Producing patient records upon request

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Healthcare providers often misunderstand their obligation to provide patient records in response to a request from a patient or third party.

Patient requests and 'designated record set'

With very limited exceptions, patients and their personal representatives generally have a right to access and/or require the disclosure of protected health information in the patient's designated record set (45 CFR § 164.524(a)).

Regarding the limited exceptions, a provider may generally decline to produce records in response to a patient's or personal representative's request if, for example, the requested records 1) are not part of the patient's "designated record set," 2) are psychotherapy notes as defined by HIPAA, 3) were compiled in reasonable anticipation of litigation, 4) were obtained from a third party under the promise of confidentiality, and disclosure would reveal the source of the information or 5) disclosure would result in substantial harm to the patient or others. (See 45 CFR § 164.524(a).)

HIPAA defines "designated record set" as a group of records maintained by or for a covered entity that is:

- The medical records and billing records about individuals maintained by or for a covered healthcare provider or
- Used, in whole or in part, by or for the covered entity to make decisions about individuals (45 CFR § 164.501). As the OCR summarizes: The Privacy Rule generally requires HIPAA-covered entities (health plans and most healthcare providers) to provide individuals, upon request, with access to the protected health information (PHI) about them in one or more "designated record sets" maintained by or for the covered entity.

This includes the right to inspect or obtain a copy or both of the PHI as well as to direct the covered entity to transmit a copy to a designated person or entity of the individual's choice. Individuals have a right to access this PHI for as long as the information is maintained by a covered entity or a business associate on behalf of a covered entity regardless of the date the information was created; whether the information is maintained in paper or electronic systems onsite, remotely or is archived or where the PHI originated (e.g., whether the covered entity, another provider, the patient). (Individuals' Right under HIPAA to Access their Health Information 45 CFR § 164.524; OCR access guidance is available at HHS.gov/HIPAA/for-professionals/privacy/guidance/access/index.html.)

In separate frequently answered questions, the OCR explains further:

What personal health information do individuals have a right under HIPAA to access from their healthcare providers and health plans?
With limited exceptions, the HIPAA Privacy Rule gives individuals the right to access, upon request, the medical and health information (protected health information or PHI) about them in one or more designated record sets maintained by or for the individuals' healthcare providers and health plans (HIPAA-covered entities). (See 45 CFR § 164.524.) Designated record sets include medical records, billing records, payment and claims records, health plan enrollment records, case management records as well as other records used in whole or in part by or for a covered entity to make decisions about individuals. (See 45 CFR § 164.501.)

Thus, individuals have a right to access a broad array of health information about themselves, whether maintained by a covered entity or a business associate on the covered entity's behalf, including medical records, billing and payment records, insurance information, clinical laboratory test reports, X-rays, wellness and disease management program information and notes (such as clinical case notes or subjective, objective, assessment and plan [SOAP] notes but not including psychotherapy notes) among other information generated from treating the individual or paying for the individual's care or otherwise used to make decisions about individuals.

Individuals do not have a right to access PHI about them that is not part of a designated record set because this information is not used to make decisions about individuals. This may include certain quality assessment

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or improvement records, patient safety activity records or business planning, development and management records that are used for business decisions more generally rather than to make decisions about individuals.

For example, peer review files, practitioner or provider performance evaluations, quality control records used to improve customer service and formulary development records may be generated from and include an individual's PHI but may not be in the covered entity's designated record set(s) to which the individual has access. (See OCR frequently asked questions at HHS.gov/HIPAA/for-professionals/FAQ/2042/what-personal-health-information-do-individuals/index.html.)

Records from other providers

As the OCR's Access Guidance affirms, the "designated record set" includes records used by the covered entity to make healthcare decisions about a patient "regardless (of) where the (record) originated (e.g., whether the covered entity, another provider, the patient, etc.)."

OCR frequently asked questions (available at HHS.gov/OCR/privacy/HIPAA/FAQ/minimum_necessary/214.html) states: A provider might have a patient's medical record that contains older portions of a medical record created by another previous provider. Will the HIPAA Privacy Rule permit a provider who is a covered entity to disclose a complete medical record even though portions of the record were created by other providers?

Answer: Yes, the Privacy Rule permits a provider who is a covered entity to disclose a complete medical record, including portions that were created by another provider, assuming that the disclosure is for a purpose permitted by the Privacy Rule, such as treatment.

The OCR's more recent access guidance confirms that not only may the provider disclose records received from other providers, it generally must disclose such outside records that are a part of the designated record set in response to the patient's or personal representative's request unless one of the limited exceptions apply; failure to do so could subject the provider to HIPAA penalties.

'Legal health record'

Healthcare entities sometimes get hung up on the concept of the "legal health record" when trying to determine what

may or must be provided in response to patient or third-party requests for protected health information.

In contrast to the designated record set, there is no uniform or regulatory definition of the "legal health record," and its meaning depends on the user and context. Some may intend it to refer to the patient's "formal" medical record as defined and maintained by a provider; others use it to describe the medical records that would be used in court or produced in response to a subpoena.

Thus, when someone refers to the "legal health record," a provider must determine just what is intended. More specifically, when responding to a request for records, the covered entity must confirm who is requesting the information and what they are seeking rather than imposing its own unilateral definition of the "legal health record":

- As discussed, if the patient or personal representative requests the patient's records or asks that the patient's records be sent to a third party, a provider generally must produce all requested records that are maintained in the patient's designated record set unless one of the limited exceptions apply. (See 45 CFR § 164.524.) If he or she chooses, a provider may ask or confirm with the patient or personal representative which records are actually wanted.
- If a provider receives a valid HIPAA authorization from a third party seeking records, the provider may (but is not

required to) produce the specific records identified in the authorization, but not others. (See 45 CFR § 164.508.) If there is any question about which records are covered by the authorization, the provider should check with the patient to confirm what should be disclosed.

- If a provider receives a subpoena, order or warrant requesting records, the provider generally must produce the specific records or information identified in the subpoena, order or warrant. (See 45 CFR § 164.512(e)-(f).)

  Remember, the party issuing the subpoena or order may define the requested records differently than the provider. The issue is not what the provider thinks should be produced or how it unilaterally defines its own medical records; the issue is what records are requested by the subpoena, order or warrant.

  If the provider fails to produce the records that are requested, the provider may be subject to contempt sanctions. If the provider produces more than the records requested, the provider may be subject to HIPAA penalties.

  Accordingly, if there is any doubt as to the scope of records requested, the provider should contact the party issuing the subpoena to confirm what is intended and only produce the records identified in the subpoena, order or warrant. In doing so, the provider should be careful to avoid disclosing protected health information in the discussion.

- If a provider is required to disclose protected health information pursuant to a statute or regulation, the provider should ensure that he or she limits the scope of the disclosure to the specific information or records identified in the statute or regulation and strictly follows the statutory or regulatory process for such disclosures. (See 45 CFR § 164.512(a).)

- If a provider is disclosing information for a purpose permitted by HIPAA without the patient's authorization (e.g., disclosures to other providers for treatment purposes or to a payer for payment purposes), the provider should generally comply with the minimum necessary standard (i.e., do not disclose more than needed for the permissible purpose. (See 45 CFR § 164.514.)

  Note that when the provider receives a request from another healthcare provider for treatment purposes, the provider may assume that the other healthcare provider needs the records requested, which may include outside records.

Conclusion

When responding to requests or demands for records, providers must be careful not to interpret or respond to the request based on their own unilateral concept of the "medical record." Instead, they must ensure that they produce the records described by applicable statutes, regulations, subpoenas, orders or warrants regardless of how the provider would characterize the records or, most often, who created the records.

Questions? Email the author at kcstanger@hollandhart.com. ■

This is number 170 in a series of articles on practice management and marketing for oral and maxillofacial surgeons developed under the auspices of the Committee on Practice Management and Professional Staff Development and AAOMS staff. Practice Management Notes from 2002 to present are available online at AAOMS.org.

EXPAREL®

(bupivacaine liposome injectable suspension)

Brief Summary
(For full prescribing information refer to package insert)

INDICATIONS AND USAGE

EXPAREL is indicated for single-dose infiltration in adults to produce postsurgical local analgesia and as an interscalene brachial plexus nerve block to produce postsurgical regional analgesia.

Limitation of Use: Safety and efficacy has not been established in other nerve blocks.

CONTRAINDICATIONS

EXPAREL is contraindicated in obstetrical paracervical block anesthesia. While EXPAREL has not been tested with this technique, the use of bupivacaine HCl with this technique has resulted in fetal bradycardia and death.

WARNINGS AND PRECAUTIONS

Warnings and Precautions Specific for EXPAREL

As there is a potential risk of severe life-threatening adverse effects associated with the administration of bupivacaine, EXPAREL should be administered in a setting where trained personnel and equipment are available to promptly treat patients who show evidence of neurological or cardiac toxicity.

Caution should be taken to avoid accidental intravascular injection of EXPAREL. Convulsions and cardiac arrest have occurred following accidental intravascular injection of bupivacaine and other amide-containing products.

Avoid additional use of local anesthetics within 96 hours following administration of EXPAREL.

EXPAREL has not been evaluated for the following uses and, therefore, is not recommended for these types of analgesia or routes of administration.

- epidural
- intrathecal
- regional nerve blocks other than interscalene brachial plexus nerve block
- intravascular or intra-articular use

EXPAREL has not been evaluated for use in the following patient population and, therefore, it is not recommended for administration to these groups.

- patients younger than 18 years old
- pregnant patients

The potential sensory and/or motor loss with EXPAREL is temporary and varies in degree and duration depending on the site of injection and dosage administered and may last for up to 5 days as seen in clinical trials.

ADVERSE REACTIONS

Clinical Trial Experience

Adverse Reactions Reported in Local Infiltration Clinical Studies

The safety of EXPAREL was evaluated in 10 randomized, double-blind, local administration into the surgical site clinical studies involving 823 patients undergoing various surgical procedures. Patients were administered a dose ranging from 66 to 532 mg of EXPAREL. In these studies, the most common adverse reactions (incidence greater than or equal to 10%) following EXPAREL administration were nausea, constipation, and vomiting. The common adverse reactions (incidence greater than or equal to 2% to less than 10%) following EXPAREL administration were pyrexia, dizziness, edema peripheral, anemia, hypotension, pruritus, tachycardia, headache, insomnia, anemia postoperative, muscle spasms, hemorrhagic anemia, back pain, somnolence, and procedural pain.

Adverse Reactions Reported in Nerve Block Clinical Studies

The safety of EXPAREL was evaluated in four randomized, double-blind, placebo-controlled nerve block clinical studies involving 469 patients undergoing various surgical procedures. Patients were administered a dose of either 133 or 266 mg of EXPAREL. In these studies, the most common adverse reactions (incidence greater than or equal to 10%) following EXPAREL administration were nausea, pyrexia, and constipation.

The common adverse reactions (incidence greater than or equal to 2% to less than 10%) following EXPAREL administration as a nerve block were muscle twitching, dysgeusia, urinary retention, fatigue, headache, confusional state, hypotension, hypertension, hypoesthesia oral, pruritus generalized, hyperhidrosis, tachycardia, sinus tachycardia, anxiety, fall, body temperature increased, edema peripheral, sensory loss, hepatic enzyme increased, hiccups, hypoxia, post-procedural hematoma.

Postmarketing Experience

These adverse reactions are consistent with those observed in clinical studies and most commonly involve the following system organ classes (SOCs): Injury, Poisoning, and Procedural Complications (e.g., drug-drug interaction, procedural pain), Nervous System Disorders (e.g., palsy, seizure), General Disorders And Administration Site Conditions (e.g., lack of efficacy, pain), Skin and Subcutaneous Tissue Disorders (e.g., erythema, rash), and Cardiac Disorders (e.g., bradycardia, cardiac arrest).

DRUG INTERACTIONS

The toxic effects of local anesthetics are additive and their co-administration should be used with caution including monitoring for neurologic and cardiovascular effects related to local anesthetic systemic toxicity. Avoid additional use of local anesthetics within 96 hours following administration of EXPAREL.

Patients who are administered local anesthetics may be at increased risk of developing methemoglobinemia when concurrently exposed to the following drugs, which could include other local anesthetics:

Examples of Drugs Associated with Methemoglobinemia:

Class	Examples
Nitrates/Nitrites	nitric oxide, nitroglycerin, nitroprusside, nitrous oxide
Local anesthetics	articaine, benzocaine, bupivacaine, lidocaine, mepivacaine, prilocaine, procaine, ropivacaine, tetracaine
Antineoplastic agents	cyclophosphamide, flutamide, hydroxyurea, ifosfamide, rasburicase
Antibiotics	dapsone, nitrofurantoin, para-aminosalicylic acid, sulfonamides
Antimalarials	chloroquine, primaquine
Anticonvulsants	Phenobarbital, phenytoin, sodium valproate
Other drugs	acetaminophen, metoclopramide, quinine, sulfasalazine

Bupivacaine

Bupivacaine HCl administered together with EXPAREL may impact the pharmacokinetic and/or physicochemical properties of EXPAREL, and this effect is concentration dependent. Therefore, bupivacaine HCl and EXPAREL may be administered simultaneously in the same syringe, and bupivacaine HCl may be injected immediately before EXPAREL as long as the ratio of the milligram dose of bupivacaine HCl solution to EXPAREL does not exceed 1:2.

Non-bupivacaine Local Anesthetics

EXPAREL should not be admixed with local anesthetics other than bupivacaine. Nonbupivacaine based local anesthetics, including lidocaine, may cause an immediate release of bupivacaine from EXPAREL if administered together locally. The administration of EXPAREL may follow the administration of lidocaine after a delay of 20 minutes or more. There are no data to support administration of other local anesthetics prior to administration of EXPAREL.

Other than bupivacaine as noted above, EXPAREL should not be admixed with other drugs prior to administration.

Water and Hypotonic Agents

Do not dilute EXPAREL with water or other hypotonic agents, as it will result in disruption of the liposomal particles

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

There are no studies conducted with EXPAREL in pregnant women. In animal reproduction studies, embryo-fetal deaths were observed with subcutaneous administration of bupivacaine to rabbits during organogenesis at a dose equivalent to 1.6 times the maximum recommended human dose (MRHD) of 266 mg. Subcutaneous administration of bupivacaine to rats from implantation through weaning produced decreased pup survival at a dose equivalent to 1.5 times the MRHD [see Data]. Based on animal data, advise pregnant women of the potential risks to a fetus.

The background risk of major birth defects and miscarriage for the indicated population is unknown. However, the background risk in the U.S. general population of major birth defects is 2-4% and of miscarriage is 15-20% of clinically recognized pregnancies.

Clinical Considerations

Labor or Delivery

Bupivacaine is contraindicated for obstetrical paracervical block anesthesia. While EXPAREL has not been studied with this technique, the use of bupivacaine for obstetrical paracervical block anesthesia has resulted in fetal bradycardia and death.

Bupivacaine can rapidly cross the placenta, and when used for epidural, caudal, or pudendal block anesthesia, can cause varying degrees of maternal, fetal, and neonatal toxicity. The incidence and degree of toxicity depend upon the procedure performed, the type, and amount of drug used, and the technique of drug administration. Adverse reactions in the parturient, fetus, and neonate involve alterations of the central nervous system, peripheral vascular tone, and cardiac function.

Data

Animal Data

Bupivacaine hydrochloride was administered subcutaneously to rats and rabbits during the period of organogenesis (implantation to closure of the hard plate). Rat doses were 4.4, 13.3, and 40 mg/kg/day (equivalent to 0.2, 0.5 and 1.5 times the MRHD, respectively, based on the BSA comparisons and a 60 kg human weight) and rabbit doses were 1.3, 5.8, and 22.2 mg/kg/day (equivalent to 0.1, 0.4 and 1.6 times the MRHD, respectively, based on the BSA comparisons and a 60 kg human weight). No embryo-fetal effects were observed in rats at the doses tested with the high dose causing increased maternal lethality. An increase in embryo-fetal deaths was observed in rabbits at the high dose in the absence of maternal toxicity.

Decreased pup survival was noted at 1.5 times the MRHD in a rat pre- and post-natal development study when pregnant animals were administered subcutaneous doses of 4.4, 13.3, and 40 mg/kg/day buprenorphine hydrochloride (equivalent to 0.2, 0.5 and 1.5 times the MRHD, respectively, based on the BSA comparisons and a 60 kg human weight) from implantation through weaning (during pregnancy and lactation).

Lactation

Risk Summary

Limited published literature reports that bupivacaine and its metabolite, pipecoloxylidide, are present in human milk at low levels. There is no available information on effects of the drug in the breastfed infant or effects of the drug on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for EXPAREL and any potential adverse effects on the breastfed infant from EXPAREL or from the underlying maternal condition.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

Geriatric Use

Of the total number of patients in the EXPAREL local infiltration clinical studies (N=823), 171 patients were greater than or equal to 65 years of age and 47 patients were greater than or equal to 75 years of age. Of the total number of patients in the EXPAREL nerve block clinical studies (N=531), 241 patients were greater than or equal to 65 years of age and 60 patients were greater than or equal to 75 years of age. No overall differences in safety or effectiveness were observed between these patients and younger patients. Clinical experience with EXPAREL has not identified differences in efficacy or safety between elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Hepatic Impairment

Amide-type local anesthetics, such as bupivacaine, are metabolized by the liver. Patients with severe hepatic disease, because of their inability to metabolize local anesthetics normally, are at a greater risk of developing toxic plasma concentrations, and potentially local anesthetic systemic toxicity. Therefore, consider increased monitoring for local anesthetic systemic toxicity in subjects with moderate to severe hepatic disease.

Renal Impairment

Bupivacaine is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. This should be considered when performing dose selection of EXPAREL.

OVERDOSAGE

Clinical Presentation

Acute emergencies from local anesthetics are generally related to high plasma concentrations encountered during therapeutic use of local anesthetics or to unintended intravascular injection of local anesthetic solution.

Signs and symptoms of overdose include CNS symptoms (perioral paresthesia, dizziness, dysarthria, confusion, mental obtundation, sensory and visual disturbances and eventually convulsions) and cardiovascular effects (that range from hypertension and tachycardia to myocardial depression, hypotension, bradycardia and asystole).

Plasma levels of bupivacaine associated with toxicity can vary. Although concentrations of 2,500 to 4,000 ng/mL have been reported to elicit early subjective CNS symptoms of bupivacaine toxicity, symptoms of toxicity have been reported at levels as low as 800 ng/mL.

Management of Local Anesthetic Overdose

At the first sign of change, oxygen should be administered.

The first step in the management of convulsions, as well as underventilation or apnea, consists of immediate attention to the maintenance of a patent airway and assisted or controlled ventilation with oxygen and a delivery system capable of permitting immediate positive airway pressure by mask. Immediately after the institution of these ventilatory measures, the adequacy of the circulation should be evaluated, keeping in mind that drugs used to treat convulsions sometimes depress the circulation when administered intravenously. Should convulsions persist despite adequate respiratory support, and if the status of the circulation permits, small increments of an ultra-short acting barbiturate (such as thiopental or thiamylal) or a benzodiazepine (such as diazepam) may be administered intravenously. The clinician should be familiar, prior to the use of anesthetics, with these anticonvulsant drugs. Supportive treatment of circulatory depression may require administration of intravenous fluids and, when appropriate, a vasopressor dictated by the clinical situation (such as ephedrine to enhance myocardial contractile force).

If not treated immediately, both convulsions and cardiovascular depression can result in hypoxia, acidosis, bradycardia, arrhythmias and cardiac arrest. If cardiac arrest should occur, standard cardiopulmonary resuscitative measures should be instituted.

Endotracheal intubation, employing drugs and techniques familiar to the clinician, maybe indicated, after initial administration of oxygen by mask, if difficulty is encountered in the maintenance of a patent airway or if prolonged ventilatory support (assisted or controlled) is indicated.

DOSAGE AND ADMINISTRATION

Important Dosage and Administration Information

- EXPAREL is intended for single-dose administration only.
- Different formulations of bupivacaine are not bioequivalent even if the milligram strength is the same. Therefore, it is not possible to convert dosing from any other formulations of bupivacaine to EXPAREL.
- DO NOT dilute EXPAREL with water for injection or other hypotonic agents, as it will result in disruption of the liposomal particles.
- Use suspensions of EXPAREL diluted with preservative-free normal (0.9%) saline for injection or lactated Ringer's solution within 4 hours of preparation in a syringe.
- Do not administer EXPAREL if it is suspected that the vial has been frozen or exposed to high temperature (greater than 40°C or 104°F) for an extended period.
- Inspect EXPAREL visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Do not administer EXPAREL if the product is discolored.

Recommended Dosing in Adults

Local Analgesia via Infiltration

The recommended dose of EXPAREL for local infiltration in adults is up to a maximum dose of 266mg (20 mL), and is based on the following factors:

- Size of the surgical site
- Volume required to cover the area
- Individual patient factors that may impact the safety of an amide local anesthetic

As general guidance in selecting the proper dosing, two examples of infiltration dosing are provided:

- In patients undergoing bunionectomy, a total of 106 mg (8 mL) of EXPAREL was administered with 7 mL infiltrated into the tissues surrounding the osteotomy, and 1 mL infiltrated into the subcutaneous tissue.
- In patients undergoing hemorrhoidectomy, a total of 266 mg (20 mL) of EXPAREL was diluted with 10 mL of saline, for a total of 30 mL, divided into six 5 mL aliquots, injected by visualizing the anal sphincter as a clock face and slowly infiltrating one aliquot to each of the even numbers to produce a field block.

Regional Analgesia via Interscalene Brachial Plexus Nerve Block

The recommended dose of EXPAREL for interscalene brachial plexus nerve block in adults is 133 mg (10 mL), and is based upon one study of patients undergoing either total shoulder arthroplasty or rotator cuff repair.

Compatibility Considerations

Admixing EXPAREL with drugs other than bupivacaine HCl prior to administration is not recommended.

- Non-bupivacaine based local anesthetics, including lidocaine, may cause an immediate release of bupivacaine from EXPAREL if administered together locally. The administration of EXPAREL may follow the administration of lidocaine after a delay of 20 minutes or more.
- Bupivacaine HCl administered together with EXPAREL may impact the pharmacokinetic and/or physicochemical properties of EXPAREL, and this effect is concentration dependent. Therefore, bupivacaine HCl and EXPAREL may be administered simultaneously in the same syringe, and bupivacaine HCl may be injected immediately before EXPAREL as long as the ratio of the milligram dose of bupivacaine HCl solution to EXPAREL does not exceed 1:2.

  The toxic effects of these drugs are additive and their administration should be used with caution including monitoring for neurologic and cardiovascular effects related to local anesthetic systemic toxicity.
- When a topical antiseptic such as povidone iodine (e.g., Betadine®) is applied, the site should be allowed to dry before EXPAREL is administered into the surgical site. EXPAREL should not be allowed to come into contact with antiseptics such as povidone iodine in solution.

Studies conducted with EXPAREL demonstrated that the most common implantable materials (polypropylene, PTFE, silicone, stainless steel, and titanium) are not affected by the presence of EXPAREL any more than they are by saline. None of the materials studied had an adverse effect on EXPAREL.

Non-Interchangeability with Other Formulations of Bupivacaine

Different formulations of bupivacaine are not bioequivalent even if the milligram dosage is the same. Therefore, it is not possible to convert dosing from any other formulations of bupivacaine to EXPAREL and vice versa.

Liposomal encapsulation or incorporation in a lipid complex can substantially affect a drug's functional properties relative to those of the unencapsulated or nonlipid-associated drug. In addition, different liposomal or lipid-complexed products with a common active ingredient may vary from one another in the chemical composition and physical form of the lipid component. Such differences may affect functional properties of these drug products. Do not substitute.

CLINICAL PHARMACOLOGY

Pharmacokinetics

Administration of EXPAREL results in significant systemic plasma levels of bupivacaine which can persist for 96 hours after local infiltration and 120 hours after interscalene brachial plexus nerve block. In general, peripheral nerve blocks have shown systemic plasma levels of bupivacaine for extended duration when compared to local infiltration. Systemic plasma levels of bupivacaine following administration of EXPAREL are not correlated with local efficacy.

PATIENT COUNSELING

Inform patients that use of local anesthetics may cause methemoglobinemia, a serious condition that must be treated promptly. Advise patients or caregivers to seek immediate medical attention if they or someone in their care experience the following signs or symptoms: pale, gray, or blue colored skin (cyanosis); headache; rapid heart rate; shortness of breath; lightheadedness; or fatigue.

PACIRA PHARMACEUTICALS, INC.

Pacira Pharmaceuticals, Inc.
San Diego, CA 92121 USA

Patent Numbers:
6,132,766 5,891,467 5,766,627 8,182,835

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*The clinical benefit of the decrease in opioid consumption was not demonstrated in the pivotal trials.

Indication

EXPAREL is indicated for single-dose infiltration in adults to produce postsurgical local analgesia and as an interscalene brachial plexus nerve block to produce postsurgical regional analgesia. Safety and efficacy have not been established in other nerve blocks.

Important Safety Information

EXPAREL is contraindicated in obstetrical paracervical block anesthesia. Adverse reactions reported with an incidence greater than or equal to 10% following EXPAREL administration via infiltration were nausea, constipation, and vomiting; adverse reactions reported with an incidence greater than or equal to 10% following EXPAREL administration via interscalene brachial plexus nerve block were nausea, pyrexia, and constipation. If EXPAREL and other non-bupivacaine local anesthetics, including lidocaine, are administered at the same site, there may be an immediate release of bupivacaine from EXPAREL. Therefore, EXPAREL may be administered to the same site 20 minutes after injecting lidocaine. EXPAREL is not recommended to be used in the following patient population: patients <18 years old and/or pregnant patients. Because amide-type local anesthetics, such as bupivacaine, are metabolized by the liver, EXPAREL should be used cautiously in patients with hepatic disease.

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Warnings and Precautions Specific to EXPAREL: Avoid additional use of local anesthetics within 96 hours following administration of EXPAREL. EXPAREL is not recommended for the following types or routes of administration: epidural, intrathecal, regional nerve blocks **other than interscalene brachial plexus nerve block**, or intravascular or intra-articular use. The potential sensory and/or motor loss with EXPAREL is temporary and varies in degree and duration depending on the site of injection and dosage administered and may last for up to 5 days, as seen in clinical trials.

Warnings and Precautions for Bupivacaine-Containing Products

Central Nervous System (CNS) Reactions: There have been reports of adverse neurologic reactions with the use of local anesthetics. These include persistent anesthesia and paresthesia. CNS reactions are characterized by excitation and/or depression. **Cardiovascular System Reactions:** Toxic blood concentrations depress cardiac conductivity and excitability which may lead to dysrhythmias, sometimes leading to death. **Allergic Reactions:** Allergic-type reactions (eg, anaphylaxis and angioedema) are rare and may occur as a result of hypersensitivity to the local anesthetic or to other formulation ingredients. **Chondrolysis:** There have been reports of chondrolysis (mostly in the shoulder joint) following intra-articular infusion of local anesthetics, which is an unapproved use. **Methemoglobinemia:** Cases of methemoglobinemia have been reported with local anesthetic use.

Please refer to brief summary of full Prescribing Information on adjacent page.
Full Prescribing Information is available at www.EXPAREL.com.
For more information, please visit www.EXPAREL.com or call 1-855-RX-EXPAREL (793-9727).

References: 1. Gupta N, Vujicic M, Blatz A. Opioid prescribing practices from 2010 through 2015 among dentists in the United States: what do claims data tell us? *J Am Dent Assoc*. 2018;149(4):237-245. **2.** Moore PA, Ziegler KM, Lipman RD, Aminoshariae A, Carrasco-Labra A, Mariotti A. Benefits and harms associated with analgesic medications used in the management of acute dental pain. *JADA*. 2018;149(4):256-268. **3.** Mont MA, Beaver WB, Dysart SH, Barrington JW, Del Gaizo DJ. Local infiltration analgesia with liposomal bupivacaine improves pain scores and reduces opioid use after total knee arthroplasty: results of a randomized controlled trial. *J Arthroplasty*. 2018;33(1):90-96.

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