

In-Office Drug Administration and Dispensing of Medications

Policy Number: DCP033.11
Effective Date: July 1, 2024

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Related Dental Policy

- [General Anesthesia and Conscious Sedation Services](#)

Coverage Rationale

Therapeutic Parenteral Drug Administration (Single or Two or More Administrations)

Therapeutic **Parenteral** drug administration may be indicated to enhance healing of surgical procedures, manage post procedure nausea and vomiting, or reduce pain and/or risk of infection. Medications include antibiotics, steroids, anti-inflammatory drugs, or antiemetics.

Infiltration of Sustained Release Therapeutic Drug (Single or Multiple Sites)

Infiltration of sustained release therapeutic drug (e.g., Exparel®) is not indicated due to insufficient evidence of efficacy and/or safety.

Drugs or Medicaments Dispensed in the Office for Home Use

Dispensing of drugs may be indicated to enhance healing of surgical procedures, reduce pain and/or risk of infection, and reduce caries risk. These include, but are not limited to oral antibiotics, oral analgesics, and topical fluoride.

Definitions

Parenteral: A technique of administration in which the drug bypasses the gastrointestinal (GI) tract [i.e., intramuscular (IM), intravenous (IV), intranasal (IN), submucosal (SM), subcutaneous (SC), intraosseous (IO)].

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

CDT Code	Description
D9610	Therapeutic parenteral drug, single administration

CDT Code	Description
D9612	Therapeutic parenteral drugs, two or more administrations, different medications
D9613	Infiltration of sustained release therapeutic drug, per quadrant
D9630	Drugs or medicaments dispensed in the office for home use

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Description of Services

Parenteral administration of drugs is any technique in which the route of administration bypasses the gastrointestinal tract. These routes include, but are not limited to, intravenous administration, intramuscular and subcutaneous injections and the use of medication patches and nasal sprays. There are many medicaments that may be given to a patient in the dental office for use at home and these include prescription strength toothpastes and mouth rinses, as well as antibiotics and pain medication.

Exparel® (Pacira Pharmaceuticals, Inc) is a sustained release, long-acting local injection that encapsulates bupivacaine in multivesicular liposomes. The liposomes gradually release bupivacaine as the lipid membranes are absorbed, resulting in sustained release and prolonged analgesia. It is purported to reduce or eliminate the need for opioids in the treatment of post-surgical pain; however, the clinical significance of opioid reduction has not been established (Noviasky).

Pursuant to CA AB2585: While not common in dentistry, nonpharmacological pain management strategies should be encouraged if appropriate.

Clinical Evidence

Gorecki et al. (2018) conducted a prospective, randomized, double-blind, placebo-controlled, parallel-group phase II single-center (ClinicalTrials.gov NCT01706588) to evaluate the efficacy, safety, and local tolerability of diclofenac HPβCD administered as a local submucosal injection prior to lower third molar surgery. Seventy-five patients requiring mandibular third molar surgery were randomized into 1 of 5 groups: 5 mg/1 mL diclofenac HPβCD, 12.5 mg/1 mL diclofenac HPβCD, 25 mg/1 mL diclofenac HPβCD, 50 mg/1 mL diclofenac HPβCD, or 1 mL placebo. The study drug was injected into the mucosal tissue surrounding the surgical site prior to surgery following achievement of local anesthesia. The primary outcome measure was the area under the curve (AUC) of cumulative pain scores from end of surgery to 6 h post-surgery. This demonstrated a global treatment effect between the active groups and placebo, hence confirming the study drug's efficacy ($p = 0.0126$). Secondary outcome measures included the time until onset of pain and the time until patients required rescue medication, both showing statistical significance of the study drug compared to placebo. The time until rescue medication ranged between 7.8 h (for 25 mg/1 mL diclofenac HPβCD) and 16 h (for 50 mg/1 mL diclofenac HPβCD). The 5-mg/1-mL solution appeared superior to the 12.5-mg/1-mL and 25-mg/1-mL solutions (time until rescue medication = 12.44 h). A total of 14% of patients experienced minor adverse drug reactions (ADRs), of which 2 cases demonstrated flap necrosis. These resolved without further intervention. The authors concluded that these results overall indicate efficacy, safety, and relative tolerability of diclofenac HPβCD used locally as a submucosal injection prior to third molar surgery.

Al-Dajani (2017) conducted a triple-blinded split-mouth randomized controlled clinical trial of 32 patients who underwent randomized bilateral extractions of impacted mandibular third molars during 2 consecutive sessions. Each patient was given a single-dose intramuscular injection of dexamethasone (0.1 mg/kg) preoperatively in 1 session and a placebo in the other session. Data were collected daily for 7 postoperative days, and 14 patient-centered outcomes were interpreted. The results showed that when administered dexamethasone, patients reported less pain, took fewer analgesics, reported less swelling, had less difficulty in eating and in enjoying food, had less difficulty in speech, and had less trismus. Additionally, they were absent less from school or work, and had less disruption of daily activities. The differences between the 2 conditions in bleeding, malaise, and sleep disturbance were not significant. The author concluded that prophylactic dexamethasone administered intramuscularly before third molar surgery can be recommended as a safe and effective strategy for decreasing pain and discomfort and enhancing oral functions and daily activities, unless contraindicated.

Arora et al. (2014) conducted a prospective randomized double-blind placebo-controlled clinical trial to evaluate whether postoperative combined amoxicillin and clavulanic acid in mandibular third molar extraction is effective in preventing inflammatory complications. Two bilaterally similar impacted mandibular third molars per head in 48 patients were randomly assigned to two treatment groups (Group I and Group II). Each patient served as his/her own control. Each patient received 625 mg of combined amoxicillin and clavulanic acid 1 h before surgery. In the case of third molars

belonging to Group I, 625 mg of combined amoxicillin and clavulanic acid TDS was continued for 3 days; in Group II, placebo was continued for 3 days. The patients were evaluated on the third and seventh postoperative days for signs of clinical infection and for microbial load evaluation. The data between the two groups were then statistically analyzed by the two-tailed Fisher's exact test, with a 95% confidence interval. The results showed no statistically significant differences between the test group and the control group with regard to erythema, dehiscence, swelling, pain, trismus, and infection based on microbial load. The data were statistically significant for alveolar osteitis, with the occurrence of alveolar osteitis (14.58%) in the placebo group. The authors concluded postoperative antibiotics are recommended only for patients undergoing contaminated, long-duration surgery.

Chugh et al. (2017) conducted a randomized controlled trial to compare the effects of the preoperative submucosal administration of equivalent doses of two commonly used steroids on the known postoperative sequelae following third molar extractions: pain, swelling, and trismus. There were 60 subjects requiring the removal of impacted mandibular third molars with a similar difficulty index. The participants were allocated randomly to three groups: the placebo group received normal saline injection (control), while the 8mg dexamethasone group and 40mg methylprednisolone group received submucosal injections of these steroids preoperatively. Each participant was assessed for postoperative pain, swelling, and trismus, along with a subjective assessment of quality of life (QOL) through a structured questionnaire. The results showed that the participants administered dexamethasone showed significant reductions in pain and trismus compared to the control group. Submucosal injection of dexamethasone was found to be superior to methylprednisolone only in terms of the reduction in swelling. QOL was minimally affected in patients administered dexamethasone as compared to methylprednisolone and control subjects. The authors concluded that within this small patient population, the preoperative submucosal use of steroids can be considered an effective, safe, and simple therapeutic strategy to reduce swelling, pain, and trismus after the surgical removal of impacted mandibular third molars.

Arteagoitia et al (2016) Prophylactic use of amoxicillin and amoxicillin/clavulanic acid, although controversial, is common in routine clinical practice in third molar surgery. The authors conducted a systematic review and meta-analysis including double-blind placebo-controlled randomized clinical trials published up to June 2015 to investigate the efficacy of amoxicillin with or without clavulanic acid on the incidence of the in the prevention of infection and dry socket after third molar extraction. There were 10 papers included in the review. The results of this review showed that the prophylactic use of amoxicillin does not significantly reduce the risk of infection and/or dry socket after third molar extraction, however with amoxicillin/clavulanic acid, the risk decreases significantly. The authors concluded however, that considering the number needed to treat, low prevalence of infection, potential adverse reactions to antibiotics and lack of serious complications in placebo groups, the routine prescription of amoxicillin with or without clavulanic acid is not justified.

Dietrich et al (2014). Diclofenac is an effective and well-tolerated nonsteroidal anti-inflammatory drug (NSAID) frequently used in the treatment of acute pain. Marketed formulations for parenteral administration usually contain 75 mg/3 mL of diclofenac sodium, which provide limited dosing flexibility, and are usually given intramuscularly. The authors conducted a randomized double-blind trial to investigate the safety and efficacy of low dose subcutaneous (SC) diclofenac containing hydroxypropyl- β -cyclodextrin (HP β CD) as a solubility enhancer for the management of acute pain. In this study, patients developing moderate-to-severe pain after third molar extraction under local anesthesia were randomized to one of the 4 SC injections: 25, 50, or 75 mg diclofenac, or placebo. The pain intensity differences were measured at 1.5 hours post dose and showed was higher in all diclofenac-treated groups than the placebo group. The authors concluded that this SC delivery of diclofenac containing (HP β CD) is effective at 25 and 50 mg levels for relieving moderate to severe pain following third molar extraction.

Mohan et al (2014) conducted a randomized, controlled clinical study to evaluate the role of antibiotics to prevent postoperative complications after routine periodontal surgery and also to determine whether their administration improved the surgical outcome. Forty-five systemically healthy patients with moderate to severe chronic periodontitis requiring flap surgery were enrolled in the study. They were randomly allocated to Amoxicillin, Doxycycline, and control groups. Surgical procedures were carried out with complete asepsis as per the protocol. Postoperative assessment of patient variables like swelling, pain, temperature, infection, ulceration, necrosis, and trismus was performed at intervals of 24 h, 48 h, 1 week, and 3 months. Changes in clinical parameters such as gingival index, plaque index, probing pocket depth, and clinical attachment level were also recorded. There was no incidence of postoperative infection in any of the patients. Patient variables were comparable in all the three groups. Though there was significant improvement in the periodontal parameters in all the groups, no statistically significant result was observed for any group over the others. The results of this study showed that when periodontal surgical procedures were performed following strict asepsis, the incidence of clinical infection was not significant among all the three groups, and also that antibiotic administration did not influence the outcome of surgery. Therefore, prophylactic antibiotics for patients who are otherwise healthy administered following routine periodontal surgery to prevent postoperative infection are unnecessary and have no demonstrable additional benefits.

Herrera-Briones FJ et al (2013) conducted a systematic literature review on the use of corticosteroids in third molar surgery. A systematic search of the literature was carried out in PubMed, Scopus, MEDLINE, and Cochrane using steroid and third molar as key words. 27 Randomized controlled trials and 1 meta-analysis were selected from among 72 articles identified and included RCTs that compared perioperative steroids given in any formulation, dose, or route with either placebo or no treatment, and included patients of any age requiring the removal of one or more impacted third molars under local anesthesia, intravenous (IV) sedation, or general anesthesia. Articles were not restricted as a function of the method used to measure pain. The authors of this review concluded the evidence shows that the administration of corticosteroids improves the postoperative experience of patients and has a significant impact on trismus and inflammation. Greater effects appear to be achieved by using the parenteral route and by administering the corticosteroid before the surgery.

Ataoglu et al (2008) conducted a study to evaluate the efficacy of antibiotic prophylaxis during removal of impacted third molars. 150 patients with impacted mandibular or maxillary third molars were divided randomly into three groups. The first was given amoxicillin 2g combined with clavulanic acid, orally daily for 5 days postoperatively; starting at the end of the operation. The second group was given the same drugs but the regimen started 5 days before the operation. The third was given no antibiotics. Pain, infection, swelling, alveolar osteitis, and interincisal mouth opening (mm) were evaluated. There were no significant differences among the groups in the incidence of these complications. The authors concluded that routine prophylactic use of oral antibiotics in third molar surgery is not recommended.

Exparel (Liposomal Bupivacaine)

The evidence regarding the safety and efficacy of Exparel in oral and maxillofacial surgery is limited. Further research is needed to determine the superior benefits of liposomal bupivacaine over standard bupivacaine administration.

James et al., (2023) conducted a parallel-arm randomized clinical trial to determine if liposomal bupivacaine infiltration (LBI) following uncomplicated extraction of bilateral, mandibular third molars significantly reduces postoperative pain when compared to standard bupivacaine. Twenty four patients were included and equally randomized to receive LBI or standard bupivacaine (control group). Following extractions under deep sedation, both groups were prescribed the same postoperative analgesic regimen of 800 mg of ibuprofen every 8 hours and oxycodone/acetaminophen 5/ 325 mg every 4-6 hours as needed. Chlorohexidine mouth rinse was also prescribed. Patients were contacted via phone at 48 hours postoperatively and asked about pain levels and narcotic medication use. Patients were seen for one week follow up and overall pain, current pain level and how much pain medication was needed up to that point. The results showed at the 48 hour follow up phone call, there were no significant differences in narcotic frequency. At the one week follow up, the results showed that patients in both groups indicated they had returned to normal activities and no longer required narcotic medication for pain. The authors concluded that LBI does not significantly reduce the need for postoperative pain control for uncomplicated third molar extractions. More research for oral surgery indications with larger patient sample sizes is needed to assess the clinical utility of LBI over standard bupivacaine administration.

In a 2021 systematic review of randomized clinical trials, Ji et al. assessed the efficacy of liposomal bupivacaine compared to placebo or other non-bupivacaine agent in postoperative pain management and opioid consumption. 63 studies with a total of 6770 subjects met inclusion criteria. Studies were categorized into the following surgical specialties: 33 orthopedic-related procedures, ten general surgery and associated subspecialty procedures, nine obstetric/gynecology (OBGYN) procedures, four oral and maxillofacial surgery procedures, and seven others. By pooling the data of all categories, overall, the results showed that in over 74% of the trials, liposomal bupivacaine did not result in significant pain relief, nor did it demonstrate a reduction in opioid consumption in almost 86%. When compared to standard bupivacaine or other active agents, there was no reduction in opioid use in 83% and 100% respectively. The authors concluded that the efficacy of liposomal bupivacaine for providing superior postoperative pain control relative to placebo or another active agent is not supported by a majority of RCTs due to low quality and a very high risk of bias. Furthermore, nearly half of the completed RCTs either did not publish their results or make them publicly available. The use of liposomal bupivacaine as an adjunct to reduce postoperative opioid consumption warrants further high-quality research. Iero et al. (2018) conducted a randomized, open-label trial to determine the efficacy and safety of an opioid-sparing postsurgical pain management protocol with or without local infiltration of liposomal bupivacaine for full-arch implant surgery (four or more implants to the maxilla and/or mandible to serve as anchors for dental prostheses). Patients scheduled to undergo full-arch implant surgery were randomly assigned to receive an opioid-sparing postsurgical pain management protocol with or without liposomal bupivacaine 266 mg at the end of surgery. All patients received infiltration with ≤ 40 mL lidocaine 2% with epinephrine at the beginning of surgery and bupivacaine 0.5% with epinephrine near the end of surgery and oral opioid or nonopioid analgesics (oxycodone 5 mg tablets or ibuprofen 600 mg), as needed, post surgically. Pain severity at the surgical site was assessed using a verbal 0 to 10 numeric rating scale (0 [no pain] to 10 [worst pain imaginable]). Patients separately assessed pain in their mandible and maxilla. Reports of treatment-emergent adverse events were collected. Sixty-nine patients were randomized to the liposomal bupivacaine 266 mg (n = 34) or control group (n = 35). At all-time points post-surgery for both the mandible and the maxilla, the liposomal bupivacaine

group reported significantly less cumulative pain than the control group. At the conclusion of the 7-day follow-up, patients in the liposomal bupivacaine group experienced one-third less cumulative postsurgical pain than patients in the control group. Seventy-seven percent of patients in the liposomal bupivacaine group and 80% in the control group experienced a treatment-emergent adverse event. A higher percentage of patients in the liposomal bupivacaine versus control group reported itching (15% vs 9%) and constipation (38% vs 23%). The authors concluded that patients receiving an opioid-sparing postsurgical pain management protocol with liposomal bupivacaine 266 mg experienced a statistically significant reduction of postsurgical pain and clinically relevant reduction in opioid consumption.

In a 2017 Cochrane Systematic Review, Hamilton et al. conducted a review of randomized, double-blind, placebo or active-controlled clinical trials in people aged 18 years or over undergoing elective surgery, at any surgical site, if they compared liposomal bupivacaine infiltration at the surgical site with placebo or other type of analgesia. The authors had planned a comparison meta-analysis however there were insufficient data to ensure a clinically meaningful answer. The findings were instead presented as two 'Summary of Findings' narratives. The authors concluded that liposomal bupivacaine at the surgical site does appear to reduce postoperative pain compared to placebo; however, the limited evidence does not demonstrate superiority to bupivacaine hydrochloride. The authors acknowledge the sparseness of data for outcomes of interest, and a number of studies with a high risk of bias are limitations of this systematic review and limit the confidence in the effect estimates.

Lieblich et al. (2017, included in Ji systematic review) conducted a meta-analysis of this randomized, placebo-controlled study, which is the first formal evaluation of liposomal bupivacaine in the setting of dental surgery. The Infiltration Trial in Third Molar Extraction Observing the Analgesic Effect of EXPAREL (INNOVATE), U.S. National Institutes of Health clinical trials identifier NCT02517905 to assess the efficacy, safety, and tolerability of a single administration of liposomal bupivacaine in subjects undergoing bilateral third molar extraction. The results showed that EXPAREL was well tolerated but was not associated with a significant improvement compared with placebo on any of the outcome measures assessed in the primary efficacy analysis. When the study data were analyzed with subjects representing protocol violations removed, treatment with liposomal bupivacaine resulted in lower least-squares mean cumulative NRS pain intensity scores during the first 48 hours after surgery (primary efficacy measure) compared with placebo. Least-squares mean scores remained significantly lower compared with placebo through 96 hours after surgery, without negatively impacting opioid consumption or subjects' satisfaction with postsurgical pain control. It is likely that the observed results were confounded by the unexpectedly large number of protocol violations that occurred during the study. The authors concluded that while the results from this study of liposomal bupivacaine for postsurgical analgesia in subjects undergoing bilateral impacted third molar extraction are encouraging, additional investigation in prospective, randomized studies that incorporate clearly defined administration technique, rigorous data collection and protocol compliance will be necessary.

Glenn et al. (2016, included in Ji systematic review) conducted a prospective, randomized, double-blind trial to compare an infiltration of bupivacaine with liposomal bupivacaine (EXPAREL, Pacira Pharmaceuticals, San Diego, CA) for postoperative numbness and pain in symptomatic patients diagnosed with pulpal necrosis experiencing moderate to severe preoperative pain. One hundred patients randomly received a 4.0-mL buccal infiltration of either bupivacaine or liposomal bupivacaine after endodontic debridement. For postoperative pain, patients were given ibuprofen/acetaminophen, and they could receive narcotic pain medication if necessary. Patients recorded their level of numbness, pain, and medication use the night of the appointment and over the next 5 days. Success was measured as no or mild postoperative pain and no narcotic use. The results showed the success rate was 29% for the liposomal group and 22% for the bupivacaine group, with no significant difference between the groups. The authors concluded that for these patients, a 4.0-mL infiltration of liposomal bupivacaine did not result in a statistically significant increase in postoperative success compared with an infiltration of 4.0 mL bupivacaine and did not result in less need for narcotic/opioid pain medication.

Bultema et al. (2016, included in Ji systematic review) conducted a study to compare an infiltration of liposomal bupivacaine versus bupivacaine for pain control in untreated, symptomatic irreversible pulpitis. Ninety-five emergency patients received 2% lidocaine with 1:100,000 epinephrine via infiltration or an inferior alveolar nerve block to relieve their initial presenting pain. Patients then randomly received either 4 mL liposomal bupivacaine (13.3 mg/mL) or 4 mL 0.5% bupivacaine with 1:200,000 epinephrine by infiltration. Patients received a diary for the day of the appointment and 3 days post injection to record soft tissue numbness, pain levels, and analgesic (non-narcotic and narcotic) use. The results showed no significant differences ($p < .05$) between the 2 anesthetic formulations for pain or the use of pain medications. A statistically higher level of soft tissue numbness was found on days 1 to 3 for the liposomal bupivacaine group. The authors concluded that although liposomal bupivacaine had some effect on soft tissue anesthesia, it did not reduce pain to manageable clinical levels in patients presenting with untreated, symptomatic irreversible pulpitis.

Clinical Guidelines

American Association of Oral and Maxillofacial Surgeons (AAOMS)

In a 2020 white paper, revised in 2023, entitled “Opioid Prescribing: Acute and Postoperative Pain Management,” the AAOMS provides the following considerations for the management of acute and postoperative pain. While oral and maxillofacial surgeons should ultimately make all final prescribing decisions, the recommendations in this AAOMS White Paper are intended to provide direction and serve as a supportive resource.

- A nonsteroidal anti-inflammatory drug administered pre-emptively may decrease the severity of postoperative pain.
- A perioperative corticosteroid (dexamethasone) may limit swelling and decrease postoperative discomfort after third-molar extractions.
- A long-acting local anesthetic (e.g., bupivacaine, etidocaine, liposomal bupivacaine) may delay onset and severity of postoperative pain.
- The oral and maxillofacial surgeon should avoid starting treatment with long-acting or extended-release opioid analgesics.
- Providers should prescribe non-steroidal anti-inflammatory drugs (NSAIDs) as first-line analgesic therapy, unless contraindicated. If NSAIDs are contraindicated, providers should prescribe acetaminophen as first-line analgesic therapy.
- NSAIDs and acetaminophen, taken simultaneously, work synergistically to rival opioids in their analgesic effect, but dosage levels and times of administration should be carefully documented to prevent overdose.
- When indicated for acute breakthrough pain, consider short-acting opioid analgesics. If opioid analgesics are considered, start with the lowest possible effective dose and the shortest duration possible.
- When prescribing opioids, state law may require prescribers to access the state prescription drug monitoring program (PDMP). If there is any suspicion of patient drug misuse, abuse and/or addiction, the OMS should access the PDMP. To assess for opioid misuse or addiction, use targeted history or validated screening tools.
- All instructions for patient analgesia and analgesic prescriptions should be carefully documented.
- When deviating from these prescribing recommendations – or those required by state laws or institutions – the oral and maxillofacial surgeon should document the justification for doing so.
- Educate patients on the expectations of postoperative pain management and the anticipated levels of relief.

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

For all drugs refer to the following website and search by drug name:

<https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm>. (Accessed March 25, 2024)

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Policy History/Revision Information

Date	Summary of Changes
07/01/2024	<p>Supporting Information</p> <ul style="list-style-type: none"> Updated <i>Clinical Evidence</i>, <i>FDA</i>, and <i>References</i> sections to reflect the most current information Archived previous policy version DCP033.10

Instructions for Use

This Dental Clinical Policy provides assistance in interpreting UnitedHealthcare standard and Medicare Advantage dental plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard dental plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Dental Clinical Policy is provided for informational purposes. It does not constitute medical advice.