

CENTRAL ASIAN JOURNAL OF MEDICAL AND NATURAL SCIENCES
https://cajmns.centralasianstudies.org/index.php/CAJMNS
*Volume: 08 Issue: 01 | Jan 2027 ISSN: 2660-4159*

*Article*

# Rational Pharmacotherapy for Painful Temporomandibular Joint Dysfunction

**Fotimakhon Xasanovna Bukharova[1], Zafar Iskandarovich Mavlyanov[2]**

1. Assistant Lecturer, Department of Oral and Maxillofacial Surgery
2. Doctor of Medical Sciences, Associate Professor, Department of Clinical Pharmacology

Correspondance: f.bukharova@tashmeduni.uz

**Abstract:** The safety and efficacy of drug treatment for painful temporomandibular joint (TMJ) dysfunction depend on the appropriateness of prescribing, the pharmacokinetics of the drug, and the patient's condition. This narrative review compares the main drug classes with regard to elimination half-life, hepatic metabolism, excretion pathways, and the effects of hepatic and renal impairment. It discusses nonsteroidal anti-inflammatory drugs (NSAIDs), paracetamol, muscle relaxants, antidepressants, gabapentinoids, benzodiazepines, tramadol, and prednisolone. Metabolism is distinguished from excretion, as are plasma elimination half-life and duration of clinical action. Hydrophilicity alone does not determine drug safety, and hepatic metabolism does not preclude renal excretion of metabolites. Organ function, drug interactions, and the risk of accumulation should be considered, while pharmacotherapy should be combined with measures to restore mandibular function. No single drug is universally the safest option for all patients with painful TMJ dysfunction.

**Keywords:** Temporomandibular joint (TMJ), painful dysfunction, pharmacotherapy safety, elimination half-life, metabolism, excretion, renal impairment, hepatic impairment

**Citation:** Bukharova, F. X & Mavlyanov, Z. I. Rational Pharmacotherapy for Painful Temporomandibular Joint Dysfunction. Central Asian Journal of Medical and Natural Science 2027, 8(1), 84-92.

Received: 10th Oct 2026
Revised: 11th Oct 2026
Accepted: 24th Oct 2026
Published: 17th Nov 2026

**Copyright:** © 2027 by the authors. Submitted for open access publication under the terms and conditions of the Creative Commons Attribution (CC BY) license (https://creativecommons.org/licenses/by/4.0/)

## 1. Introduction

Temporomandibular disorders (TMDs) encompass disorders of the joint, masticatory muscles, and associated pain syndromes. Similar pain intensity may occur in different clinical conditions; therefore, medication selection requires an accurate diagnosis. A longer duration of action or a pronounced analgesic effect does not necessarily indicate a more favourable safety profile [1]–[4].

Two interrelated questions are important in clinical practice: whether a drug is likely to benefit the identified pain mechanism, and whether the patient's body can tolerate and eliminate it without unacceptable risk. Reduced clearance may lead to accumulation of the parent compound or active metabolites. However, organ injury may also occur without drug accumulation, for example because of the effects of NSAIDs on renal haemodynamics [5]–[9].

## 2. Materials and Methods

This narrative review concerns adult patients. Clinical considerations were compared with the DC/TMD framework, the 2023 BMJ guideline, NIDCR materials, and publications on drug treatment. Pharmacokinetic characteristics and restrictions in organ

impairment were checked against official summaries of product characteristics (SmPCs) and prescribing information published in DailyMed and on manufacturers' websites. The review was updated on 17 September 2026. No systematic search with formal appraisal of all studies or quantitative meta-analysis was performed. No original clinical results are presented [1]–[27].

The BMJ recommendations address chronic pain associated with temporomandibular disorders lasting at least three months and are not intended for the management of acute pain. Inflammatory TMJ involvement in systemic rheumatic disease requires a separate decision that takes treatment of the underlying disease into account [3], [27]–[30].

Sources were grouped into four sets: classification criteria and clinical guidelines [2], [3], [27], systematic-review and trial evidence on pharmacological treatment [4], [10], product information for the individual drugs [5]–[9], [11]–[23], and clinical reference materials [24]–[26]. The authors' own studies of rheumatoid TMJ involvement and imaging [28]–[34] were cited for inflammatory TMJ involvement and for the choice of imaging.

## 3. Results

The review covers 18 systemic drugs from eight classes: NSAIDs, paracetamol, muscle relaxants, antidepressants, gabapentinoids, benzodiazepines, tramadol and prednisolone [5]–[9], [11]–[23]. For chronic TMD pain, the BMJ guideline gives conditional recommendations against routine use of paracetamol, gabapentinoids and several injection-based treatments, and a strong recommendation against combining NSAIDs with opioids [3]. Elimination half-life, hepatic metabolism and renal excretion differ markedly between drugs, as Table 1 shows. Gabapentin, pregabalin and baclofen depend on renal elimination and may accumulate when renal function is reduced [13], [18], [19]. NSAIDs can harm the kidneys through effects on renal haemodynamics regardless of the extent of hepatic metabolism [5]–[9]. Table 2 summarises how renal and hepatic dysfunction change drug selection.

Assessment before prescribing: DC/TMD assesses physical manifestations of the disorder under Axis I and psychosocial factors, pain intensity, and activity limitations under Axis II. Tools include the Graded Chronic Pain Scale (GCPS) and the Jaw Functional Limitation Scale. Clinicians assess the relationship of pain to chewing and movement, mouth-opening range, joint and muscle tenderness, and whether examination reproduces the patient's familiar pain [2].

Further investigations are selected according to the clinical question: MRI helps assess the disc and soft tissues, while CT or cone-beam CT evaluates osseous changes. Odontogenic sources and other causes of facial pain must be excluded. Progressive swelling, fever, neurological deficits, marked limitation of mouth opening, and systemic symptoms require further diagnostic assessment. Chronic pain alone does not confirm trigeminal nerve pathology and is not sufficient justification for prescribing medication for neuropathic pain [1], [2], [31]–[34].

Clinical role and limitations of the main drug classes: Nonsteroidal anti-inflammatory drugs. Ibuprofen and naproxen may be used for short-term pain relief, particularly when an inflammatory component is present. Meloxicam, ketorolac, and nabumetone have not been shown to form a superior treatment hierarchy over other NSAIDs for painful TMJ dysfunction. Duration of action, analgesic efficacy, and safety should be assessed separately. Evidence for specific regimens across different TMD presentations is heterogeneous [1], [4]–[9].

NSAIDs increase the risk of gastrointestinal bleeding, fluid retention, and impaired renal function. Risk rises with dehydration, heart failure, chronic kidney disease, and concurrent use of a diuretic with an ACE inhibitor or angiotensin receptor blocker. Two systemic NSAIDs are generally not prescribed together. Gastroprotection, when indicated,

reduces certain gastrointestinal risks but does not prevent renal or cardiovascular complications [5]–[9].

The BMJ guideline does not recommend avoiding all NSAIDs in every circumstance: cognitive behavioural therapy combined with an NSAID received a conditional recommendation in favour. A strong recommendation was made against combining NSAIDs with opioids. This does not justify prolonged NSAID use without an individual benefit–risk assessment [3]. The US prescribing information for ketorolac limits total systemic use to five days; the regimen must follow the instructions for the locally registered product [8].

Paracetamol. This drug has analgesic activity but does not provide a pronounced peripheral anti-inflammatory effect. Selection should account for total intake from all combination products, liver disease, alcohol consumption, inadequate nutrition, and body weight. Overdose can cause severe liver injury. For chronic pain associated with TMD, the BMJ guideline conditionally recommends against routine paracetamol use, including the combinations considered [3], [11].

Muscle relaxants. Cyclobenzaprine, baclofen, and metaxalone differ pharmacokinetically and are not interchangeable treatments for all types of muscle pain. Cyclobenzaprine is notable for prolonged elimination, sedation, and anticholinergic effects; baclofen may accumulate in renal impairment; metaxalone has restrictions in severe hepatic and renal impairment. Prescribing requires a specific clinical indication and assessment of tolerability. Sedation is intensified by alcohol and other central nervous system (CNS) depressants; patients who experience it should not drive [12]–[14].

Antidepressants. Amitriptyline may be considered for selected chronic pain conditions, although evidence specifically for TMD is limited. Its use requires assessment of cardiac conduction risk, anticholinergic effects, and falls. Sertraline and duloxetine should not be prescribed solely because a patient has TMJ pain; an independent indication and rationale are required. Combining serotonergic drugs with tramadol increases the risk of serotonin syndrome; selective serotonin reuptake inhibitors (SSRIs) and serotonin–noradrenaline reuptake inhibitors (SNRIs) may also increase bleeding risk when taken with NSAIDs [15]–[17], [22].

Gabapentinoids. A small randomised trial of gabapentin for chronic masticatory muscle pain does not establish universal efficacy across all TMDs [10]. The BMJ guideline conditionally recommends against routine use for chronic pain in this group [3]. Gabapentin and pregabalin undergo little hepatic metabolism but require dose adjustment when renal function is reduced. Drowsiness, dizziness, and respiratory-depression risk are especially relevant when they are combined with other CNS depressants [18], [19].

Benzodiazepines and tramadol. Alprazolam and clonazepam are not standard treatments for painful TMJ dysfunction; dependence, sedation, and withdrawal may occur. Tramadol is an opioid analgesic with additional serotonergic activity; routine use for chronic TMD pain is not justified. Combining opioids with benzodiazepines increases the risk of respiratory depression. Regularly used drugs in these classes should be discontinued according to an individual plan that accounts for withdrawal risk [3], [20]–[22].

Glucocorticoids. Prednisolone should be used for a defined inflammatory indication, not for every flare of pain. In rheumatoid arthritis, management of TMJ involvement should be coordinated with a rheumatologist; symptomatic treatment does not replace disease-modifying therapy. Safety considerations include dose, duration, infection risk, hyperglycaemia, fluid retention, and suppression of the hypothalamic–pituitary–adrenal axis [23], [27].

Local and injection-based approaches. For chronic TMD pain, the BMJ guideline conditionally recommends against routine injections of botulinum toxin, hyaluronic acid, or glucocorticoids, topical capsaicin, and trigger-point injections [3]. A single plasma elimination half-life or general excretion organ cannot be assigned to these interventions

without specifying the product and route of administration. Intra-articular residence time and duration of clinical effect are not equivalent to plasma T½. Table 1 therefore covers all 18 systemic drugs discussed in this review; pharmacokinetics of local treatments should be assessed using the instructions for the specific product.

Elimination half-life and routes of elimination: Elimination half-life (T½) is the time required for the plasma concentration of a substance to decrease by 50% during the relevant elimination phase. It should be distinguished from time to peak concentration, dosing interval, and duration of analgesia. For nabumetone, the half-life of the active metabolite 6MNA is clinically relevant; for tramadol, O-desmethyltramadol must also be considered. The biological effects of prednisolone last longer than its plasma elimination half-life [8], [9], [22], [23].

Metabolism is the chemical transformation of a substance; excretion is its removal from the body unchanged or as metabolites. The liver is the principal site of biotransformation for many of the drugs considered, while the kidneys are the main route of elimination for several parent compounds and their metabolites. Biliary and intestinal routes are also important for some medicines. The statement 'metabolised in the liver' does not mean 'excreted only by the liver' [5]–[9], [11]–[23].

Table 1. Pharmacokinetic characteristics of systemic drugs

| Drug | T½ | Metabolism | Organ and route of excretion |
|---|---|---|---|
| Ibuprofen [5] | About 2 h | Liver; inactive metabolites | Kidneys: mainly metabolites and conjugates, with a small proportion of unchanged drug. |
| Naproxen [6] | 12–15 h | Liver; demethylation and conjugation | Kidneys: about 95% of the dose, mainly as conjugates and metabolites. |
| Meloxicam [7] | 13–25 h | Liver; mainly CYP2C9, also CYP3A4 | Kidneys and intestine: approximately equal proportions of metabolites; little unchanged drug. |
| Ketorolac [8] | 5–6 h | Partly hepatic; hydroxylation and conjugation | Kidneys: about 91% of the dose as parent drug and metabolites; about 6% in faeces. |
| Nabumetone [9] | About 24 h for 6MNA | Liver: formation of active 6MNA followed by further metabolism | Kidneys: about 80% of the dose, mainly metabolites and conjugates; about 9% in faeces. |
| Paracetamol [11] | 1–4 h | Liver; mainly conjugation, with a small proportion undergoing oxidation | Kidneys: mainly conjugated metabolites, with a small proportion of unchanged drug. |
| Cyclobenzaprine [12] | Mean 18 h; range 8–37 h | Liver; CYP3A4, CYP1A2, and to a lesser extent CYP2D6 | Kidneys: mainly glucuronides. Data refer to immediate-release tablets. |
| Baclofen [13] | 3–4 h | Minimal metabolism | Kidneys: about 75% of the dose over 72 h, mainly unchanged. |
| Metaxalone [14] | About 9 h fasting | Liver; several CYP enzymes | Kidneys: metabolites. Food and formulation affect pharmacokinetics; data refer to Skelaxin 800 mg. |
| Amitriptyline [15] | About 25 h; range 16–40 h | Liver; active nortriptyline is formed, followed by other metabolites | Kidneys: mainly metabolites; about 2% of amitriptyline is excreted unchanged. |
| Sertraline [16] | About 26 h | Liver; N-desmethylsertraline has a T½ of 62–104 h and lower activity | About 40–45% of the radioactive label is recovered in urine and faeces, respectively; unchanged sertraline is not detected in urine. |
| Duloxetine [17] | Mean 12 h; range 8–17 h | Liver; CYP1A2 and CYP2D6, followed by conjugation | Kidneys: mainly inactive metabolites. |

| | | | |
|---|---|---|---|
| Gabapentin [18] | 5–7 h | No clinically significant metabolism | Kidneys: absorbed drug is excreted unchanged. |
| Pregabalin [19] | About 6.3 h | Minimal metabolism | Kidneys: mainly unchanged drug. |
| Alprazolam [20] | Mean 11.2 h; range 6.3–26.9 h | Liver; mainly CYP3A4 | Kidneys: parent drug and metabolites. |
| Clonazepam [21] | 20–60 h | Liver; extensive biotransformation | 50–70% of the radioactive label in urine and 10–30% in faeces; mainly metabolites. |
| Tramadol [22] | About 6 h; active metabolite about 8 h | Liver; CYP2D6 and CYP3A4; active O-desmethyltramadol is formed | Kidneys: about 90% of the dose as parent drug and metabolites. Data refer to the immediate-release formulation. |
| Prednisolone [23] | About 3 h in plasma | Mainly liver | Kidneys: free and conjugated metabolites, with a small amount of unchanged drug. |

Note. Approximate values are presented for adults with preserved organ function receiving systemic, predominantly oral formulations. Ranges vary by product information, study design, and population; T½ may increase in organ impairment. Excretion proportions reflect individual pharmacokinetic studies and may not add up to 100%. They must not be used alone to calculate a dose. CYP, cytochrome P450 enzymes; 6MNA, 6-methoxy-2-naphthylacetic acid.

## 4. Discussion

The results show that elimination half-life, hepatic metabolism and route of excretion must be read together and not one by one. The following sections interpret them for clinical prescribing.

Hydrophilicity and the roles of the liver and kidneys: Many lipophilic substances undergo biotransformation, including in the liver, producing more polar and often more water-soluble metabolites. This facilitates elimination, particularly in urine. However, metabolism does not always result in complete inactivation: nabumetone and tramadol produce active metabolites. Formation of a metabolite in the liver and its subsequent renal elimination are sequential stages, not alternative routes of elimination [9], [22].

Hydrophilic compounds are often eliminated by the kidneys with limited hepatic metabolism. Among the drugs reviewed, gabapentin and pregabalin illustrate this principle; baclofen is also excreted mainly unchanged by the kidneys. Reduced renal function may therefore lead to accumulation. It is incorrect to state that 'hydrophilic drugs are excreted by the liver' [13], [18], [19].

Solubility alone cannot identify the organ of excretion or determine which drug is safe. Protein binding, active transport, volume of distribution, active metabolites, and intrinsic toxic effects also matter. NSAIDs are a useful example: hepatic metabolism does not remove the risk of reduced renal perfusion. Paracetamol, in turn, is eliminated mainly by the kidneys as metabolites, but its most important overdose risk is liver toxicity [5]–[9], [11].

Assessment of organ function before prescribing: Renal function. Review chronic kidney disease, recent acute kidney injury, dehydration, and concomitant treatment. When indicated, assess creatinine, estimated glomerular filtration rate (eGFR), electrolytes, and urine output. Dose selection should use the measure specified in the product information for the particular drug. Creatinine clearance (CrCl, commonly calculated using Cockcroft–Gault, mL/min) and eGFR indexed to 1.73 $m^2$ are not fully interchangeable. Estimates may be inaccurate when creatinine is changing rapidly or muscle mass is extreme [25].

Liver status. Assess a history of hepatitis, cirrhosis, alcohol use, drug-induced liver injury, and signs of decompensation. ALT and AST mainly reflect cellular injury; ALP and GGT help assess cholestasis. Bilirubin, albumin, and prothrombin time/INR should be interpreted together with the clinical picture. Normal transaminase levels do not prove that all liver functions are preserved. In cirrhosis, use the Child–Pugh class when referenced by the drug information. Low albumin may increase the free fraction of some drugs but does not, by itself, establish hepatic failure [24].

The extent of laboratory monitoring depends on the drug, treatment duration, and risk factors. These tests do not imply that every healthy patient requires a full work-up before a single dose of an analgesic. For patients with liver or kidney disease, polypharmacy, or planned repeat prescribing, baseline assessment and follow-up intervals should be determined in advance. Table 2 summarises how organ dysfunction affects the selection of each systemic drug reviewed.

Table 2. Implications of renal and hepatic dysfunction for drug safety

| Drug | In renal impairment | In hepatic impairment |
|---|---|---|
| Ibuprofen [5] | Contraindicated in severe renal impairment; use caution, ensure adequate hydration, and monitor in other forms of impairment. | Contraindicated in severe hepatic impairment; use caution in less severe dysfunction. |
| Naproxen [6] | According to the cited SmPC, contraindicated when CrCl <30 mL/min. For other degrees of impairment, consider a lower dose and monitoring. | Contraindicated in severe impairment. The free fraction may increase in cirrhosis. |
| Meloxicam [7] | Contraindicated in severe impairment without dialysis; a special regimen is used in dialysis. Even when dose adjustment is not required, NSAID-related risks should be monitored. | Mild or moderate impairment usually does not require dose reduction under the SmPC; severe impairment is a contraindication. |
| Ketorolac [8] | Contraindicated in marked impairment and when hypovolaemia places the patient at risk of renal failure. With reduced renal function, T½ may reach 6–19 h. | Use cautiously in liver disease; monitor if symptoms of dysfunction occur. No major change in T½ does not exclude adverse reactions. |
| Nabumetone [9] | Dose reduction is required according to the product information in moderate or severe dysfunction; the T½ of active 6MNA increases. | Severe dysfunction has been insufficiently studied; formation of the active metabolite and its subsequent breakdown may both change. |
| Paracetamol [11] | Individualise the regimen in renal impairment; in severe impairment, observe the restrictions in the specific product information. | Consider active liver disease, alcohol use, nutrition, and total dose. Individualise the regimen in marked dysfunction; overdose is hepatotoxic. |
| Cyclobenzaprine [12] | The cited prescribing information provides no reliable standard CrCl-based adjustment scheme; this does not establish safety in severe chronic kidney disease. | In mild impairment, use a lower starting dose and slow titration; use is not recommended in moderate or severe impairment. |
| Baclofen [13] | Dose reduction and close monitoring are essential in renal impairment; neurotoxicity may occur even at low doses in severe impairment. | The liver plays a limited role in elimination, but use caution; liver enzymes may increase. |
| Metaxalone [14] | Contraindicated in severe impairment; use cautiously and monitor in mild or moderate impairment. Evidence for precise dose calculation is limited. | Contraindicated in severe impairment; use cautiously and monitor in mild or moderate impairment. |

| | | |
|---|---|---|
| Amitriptyline [15] | Renal impairment usually does not require dose adjustment for pharmacokinetic reasons, but clinical tolerability must still be assessed. | Concentrations may increase and a lower dose may be needed; severe liver disease is a contraindication under the SmPC. |
| Sertraline [16] | According to the cited prescribing information, dose adjustment is usually unnecessary in mild to severe renal impairment. | In mild impairment, the starting dose and therapeutic range are halved; use is not recommended in moderate or severe impairment. |
| Duloxetine [17] | Contraindicated according to the cited SmPC when CrCl <30 mL/min. | Contraindicated in liver disease causing hepatic dysfunction; exposure increases substantially in moderate dysfunction. |
| Gabapentin [18] | Select dose and frequency according to CrCl; a separate regimen is provided for haemodialysis. Accumulation may increase CNS depression. | There is no substantial hepatic metabolism; separate adjustment solely for liver function is usually unnecessary. |
| Pregabalin [19] | Dose adjustment based on CrCl is required when renal function declines; use a specific regimen for haemodialysis. | Hepatic dysfunction is not expected to materially affect concentrations; hepatic dose adjustment is usually unnecessary. |
| Alprazolam [20] | The cited prescribing information does not establish a universal CrCl-based adjustment; individual assessment and monitoring for sedation are required. | Reduce the initial dose and titrate according to tolerability; elimination may be slower in liver disease. |
| Clonazepam [21] | Pharmacokinetic data do not require automatic adjustment; the SmPC recommends caution and individualised dosing. | Contraindicated in severe impairment; a lower dose is usually required in mild or moderate impairment. |
| Tramadol [22] | Elimination of the parent drug and active metabolite is delayed; reconsider the interval and regimen according to the product information, especially in severe impairment. | In cirrhosis, T½ of the parent drug and active metabolite increases, requiring regimen review. Not intended for routine TMD treatment. |
| Prednisolone [23] | Do not determine the dose solely by CrCl. Consider sodium and fluid retention, blood pressure, potassium, and coexisting heart failure. | Liver disease may slow elimination; hypoalbuminaemia increases the free fraction and may intensify adverse effects. |

Note. Restrictions are based on specific product information [5]–[9], [11]–[23]; regulatory conditions may differ between countries and formulations. 'Dose adjustment usually not required' means that no standard pharmacokinetic adjustment is specified, not that the drug is free of toxicity. The severity of organ impairment and the permissible regimen must be checked against the information for the selected product.

Special patient groups and outcome assessment: In older adults, reduced renal clearance, polypharmacy, and increased sensitivity to sedatives raise the risk of complications. NSAIDs, benzodiazepines, anticholinergic drugs, and combinations of CNS depressants require particular caution. During pregnancy and breastfeeding, every prescription should be assessed individually. The FDA recommends limiting NSAID use from 20 weeks of pregnancy because of the risk of fetal renal dysfunction and oligohydramnios, and avoiding them from approximately 30 weeks because of the additional risk of premature closure of the ductus arteriosus. Adult data should not automatically be extrapolated to adolescents [5]–[9], [11]–[23], [26].

Before treatment, record pain intensity, limitations in chewing and mouth opening, the expected benefit, and the time for reassessment. Depending on the clinical question, use a numerical rating scale or visual analogue scale (VAS), GCPS, and the Jaw Functional

Limitation Scale. At follow-up, assess not only pain but also daily activity, sleep, adverse effects, and laboratory parameters when indicated [2]. If treatment is ineffective, reassess the diagnosis and rationale for therapy; adding more drugs does not, by itself, solve the problem.

Medication should form part of a functional rehabilitation programme that includes patient education, reduction of provoking chewing loads, avoidance of habitual tooth clenching, and individually selected exercises. Behavioural therapies are also supported for chronic pain [1], [3]. Persistent pain, suspected neuropathic mechanisms, or systemic arthritis warrants referral to the appropriate specialist. In substantial organ impairment, the regimen should be agreed with the treating physician and, when needed, a clinical pharmacologist.

Limitations. This is a narrative review without a systematic search or formal appraisal of all studies, so the selection of sources may be biased and the strength of evidence was not graded. The values in Tables 1 and 2 are approximate, apply to adults with preserved organ function, and may differ between products and countries. Trials of drugs specifically for TMD are few and small, as the gabapentin trial shows [10].

Implications for practice. The findings support an individual approach: confirm the diagnosis and the pain mechanism, check renal and hepatic function and interacting drugs, choose the drug whose elimination profile fits the patient, and reassess early [2], [3]. Because no single drug is safest for all patients, prescribing should be linked to functional rehabilitation and patient education and not to a growing drug burden [1], [3].

## 5. Conclusion

The safety of pharmacotherapy for painful TMJ dysfunction depends on clinical justification and individual tolerability. Drug selection should take account of elimination half-life, active metabolites, hepatic metabolism, and the actual route of excretion. Assessing only one 'organ of elimination' is insufficient: a drug may be metabolised in the liver while its metabolites are removed by the kidneys.

In reduced renal function, accumulation of gabapentin, pregabalin, and baclofen is a particular concern; liver disease may slow the elimination of some antidepressants, benzodiazepines, and other drugs. Renal risks from NSAIDs must be assessed regardless of the extent of hepatic metabolism. Hydrophilicity is not an independent criterion of safety. Rational prescribing requires matching the diagnosis to the indication, minimising unnecessary medication burden, checking interactions, and reassessing benefits and adverse effects in a timely manner. A universal ranking of drugs as the 'most effective' or 'safest' for all patients is not scientifically justified.

## REFERENCES

Electronic prescribing information and reference materials were used to update this review on 17 September 2026. Before prescribing, consult the current information for the specific registered product.

[1] National Institute of Dental and Craniofacial Research, “TMD (Temporomandibular Disorders).” [Online]. Available: https://www.nidcr.nih.gov

[2] E. Schiffman et al., “Diagnostic criteria for temporomandibular disorders (DC/TMD) for clinical and research applications,” J. Oral Facial Pain Headache, vol. 28, no. 1, pp. 6–27, 2014, doi: 10.11607/jop.1151.

[3] J. W. Busse et al., “Management of chronic pain associated with temporomandibular disorders: A clinical practice guideline,” BMJ, vol. 383, Art. no. e076227, 2023, doi: 10.1136/bmj-2023-076227.

[4] H. R. Mujakperuo, M. Watson, R. Morrison, and T. V. Macfarlane, "Pharmacological interventions for pain in patients with temporomandibular disorders," Cochrane Database Syst. Rev., no. 10, Art. no. CD004715, 2010, doi: 10.1002/14651858.CD004715.pub2.
[5] Viatris, "Brufen 400 mg tablets," Summary of Product Characteristics.
[6] Atnahs Pharma UK Ltd., "Naprosyn 250 mg tablets," Summary of Product Characteristics.
[7] "Meloxicam 15 mg tablets," Summary of Product Characteristics, Electronic Medicines Compendium. [Online]. Available: https://www.medicines.org.uk/emc
[8] "Ketorolac tromethamine injection," Prescribing information, DailyMed. [Online]. Available: https://dailymed.nlm.nih.gov
[9] "Nabumetone tablets," Prescribing information, DailyMed. [Online]. Available: https://dailymed.nlm.nih.gov
[10] P. Kimos et al., "Analgesic action of gabapentin on chronic pain in the masticatory muscles: A randomized controlled trial," Pain, vol. 127, no. 1–2, pp. 151–160, 2007, doi: 10.1016/j.pain.2006.08.028.
[11] Haleon UK Trading Ltd., "Anadin paracetamol tablets," Summary of Product Characteristics.
[12] "Cyclobenzaprine hydrochloride tablets," Prescribing information, DailyMed. [Online]. Available: https://dailymed.nlm.nih.gov
[13] Novartis Pharmaceuticals UK Ltd., "Lioresal tablets 10 mg," Summary of Product Characteristics.
[14] "Skelaxin (metaxalone)," U.S. prescribing information.
[15] Brown & Burk UK Ltd., "Amitriptyline 10 mg film-coated tablets," Summary of Product Characteristics.
[16] "Sertraline tablets," Prescribing information, DailyMed. [Online]. Available: https://dailymed.nlm.nih.gov
[17] "Duloxetine 30 mg gastro-resistant capsules," Summary of Product Characteristics, Electronic Medicines Compendium. [Online]. Available: https://www.medicines.org.uk/emc
[18] Morningside Healthcare Ltd., "Gabapentin 100 mg hard capsules," Summary of Product Characteristics.
[19] "Alzain 100 mg capsules, hard (pregabalin)," Summary of Product Characteristics, Electronic Medicines Compendium. [Online]. Available: https://www.medicines.org.uk/emc
[20] "Xanax (alprazolam)," U.S. prescribing information.
[21] "Clonazepam Aristo 0.5 mg tablets," Summary of Product Characteristics, Electronic Medicines Compendium. [Online]. Available: https://www.medicines.org.uk/emc
[22] Aurobindo Pharma – Milpharm Ltd., "Tramadol 50 mg capsules," Summary of Product Characteristics.
[23] "Prednisolone tablets BP 5 mg," Summary of Product Characteristics, Electronic Medicines Compendium. [Online]. Available: https://www.medicines.org.uk/emc
[24] NHS Specialist Pharmacy Service, "Assessing liver function and interpreting liver blood tests." [Online]. Available: https://www.sps.nhs.uk
[25] NHS Specialist Pharmacy Service, "Calculating kidney function." [Online]. Available: https://www.sps.nhs.uk
[26] U.S. Food and Drug Administration, "FDA recommends avoiding use of NSAIDs in pregnancy at 20 weeks or later because they can result in low amniotic fluid," Drug Safety Communication, 2020.
[27] L. Fraenkel et al., "2021 American College of Rheumatology guideline for the treatment of rheumatoid arthritis," Arthritis Care Res. (Hoboken), vol. 73, no. 7, pp. 924–939, 2021, doi: 10.1002/acr.24596.
[28] F. Kh. Bukharova, D. Sh. Abdullaev, and Z. B. Abdashimov, "Features of painful temporomandibular joint dysfunction in patients with rheumatoid arthritis," presented at the VI Int. Sci. Pract. Conf., Tashkent State Med. Univ., Dept. Oral Maxillofac. Surg., Tashkent, Uzbekistan, Feb. 6, 2026.
[29] Sh. Yu. Abdullaev and F. Kh. Bukharova, "Densitometry in temporomandibular joint dysfunction at the early stage of rheumatoid arthritis," Innov. Technol. Sci. Educ., vol. 4, no. 31, pp. 21–25, Feb. 2026, ISSN 2181-371X. [Online]. Available: https://sr-journals.org/index.php/FJI
[30] F. Kh. Bukharova, "Correlation between condylar dimensions on CT and TMJ disc position on MRI," Scholar, vol. 4, no. 3, pp. 101–109, Feb. 2026, ISSN 2181-4147, doi: 10.5281/zenodo.18713464.
[31] Sh. Yu. Abdullaev and F. Kh. Bukharova, "Current issues in the diagnosis and treatment of temporomandibular joint arthritis and osteoarthritis," Res. Educ., vol. 5, no. 2, pp. 11–19, Feb. 2026, ISSN 2181-3191, doi: 10.5281/zenodo.18860705.
[32] F. Kh. Bukharova, D. Sh. Abdullaev, and Z. B. Abdashimov, "Assessment of painful temporomandibular joint dysfunction in rheumatoid arthritis using cone-beam computed tomography," Int. J. Conf. Ser. Educ. Social Sci. (IJORCES), vol. 5, no. 2, pp. 23–24, 2025, ISSN 2717-7076. [Online]. Available: https://www.ijorces.org/index.php/ojs/issue/view/26
[33] F. Kh. Bukharova, D. Sh. Abdullaev, and Z. B. Abdashimov, "MRI assessment of painful temporomandibular joint dysfunction in rheumatoid arthritis: Diagnosis of inflammatory changes and their correlation with clinical signs," Int. J. Conf. Ser. Educ. Social Sci. (IJORCES), vol. 5, no. 2, pp. 20–22, 2025, ISSN 2717-7076. [Online]. Available: https://www.ijorces.org/index.php/ojs/issue/view/26
[34] Sh. Yu. Abdullaev, F. Kh. Bukharova, and Z. B. Abdashimov, "MRI assessment of painful temporomandibular joint dysfunction in rheumatoid arthritis: A review of current evidence," Med. Radiol. Uzbekistan, vol. 1, no. 4, pp. 1–19, 2024.