*Supplemental Table 1: Summary of Pharmacological Agents Used for Temporomandibular Disorder-associated Pain*

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Therapy |

|  |
| --- |
| **Description of the Therapy** |

|  |
| --- |
|  |

 |

|  |
| --- |
| **Evidence Level** |

|  |
| --- |
|  |

|  |
| --- |
|  |

 | Implications for Clinical Practice | References |
| Non-opioids analgesics | Use of oral non-opioid analgesics, as acetaminophen or non-steroid anti-inflammatory drugs (NSAIDs) to alleviate pain | **Moderate** Systematic reviews and meta-analyses confirm pain relief, but must be combine with physical therapy or behavioral interventions | Acetaminophen is commonly recommended as fist-line pharmacological treatment for managing temporomandibular (TMD) pain, associated with other non-pharmacological approach. NSAIDs can be used too, and have an anti-inflammatory role too, but must be used in a short time period, because of their side effects. | [12–15] |
| Muscle relaxants | Use of myorelaxants (e.g. cyclobenzaprine) to alleviate muscle tension and pain | **Low** Some studies find effectiveness in decreasing muscle hyperactivity, but with significant side effects | Not commonly used in TMD, because of the lack of evidence and significant side effects | [5,12,14,15,19] |
| Antidepressants | Use of antidepressants, especially tricyclic antidepressants or Serotonin and Norepinephrine Reuptake Inhibitors (SNRIs), to treat chronic pain | **Low** High level of evidence for chronic pain, but data about its efficacy in monotherapy for TMD is lacking | In patients with psychiatric comorbidities, may be used in addition to physical therapy and behavioral interventions, with close monitoring of the side effects | [12,13,15] |
| Anti-convulsants | Use of oral anticonvulsants (e.g. gabapentinoids or pregabalin) to modulate nociceptive signal | **Low** Some studies have shown significant reduction of chronic TMJ pain, but with side effects | May be tried to reduce the pain signal in association with physical therapy or behavioral interventions | [12,15,27] |
| Botulinum toxin injections | Use of Botulinum toxin injection to suppress muscle contraction and therefore alleviate pain and improve function | **Moderate** A recent meta-analysis revealed no conclusive evidence, with significant side effects | Botulinum toxin injections are not recommended for TMD management | [19,22,27] |
| Opioids | Use of different opioids (morphine, codeine, oxycodone) against TMD pain | **Strong** Systematic reviews and meta-analyses confirm the high risk of addiction with the use of opioids for chronic pain | Opioids should be avoided in TMD management | [12,17,27] |
| Cortico-steroids | Use of oral or intra-articular injection of corticosteroids, such as prednisone or triamcinolone, for their anti-inflammatory effect on TMD | **Moderate**Some studies describe a short-time relief, but their long-term use is limited by side effects | Systemic corticosteroids should not be used in TMD managementLocal injections can be considered, but also limited evidence and side effects | [13,15] |
| Benzo-diazepines | Use of oral benzodiazepines against TMD pain | **Moderate**Studies comparing benzodiazepines with a placebo for TMD pain indicate no significant difference in pain relief. | Benzodiazepines should not be used in TMD management because of their lack of significative pain relief and their side effects | [25] |
| Beta-blockers | Use of oral beta-blockers to inhibit adrenergic neurotransmission  | **Low** Two recent meta-analyses recommend against their use in clinical practice, with potentially more harm than benefits | Beta-blocker should not be routinely used in TMD management, unless the patient has other comorbidities where beta-blockers may be beneficial | [12,13,15,16,27,28] |
| Cannabinoids | Use of oral cannabinoids to modulate nociceptive signals | **Low**Studies with medical cannabinoids in TMD are lacking  | Not recommended because of lack of evidence, may be tried based on patient preferences | [46] |
| Glucosamine and chondroitin sulfate | Oral substitution in the primary component of the articular cartilage to alleviate arthritic TMD pain | **Low** Lack of high-quality studies with these components | Glucosamine and chondroitin sulfate should not be recommended in TMD management  | [30,32–34] |
| Ozone therapy | Injection of ozone in the joint space to reduce inflammation and promote tissue oxygenation, potentially reducing pain and improving jaw function | **Low** Studies showing a potential pain improvement are lacking | Not recommended because of lack of evidence  | [22] |
| Topical therapies | Use of topical patches of lidocaine, capsaicin or methyl salicylate to alleviate pain | **Low**Lack of studies evaluating its utility in TMD management, despite the absence of major side effects | Topical patches are not recommended because of lack of evidence | [16,27,41,45] |

**Supplementary Table 1.** Summary of pharmacological therapies for temporomandibular disorder (TMD)-associated chronic pain, including descriptions, evidence levels, clinical implications, and key references.