effects like nausea but also serious reactions such as seizures and serotonin syndrome. Furthermore, tramadol interacts with a number of drugs, many of which are used to treat different types of pain.

Before prescribing COX-2 selective or conventional NSAIDs, review risk of peptic ulcer, cardiac disease or renal impairment

For patients in whom you would not otherwise use an NSAID, a COX-2 selective NSAID may be equally inappropriate. All NSAIDs should be used with caution in patients with renal or cardiac problems and should be avoided in patients with active peptic ulcer disease.

NPS has again arranged for your prescribing data from the HIC database to be extracted confidentially and accompany this *PPR*. We anticipate this snapshot of your recent prescribing patterns will assist you to consider our evidence-based messages regarding analgesic use.

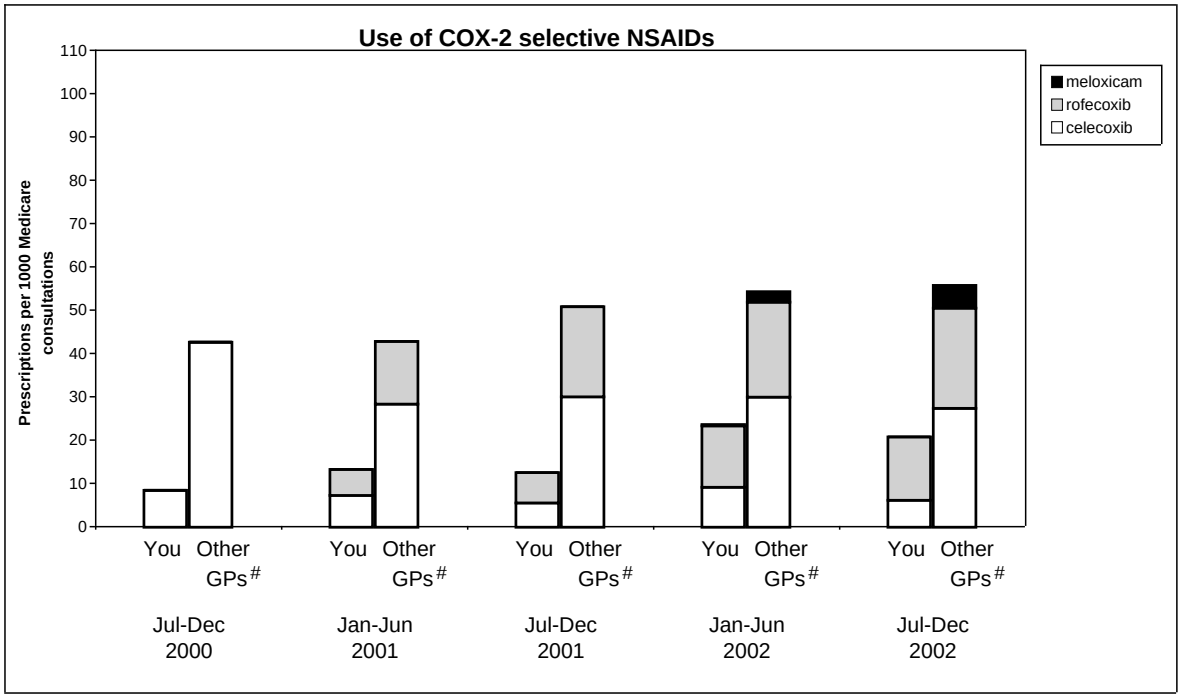
Finally, this *PPR* contains an invitation to enrol in the NPS clinical audit, *Analgesics in musculoskeletal pain*, providing an opportunity to review your approach to prescribing analgesics.

Yours sincerely,

Dr Stephen Phillips
Chair, NPS Board

005080 - V4

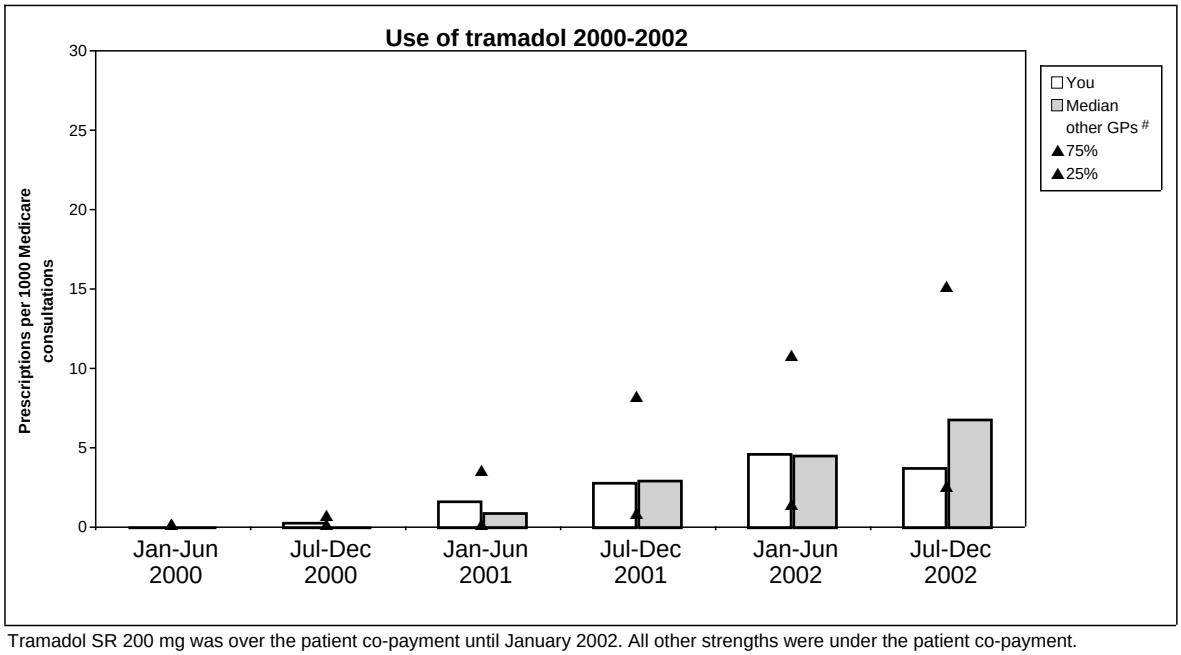
Your confidential prescribing data



Your prescribing of COX-2 selective NSAIDs and meloxicam (which is COX-2 selective only at lower doses) and the median for other GPs[#] in a similar region.
All COX-2 selective NSAIDS were over the patient co-payment in this period.

Practice Points

- Has your prescribing changed now that the benefits and harms of the COX-2 selective NSAIDs are clearer?
- Are you prescribing COX-2 selective NSAIDs only in those patients most likely to benefit?
- Are you reviewing the risk of peptic ulcer, cardiac disease or renal impairment before prescribing COX-2 selective NSAIDs?



Tramadol SR 200 mg was over the patient co-payment until January 2002. All other strengths were under the patient co-payment.

Practice Points

- Review the potential for drug interactions before prescribing tramadol.
- Has the adverse effect profile of tramadol influenced your prescribing of this drug?

Range of strengths of COX-2 selective NSAIDs used in 2001 and 2002

Year	Percentage of prescriptions*											
	celecoxib				rofecoxib				meloxicam			
	Lower strength 100 mg		*Higher strength* 200 mg		*Lower strength* 12.5 mg		*Higher strength* 25 mg		*Lower strength* 7.5 mg		*Higher strength* 15 mg	
	2001	2002	2001	2002	2001	2002	2001	2002	2001	2002	2001	2002
You	2	0	98	100	88	77	12	23	0	100	0	0
Median other GPs[#]	10	9	90	91	48	38	52	62	0	47	0	53

All agents are over the patient co-payment. * Prescriptions may not total 100%.

Practice Points

- Are you minimising the risk associated with these agents by using the lowest effective dose for the shortest period of time?
- Dose range: celecoxib 200 mg - 400 mg per day
  rofecoxib 12.5 mg - 25 mg per day
  meloxicam 7.5 mg - 15 mg per day
- COX-2 selective NSAIDs are not more effective than conventional NSAIDs and have a similar range of adverse effects.

Range of strengths of tramadol used in 2002

Percentage of prescriptions*				
	Lower strengths		*Higher strengths*	
	50 mg capsules	100 mg SR tablets	150 mg SR tablets	200 mg SR tablets
You	93	7	0	0
Median other GPs[#]	46	28	12	15

All agents are under the patient co-payment. * Prescriptions may not total 100%.

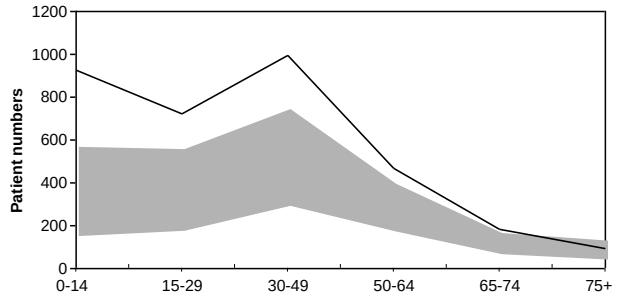
Practice Points

- Avoid sustained release formulations as intial therapy since gradual upward titration may be required to minimise adverse effects.
- If tramadol is being used for acute musculosketetal pain, lower doses (50 mg four times a day) are recommended.
- Dose adjustment should be used in renal and hepatic impairment and people aged over 70 years.
- Does your prescribing reflect the age, risk profile and presenting problems of patients in your practice?

Practice profile

These data below, based on Medicare claims, are provided to help you review your prescribing data within the profile of your practice and the limitations of the data capture for under co-payment items.

Age profile of your practice
1 Jan 2002 to 31 Dec 2002



The black line represents the age profile of patients in your practice. 25% to 75% of other GPs[#] fall within the shaded area.

Medicare patients and concession cardholders in your practice

Patients:	You	Median other GPs[#]
Total Medicare	1,110	727
Concession cardholders	191	210

Concession cardholders include patients who have reached the Safety Net. Data from a three month period (1 April 2002 to 30 June 2002) that best represents your patient mix have been provided.

Notes

@ Data shown is an aggregate for all your provider locations.
# The comparator group "other GPs" includes all prescribers who are currently located in a similar geographical region ie captial city, other metropolitan area, large rural centre, small rural centre, other rural area, remote centre and other remote area.
▲ 25% to 75% of all doctors in the comparator group fall in the range shown by the triangular symbols.

Source: Health Insurance Commission, PBS claims database. Extracted for your personal review only.

July 2003

National Prescribing Service Limited

PPR twenty two

Prescribing Practice Review—*PPR* For General Practice

Optimising safe and effective use of analgesics in musculoskeletal pain

Key messages

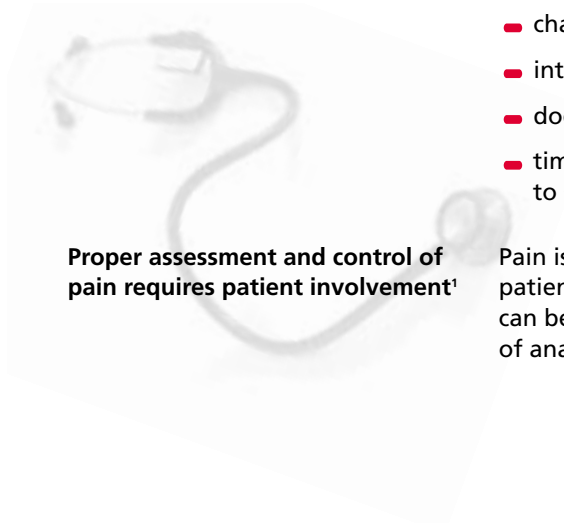
- Assess and document characteristics of pain in order to individualise and monitor effectiveness of treatment
- Use paracetamol first: it is effective when taken regularly in appropriate doses and has a good safety profile
- Consider the range of adverse effects and serious drug interactions with tramadol when selecting therapy where pain requires an opioid or opioid-like analgesic
- Before prescribing COX-2 selective or conventional NSAIDs, review risk of peptic ulcer, cardiac disease or renal impairment
  - COX-2 selective NSAIDs are not more effective than conventional NSAIDs and have a similar range of adverse effects

Assess the pain to guide treatment choice and review its effectiveness

Obtain a 'pain history' in addition to the physical examination[1,2]

A pain history attempts to determine the mechanisms producing pain and factors influencing the painful experience. The history should consider:

- location—is there more than one site affected?
- what makes the pain better or worse?
- character of the pain (e.g. throbbing, aching, sharp, burning)
- intensity/severity of pain
- does the pain radiate anywhere?
- timing—is the pain continuous or does it fluctuate or relate to specific events (e.g. sleep, movement)?



Proper assessment and control of pain requires patient involvement[1]

Pain is always subjective so measuring pain must rely on recording the patient's report. A common method uses visual analogue scales which can be a sensitive and consistent means of assessing the effectiveness of analgesia on an individual basis.[3]

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Figure 1: Pain relief scale

No relief of pain — Complete relief of pain

Pain relief scales (as above) may be more convenient than pain intensity scales because patients have the same baseline relief (zero) whereas they could start with different baseline intensities (e.g. moderate or severe).[3]

Pain is best treated early because established or severe pain is more difficult to treat[1]

The effectiveness of analgesia should be reviewed regularly. Inadequate pain relief can result in the patient progressing from acute pain to chronic pain.[1,2] Although beyond the scope of this discussion, non-drug therapies should also be employed to modify pain.

Paracetamol is the drug of first choice in acute pain

Paracetamol is an effective analgesic when used regularly and in appropriate doses

Good efficacy and safety, together with its low cost relative to other analgesics, makes paracetamol the drug of first choice for managing acute pain conditions.

Systematic reviews of randomised controlled trials have confirmed that paracetamol is an effective analgesic for a wide range of painful conditions.[4,5] Paracetamol continues to be recommended as a first choice analgesic for osteoarthritis.[2,6]

The dosage of paracetamol is often insufficient, leading to perceptions that it is ineffective. Regular use of therapeutic doses provides relief from mild to moderate pain.

Paracetamol has an excellent safety record at therapeutic doses

Paracetamol is well tolerated and toxicity at therapeutic doses is extremely rare. Most cases of paracetamol-induced hepatotoxicity have resulted from either deliberate self-poisoning or accidental overdoses with therapeutic intent.[7]

The risk of paracetamol toxicity increases in those who are fasting or dehydrated (poor fluid intake > 24 hours), with concurrent illness (fever, vomiting, or diarrhoea) causing dehydration, or with underlying hepatic disease.

Achieving pain relief when paracetamol is inadequate

Paracetamol should be used as an adjunct when other forms of analgesia are employed

The WHO 'analgesic ladder' is a stepwise approach to managing pain, starting with a non-opioid analgesic (with or without non-drug therapies) and moving up to potent opioid analgesics. Throughout any progression, the non-opioid analgesic should be continued.

NSAIDs can be added to, or substituted for, paracetamol when pain is of an inflammatory nature

NSAIDs are particularly useful in pain resulting from inflammation. Combining paracetamol with an NSAID may enable lower doses of the NSAID to be used,[8] thus decreasing the risk of gastrointestinal adverse effects.

Add a weak opioid or opioid-like analgesic when paracetamol alone is inadequate…

An alternative to using an NSAID (particularly in pain without inflammatory origins) is to add a weak opioid (such as codeine) to paracetamol or an opioid-like analgesic such as tramadol.

…but avoid combinations of paracetamol and dextropropoxyphene

Avoid paracetamol/dextropropoxyphene combinations (Capadex, Di-Gesic, Paradex)—they are no more effective than paracetamol alone.[9,10] Furthermore, these fixed-dose combinations are generally taken at a frequency that increases the risk of adverse effects from accumulation of dextropropoxyphene and its cardiotoxic metabolite. Dextropropoxyphene can also cause dependency.

Tramadol has potentially serious adverse effects and drug interactions which make it less preferable

Consider adverse effects and drug interactions when choosing between add-on analgesics

The efficacy of paracetamol 1000 mg/codeine 60 mg and tramadol 100 mg is comparable.[3,11] Thus the prescriber needs to consider safety issues when choosing between these alternatives.

Typical opioid adverse effects associated with codeine (particularly constipation but also nausea, drowsiness, dizziness and dry mouth) are well-known to prescribers and greatly influence how well the patient tolerates the paracetamol/codeine combination at higher codeine doses.

Tramadol is associated with serious adverse effects…

Similarly, tolerability can be an issue with tramadol. Almost one-third of patients stopped taking tramadol in clinical trials, predominantly due to adverse effects.[12]

Nausea occurs in at least 1 in 10 patients,[13] often limiting therapy.[14] Serious adverse effects include hallucinations, raised blood pressure and hypersensitivity reactions.[15] Tramadol may induce seizures, particularly in patients with epilepsy or a recognised risk of seizure.[2,8]

The Australian Adverse Drug Reactions Advisory Committee (ADRAC) has received 20 reports of serotonin syndrome with tramadol[15]; this syndrome is more likely to occur with high doses of tramadol.[16]

…abuse and withdrawal reactions have been reported…

Case reports have revealed dependence, abuse and withdrawal symptoms with tramadol, mainly after long-term treatment[14] of several months or longer. ADRAC has received 11 reports of withdrawal symptoms with tramadol.[15]

…and clinically important drug interactions

Concomitant use of tramadol with drugs which lower the seizure threshold, such as tricyclic antidepressants, selective serotonin re-uptake inhibitors (SSRIs), bupropion, or opioids, may precipitate convulsions.[14,15]

Additionally, combining tramadol with drugs which increase serotonin activity in the brain increases the risk of serotonin syndrome; such drugs include tricyclic antidepressants, SSRIs, venlafaxine, monoamine oxidase inhibitors (including moclobemide), pethidine, St. John's wort and sibutramine.[2,8,14]

As tramadol may increase the effect of warfarin,[15] INR should be monitored in patients taking warfarin who either commence or cease tramadol therapy.

Review analgesic effectiveness and patient tolerability of the drug therapy regularly

For patients in whom tramadol is used, it would seem prudent to initiate therapy with the immediate-release dosage form (to assess a patient's response) and only switch to the modified-release formulation if tolerability is established.

Little difference between COX-2 selective NSAIDs and other NSAIDs for analgesia and adverse effects

Consider the overall benefit/harm of both gastrointestinal and non-gastrointestinal adverse effects when prescribing all NSAIDs

COX-2 selective NSAIDs are not more effective than other NSAIDS. Therefore, the overall benefit/harm profile should be considered before prescribing.

The safety profile for COX-2 selective NSAIDs depends on the cumulative effects of both gastrointestinal *and* non-gastrointestinal adverse effects; these data remain controversial and incomplete at present.[17]

It remains unresolved whether COX-2 selective NSAIDs are prothrombotic compared to other NSAIDs. On current evidence, prescribing COX-2 selective NSAIDs preferentially over conventional NSAIDs is not justified in patients requiring prophylactic low-dose aspirin.[18]

Review the patient's risk of peptic ulcer, cardiac disease or renal impairment before prescribing NSAIDs, including COX-2 selective NSAIDs

There is no evidence that COX-2 selective NSAIDs can be used in patients with active peptic ulcer disease. Gastrointestinal complications (perforation, obstruction, or bleeding) do occur with celecoxib and rofecoxib. Improved gastrointestinal safety has been questioned, particularly with celecoxib use exceeding 6 months.[19] Meloxicam has less COX-2 specificity at higher doses[8] and its gastrointestinal safety has not been assessed adequately in clinical outcome trials.

Caution is advised if NSAIDs or COX-2 selective NSAIDs are used in patients at risk of heart failure or acute renal failure, particularly the elderly or in those taking ACE inhibitors and thiazide diuretics concurrently. Assess renal function and blood pressure prior to prescribing and during therapy in those considered at risk.

Reviewer:

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The information contained in this material is derived from a critical analysis of a wide range of authoritative evidence. Any treatment decisions based on this information should be made in the context of the individual clinical circumstances of each patient.

National Prescribing Service Limited

Our goal To improve health outcomes for Australians through prescribing that is: safe effective cost-effective
Our programs To enable prescribers to make the best prescribing decisions for their patients, the NPS provides information education support resources

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