

## Paracetamol and tramadol combination products

This is one of a number of bulletins providing further information on medicines that should be given low priority, are poor value for money, are suitable for self care or for which there are safer, more suitable alternatives. This guidance will support Clinical Commissioning Groups (CCGs) in taking action on items that should not routinely be prescribed in primary care or on the NHS. Further bulletins, including the overarching low value medicines information bulletin are available on the PrescQIPP website: <https://www.prescqipp.info/drop-list/headline-areas/the-prescqipp-drop-list#low-value-medicines-lvm>

This bulletin focuses on paracetamol and tramadol combination products and provides the rationale for therapy to be switched to alternative treatments or discontinued as appropriate and for new patients not to be started on paracetamol and tramadol combination products.

### Recommendations

- Commence new patients requiring analgesia on paracetamol taken on a regular basis. Those requiring a weak opioid analgesic can have codeine added to their paracetamol.
- Review all patients on paracetamol/tramadol combination products for suitability for switching to paracetamol alone or paracetamol with codeine.
- Switch all suitable patients to paracetamol alone or paracetamol and codeine. As with all switches, these should be tailored to the individual patient.

### Background

The NHS England guidance on items which should not routinely be prescribed in primary care lists products that are regarded as low priority for funding, poor value for money or for which there are safer alternatives (<https://www.england.nhs.uk/publication/items-which-should-not-be-routinely-prescribed-in-primary-care-guidance-for-ccgs/>). Paracetamol and tramadol combination products (Tramacet®) feature on the list as an item that is poor value for money, as although it is clinically effective, more cost-effective products are available.

Combination products containing 325mg paracetamol and 37.5mg tramadol are currently available as both tablets and effervescent tablets.<sup>1</sup> The tablets were previously available as the brand Tramacet® but are now also available generically.<sup>2</sup> Both active ingredients are analgesics - paracetamol is a simple analgesic and tramadol is an opioid analgesic and schedule 3 controlled drug.<sup>1</sup>

Tramacet® and the generic equivalent combination products of paracetamol and tramadol are licensed for the symptomatic treatment of moderate to severe pain.<sup>3</sup> There is no evidence that paracetamol/tramadol combination products are more effective or safer than paracetamol 500mg and codeine 30mg (both as individual drugs, or combined as co-codamol 30/500).<sup>4,5</sup> Although paracetamol and tramadol combination products are licensed for the treatment of moderate to severe pain, they have not been shown to be either more effective or better tolerated than other weak opioid analgesics, such as codeine.<sup>4,5</sup> For severe pain, strong opioids are more effective.<sup>4</sup> In fact, paracetamol 325mg/tramadol 37.5mg contains sub-therapeutic doses of both active ingredients<sup>1</sup> and there have been an increased number of reports of misuse and harms associated with tramadol, which have resulted in an increase in the number of tramadol related deaths.<sup>6</sup>

In terms of cost-effectiveness, most formulations of paracetamol/tramadol combination products are also significantly more expensive than paracetamol and codeine (alone or combined).<sup>7</sup> Consequently, paracetamol 325mg/tramadol 37.5mg products are not recommended for NHS prescribing.

## National guidance

Tramadol is not included in the advice given by the British Pain Society and Medicines and Healthcare Products Regulatory Agency (MHRA) for options in the management of mild to moderate pain.<sup>8</sup> There is little evidence for the efficacy of tramadol from clinically useful trials (particularly in primary care, chronic pain and cancer pain).<sup>9</sup> For cancer pain in particular, it is neither more effective nor better tolerated than other, less expensive analgesics and, in severe pain, strong opioids are likely to be more effective.<sup>10</sup>

Tramacet® (the brand available at the time) was reviewed by the Scottish Medicines Consortium (SMC) in February 2006 and they did not recommend it for use within NHS Scotland for the treatment of moderate to severe pain.<sup>9</sup> It had similar efficacy to co-codamol 30/300mg in clinical studies, though the dose of paracetamol in the co-codamol preparation it was compared to was lower than that usually used in the UK.<sup>9</sup> The SMC also noted that the combination product costs significantly more than its individual components (i.e. tramadol and paracetamol) prescribed separately.<sup>7,9</sup>

## Safety

In terms of safety, paracetamol/tramadol combination products have a similar profile of side effects and possible interactions as tramadol.<sup>1</sup> Due to the opioid component, dizziness and constipation are very common side effects, occurring in more than 10% of patients treated.<sup>11</sup> Hallucinations, confusion and convulsions, as well as rare cases of drug dependence and withdrawal, have been reported with tramadol at therapeutic doses.<sup>11</sup> To minimise the risk of convulsions, the Committee on Safety of Medicines (CSM) recommended that patients with a history of epilepsy take tramadol only if there are compelling reasons. In addition, tramadol should be used with caution in patients taking concomitant drugs that can lower the seizure threshold, such as tricyclic antidepressants or selective serotonin reuptake inhibitors.<sup>12</sup>

As a result of the increased incidence of tramadol related deaths, the Advisory Council on the Misuse of Drugs recommended that tramadol was reclassified as a Class C substance under the Misuse of Drugs Act 197. Consequently, it has been a schedule 3 drug since June 2014.<sup>13,14</sup> This includes the combination products.

Compound analgesic preparations that contain a simple analgesic (such as paracetamol) with an opioid component in the same product, reduce the scope for effective titration of the individual components in the management of pain of varying intensity.<sup>1</sup> Furthermore, the dose of paracetamol contained in Tramacet is not optimal – 650mg versus 1000mg.<sup>1</sup>

The advantages of using compound analgesic preparations have not been substantiated. The addition of a low dose of an opioid can result in opioid side-effects (e.g. constipation) and can complicate treatment of overdose without any additional pain relief.<sup>1</sup> The elderly are particularly susceptible to the side effects of opioids.<sup>1</sup>

## Costs and savings

The table below shows the cost of paracetamol/tramadol products compared to alternative analgesics.<sup>7</sup>

Drug	Cost per 100
Tramadol 37.5mg/Paracetamol 325mg tablets	£5.03
Tramadol 37.5mg/Paracetamol 325mg effervescent tablets	£16.13
Tramadol 75mg/Paracetamol 650mg tablets	£32.50 (for 50)
Paracetamol 500mg tablets	£0.97p
Codeine 30mg tablets	£2.71p
Co-codamol 30/500 capsules	£3.88p

## 208. Paracetamol tramadol combination 2.0

In England and Wales, over £608,000 is spent annually on paracetamol and tramadol combination products. (ePACT May to July 2018). Switching to paracetamol alone at its optimal dose **could save up to £ 268,000 annually, which equates to £447 per 100,000 patients**. Eighty percent of prescribing is currently for the more costly high strength or soluble formulations and these patients should be prioritised for review. As with all switches, individual patient circumstances need to be considered.

### Suggested alternatives

Paracetamol 500mg tablets (or soluble tablets) – two tablets to be taken four times a day for pain	PLUS	Codeine 30mg tablets (or soluble tablets) – one tablet to be taken four times a day for pain
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OR

Co-codamol 30/500 capsules (or effervescent tablets). Take two capsules up to four times a day for pain

Full data pack available here:

[https://pdata.uk/views/B208\\_Tramacet/FrontPage?iid=1&isGuestRedirectFromVizportal=y&embed=y](https://pdata.uk/views/B208_Tramacet/FrontPage?iid=1&isGuestRedirectFromVizportal=y&embed=y)

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