

# Gebauer's Pain Ease®

Topical Anesthetic Skin Refrigerant

## TECHNICAL DATA DOCUMENT

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Gebauer's  
**PainEase®**  
The INSTANT topical anesthetic

 **Gebauer Company**

# GEBAUER'S PAIN EASE®

## Topical Aerosol Skin Refrigerant

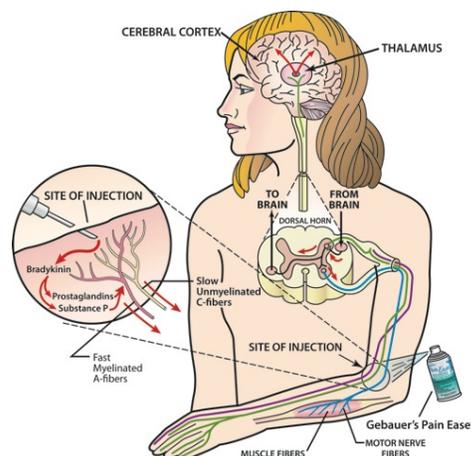
### Description

Gebauer's Pain Ease consists of a proprietary blend of 1,1,1,3,3-Pentafluoropropane (high purity HFC-245fa) and 1,1,1,2-Tetrafluoroethane (pharma grade HFC-134a) that produces an instantaneous cooling effect upon contact with the skin, intact mucous membranes and minor open wounds. The product is delivered in the form of an aerosol in either a mist or medium stream spray. Upon contact with the skin or mucosal membranes, the product evaporates immediately due to the low boiling point of the chemical blend and the unique delivery system. This evaporation of the product draws heat away from the skin and results in a cooling effect on the skin.

Gebauer's Pain Ease is non-flammable.

### Mechanism of Action

When topically applied to the skin or intact mucous membranes, Gebauer's Pain Ease creates an instantaneous cooling effect on the surface of the application site by the immediate evaporation of the product from the skin surface. The coldness created by the spray decreases the nerve conduction velocity of the C fibers and A-delta fibers that make up the peripheral nervous system, thus interrupting the nociceptive inputs to the spinal cord.<sup>1</sup>

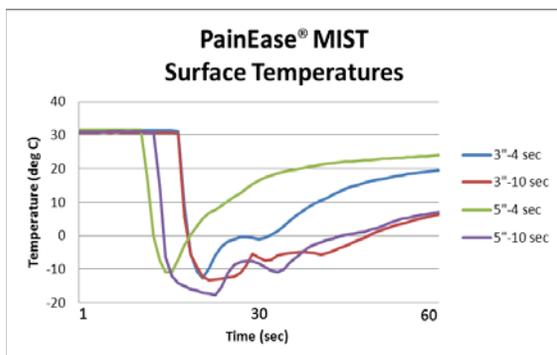


*Cooling Effect:* When Gebauer's Pain Ease begins to evaporate from the surface of the target area after application, a cooling effect results. The cooling sensation produced is directly related to the type of stream and the distance from the point of contact.

The mist produces very fine droplets that create instantaneous cold at the points of contact. The fine droplets are dispersed in a circular pattern with an approximate 2-inch diameter when sprayed from a distance of 4 inches from the target. The medium stream spray produces a pinpoint stream that contacts the skin surface at a specific single location.

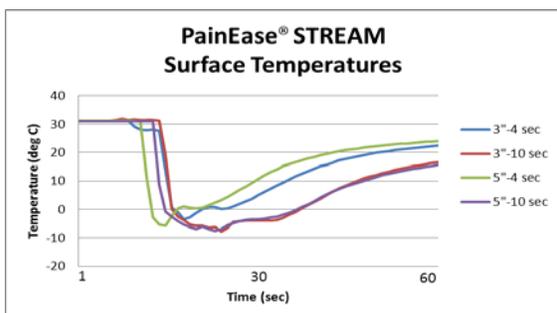
As the distance from the target surface is increased, the dispersion of the droplets in both the mist and medium stream is increased. Increasing the surface area of contact and decreasing the size of the droplets increases the evaporation rate. The increase in evaporation rate correlates to an increase in the cooling effect.

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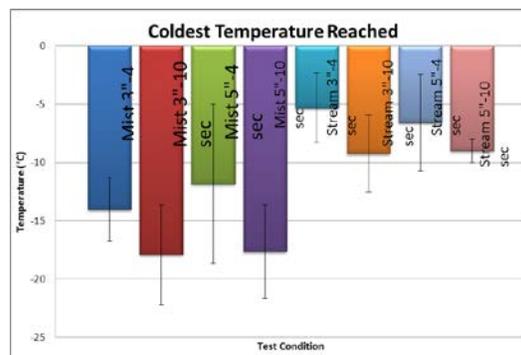
*\* Data is an average of individual results collected during a clinical trial at The Ohio State University by Dr. M. Merrick.*

Gebauer's Pain Ease Mist is most effective for general cooling of the skin, intact mucous membranes, and minor open wounds where precise contact is not indicated. Since the evaporation rate is increased, a more intense cooling effect will be created at the initial point of application over a larger area.



*\* Data is an average of individual results collected during a clinical trial at The Ohio State University by Dr. M. Merrick.*

Gebauer's Pain Ease Medium Stream is most effective for creating an anesthetic effect on the skin or intact mucous membranes at a specific pinpoint site.



*\* Data is an average of individual results collected during a clinical trial at The Ohio State University by Dr. M. Merrick.*

According to a study performed at The Ohio State University by Dr. M. Merrick, the comparison between Gebauer's Pain Ease Mist and Stream products yielded results that indicated lowest average temperature reached over various distances and dispense time. The data of the clinical trial concluded that on average the mist product showed a lower temperature reached on the skin compared to the stream product. However, both Gebauer's Pain Ease product variations demonstrated an initial cooling that created an anesthetic effect on the skin. <sup>2</sup>

## Indications and Use

Gebauer's Pain Ease Medium Stream and Mist configurations are safe for use on skin, intact mucous membranes (oral cavity, nasal passages and lips) and minor open wounds for the following indications:

### *Pain Management due to*

- Injections such as venipuncture, IV starts and cosmetic procedures
- Minor surgical procedures such as lancing boils, incisions,

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drainage of small abscesses and suturing

- Minor sports injuries such as sprains, bruising, cuts and abrasions

*The Medium Stream is also intended as a counterirritant in the management of*

- Myofascial Pain
- Restricted Motion
- Muscle Tension

### **Contraindications**

Gebauer's Pain Ease is contraindicated in individuals with a history of hypersensitivity to 1,1,1,3,3-Pentafluoropropane and 1,1,1,2-Tetrafluoroethane. If skin irritation develops, discontinue use.

### **Warnings**

Gebauer's Pain Ease is for external use, for use on minor open wounds, and for use on intact mucous membranes only.

The contents are under pressure. Do not puncture or incinerate the container. Do not expose to heat or store at temperatures above 50°C (120°F).

Dispose of in accordance with local and national regulations.

### **Adverse Reactions**

Cutaneous sensitization may occur in rare cases.

Freezing can occasionally alter skin pigmentation. Injury to the skin due to extreme cold or irritation may create post inflammatory hypopigmentation due to death of melanocytes in the epidermal layer of the skin. This reaction

may be more apparent in people with dark complexions. Often, pigmentary changes slowly return to normal over several months. The effects of post-inflammatory hypopigmentation may be permanent.<sup>3</sup>

### **Precautions**

The following precautions should be observed when using Gebauer's Pain Ease:

- 1) Do not spray in the eyes. Do not use this product on persons with poor circulation or insensitive skin.
- 2) When used to produce local freezing of tissues, adjacent skin areas should be protected by an application of petroleum.
- 3) The freezing and thawing process may be painful, and freezing may lower local resistance to infection and delay healing.
- 4) Over application of the product might cause frostbite and/or alter skin pigmentation.
- 5) Do not use on large areas of damaged skin, puncture wounds, animal bites or serious wounds.
- 6) Apply only to intact mucous membranes.
- 7) Do not use on genital mucous membranes.

### **Keep Out of the Reach of Children**

As the safety for the use of the Pain Ease in pediatric patients has not been established, it is recommended that the device should not be used on patients under the age of 4 years without consultation of a pediatrician.

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### **Biocompatibility**

All biocompatibility and toxicology testing was performed in accordance with ISO 10993-1: *Biological Evaluation of Medical Devices within a Risk Management Process* and Attachment A of FDA's *Guidance on ISO 10993-1 Risk Based Approach*. All testing was performed by independent testing laboratories.

*Cytotoxicology:* Gebauer's Pain Ease was tested for cytotoxicity in accordance to ISO 10993-5 *Tests for Cytotoxicity – In Vitro Tests* and was found to be non-toxic when used as recommended.

Acute cytotoxicity of the product was tested by observing the % inhibition of the cell viability of L-929 mouse fibroblast cells when Gebauer's Pain Ease was "sprayed" on the cells for 5 seconds and incubated at 5% CO<sub>2</sub> and 37°C. The 5 second dosage was not found to be cytotoxic and had little effect on the L-929 mouse fibroblast cell viability.

*Dermal Sensitization:* A dermal sensitization study was performed in accordance with ISO 10993-10, *Tests for Irritation and Sensitization* on guinea pigs using a modified Buehler method to determine the dermal sensitization in the guinea pig with repeated dermal exposure of 7 seconds of Gebauer's Pain Ease. The animals were exposed to the product three times a week for three weeks. The animals remained in good health throughout the induction phases and no abnormal clinical findings were observed. There was slight erythema noted in one animal at the first induction exposure. There were no incidents of edema noted during the induction

phases. During the challenge phase of the study, one animal had minimal erythema at the 24-hour stage. No incidents of edema were observed during the challenge stage. Based on these results, Gebauer's Pain Ease did not produce dermal sensitization in guinea pigs under the conditions of the study.

*Acute Dermal Toxicity:* An acute dermal toxicity study was performed in accordance to US EPA, OPPTS Health Effects Test Guidelines 870.1200, *Tests for Acute Dermal Toxicity* on Sprague-Dawley Rats to determine the acute dermal toxicity of Gebauer's Pain Ease. No animals died during the study, and the animals gained weight as expected. Observations made at 1 hour, 2.5 hours, 4 hours, 1 day and daily up to 14 days showed no clinical effects as a result of the treatment. Necropsy of the tissues at the end of the study were found to be grossly normal. Gebauer's Pain Ease does not produce acute dermal toxicity.

*Oral Irritation:* A study was executed in accordance to ISO 10993-10, *Tests for Irritation and Sensitization* on Syrian Hamsters to determine the acute oral irritation produced by exposure to Gebauer's Pain Ease. A group of hamsters was exposed to the product by directly spraying the cheek pouch with product on a single occasion for 6 seconds and observing for signs of irritation. In addition, a second group of hamsters was exposed to the product 5 times in a 4-hour period by directly spraying the cheek pouch with product and observing for signs of irritation. Oral observations showed that no irritation was observed for the single dosage group, and an irritation score of <1 was observed for the 5 doses over a

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4-hour period, which shows that the irritation observed was between no erythema and very slight erythema (hardly perceptible). Histopathology was performed on the cheek pouches and compared to the control group. Based on the results of the oral irritation histopathology report, Gebauer's Pain Ease is a non-irritant when applied as a single dose. Gebauer's Pain Ease is a minimal irritant when applied five times over a period of four hours.

The results of this study confirm the indication for use of Gebauer's Pain Ease on intact mucous membranes.

*Inhalation Toxicity:* Gebauer's Pain Ease has a very low to minimal toxicity by inhalation. Studies performed on mice/rats showed that 1,1,1,2-Tetrafluoroethane and 1,1,1,3,3-Pentafluoropropane were non-toxic by inhalation. A series of 28-Day and 13-Week Inhalation studies were performed using 1,1,1,3,3-Pentafluoropropane. In a snout-only exposure to 1,1,1,3,3-Pentafluoropropane with mice, no lethality was seen even with exposure levels over 100,000 ppm for 4 hours. In rats, 4-hour whole body exposures to levels as high as 203,000 ppm did not cause mortality. Although some signs of mild central nervous system depression were seen with exposures at 143,000ppm and 203,000 ppm, these were only seen during exposure, with the animals showing recovery within 30 minutes of the end of the exposure period. These findings indicate that 1,1,1,3,3-Pentafluoropropane is not acutely toxic by inhalation and that even high-level exposures do not result in marked signs of toxicity.<sup>4</sup>

Subchronic and chronic studies were carried out in the rat with exposures to 1,1,1,2-Tetrafluoroethane by inhalation. Repeated exposure to 50,000 ppm of 1,1,1,2-Tetrafluoroethane for 13, 52, and 104 weeks elicited no effect on clinical condition, growth, and survival, or on a variety of hematological, clinical chemistry, and urinary parameters. Treatment-related pathological changes were seen only at study termination at 2 years and were confined to increased incidence of Leydig cell hyperplasia and adenoma in male rats exposed to 50,000 ppm. The tumors were benign and not life threatening. These studies demonstrate that 1,1,1,2-Tetrafluoroethane has very low toxicity by inhalation.<sup>6</sup>

*Effects on Fertility:* Gebauer's Pain Ease is safe for use during pregnancy when used as directed. Studies performed on rats showed that 1,1,1,2-Tetrafluoroethane and 1,1,1,3,3-Pentafluoropropane were non-teratogenic and did not cause fetal effects at levels of 50,000 ppm. Rats exposed daily to levels of 50,000 ppm 1,1,1,2-Tetrafluoroethane for six hours from day 6 to day 19 of gestation at the 50,000 ppm level had a reduction in body weight and food consumption. No significant effects were seen on fetal parameters. Pup weight, litter size, and uterine weights were slightly reduced when compared to controls. The incidents of malformation, skeletal and visceral anomalies, and skeletal variants were comparable to the control group.<sup>4</sup> When exposed daily to 300,000 ppm of 1,1,1,2-Tetrafluoroethane during day 6 through 15 of gestation, there was a significant reduction in fetal weight and increase in skeletal variations.<sup>6</sup>

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### *Cardiac Sensitization:*

1,1,1,3,3-Pentafluoropropane and 1,1,1,2-Tetrafluoroethane are known to be cardiac sensitizers when inhaled in quantities greater than 80,000 ppm<sup>4</sup> and 44,000 ppm<sup>5</sup> respectively. In studies performed on beagle dogs, fatal ventricular fibrillation was seen at 74,000 ppm, one incident of ventricular defibrillation occurred at 44,000 ppm, and no incidents of cardiac sensitization were seen at 34,100 ppm for 1,1,1,3,3-Pentafluoropropane.<sup>4</sup>

*Carcinogenesis:* Gebauer's Pain Ease is not carcinogenic. When 1,1,1,2-Tetrafluoroethane was administered to rats for 104 weeks, there was a slight increase in the incidence of testicular Leydig cell adenomas in the male rats. This type of tumor does not progress to malignancy in humans, and the lack of genotoxicity supports the conclusion that

1,1,1,2-Tetrafluoroethane is not carcinogenic.<sup>6</sup> Genotoxicity in 1,1,1,3,3-Pentafluoropropane has not been shown, and various inhalation studies have produced no carcinogenic effects.<sup>4</sup>

### **Performance**

Gebauer Company has executed the following performance testing to verify that Gebauer's Pain Ease provides a safe and effective product.

*Number of Applications:* Gebauer's Pain Ease products have approximately 50 doses per can when applied for an average time of 5 seconds per dose.

*Chemical Compatibility:* Chemical compatibility testing was performed by the manufacturers of 1,1,1,3,3-Pentafluoropropane and 1,1,1,2-Tetrafluoroethane to determine the chemical stability of the Gebauer's Pain Ease blend. In chemical stability studies 1,1,1,3,3-Pentafluoropropane and 1,1,1,2-Tetrafluoroethane were both found to be stable at temperatures up to 400°F. A mixture of 1,1,1,3,3-Pentafluoropropane and 1,1,1,2-Tetrafluoroethane was stored in a tin-plated aerosol can with a valve and dip tube for a period of two months in ambient conditions. Results from GC/MS analysis confirmed that there were no new compounds formed during the storage due to chemical incompatibility.

*Material Compatibility:* Material compatibility data for the following materials has been performed with Gebauer's Pain Ease in order to show package integrity. Results of the compatibility analysis can be found in Table 1.

**Table 1**  
**Material Compatibility of**  
**Gebauer's Pain Ease**

Material	Compatibility
Butyl	Excellent
Poly-propylene	Excellent
Nylon	Excellent
Epoxy	Excellent
Buna N	Excellent

The packaging materials tested show excellent material compatibility characteristics. Based on the results, there was no evidence of leachables or breakdown of the packaging components that would lead to contamination or product malfunctioning.

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*Product Stability:* Stability studies are routinely conducted to determine the chemical stability and packaging integrity of Gebauer's Pain Ease in accordance with Q1A Stability Testing of New Drug Substances and Products, ICH Guidance for Industry; Rev. 1, August 2001. Stability is performed over the shelf-life of the product. This testing consists of the following: appearance, percent purity, and ratio composition. Table 2 contains the results of the stability study.

**Table 2**  
**Results of Stability Testing for Gebauer's Pain Ease**

	Appearance	Ratio Composition	% Purity
Initial	N/A	Pass	99.9
1 Year	No change observed	Pass	99.9
2 Year	No change observed	Pass	99.9
3 years	No change observed	Pass	99.9

Based on the results of the stability testing, Gebauer's Pain Ease is determined to be chemically stable over the 3-year shelf-life.

### **Microbiological Testing**

*Controlled Manufacturing Environment:* The chemicals themselves that are used to comprise Pain Ease are filtered to screen out particulates larger than 0.2 microns. In addition, Pain Ease is filled in a controlled environment that is monitored for temperature, humidity and positive pressure. The air in this manufacturing environment has HEPA filtration which maintains air particulates

to levels established for a Class 100,000 clean room.

The room also undergoes microbial monitoring during each manufacturing run of Pain Ease. It includes an assessment of the air, surfaces, as well as the personnel. This assessment is based on the recommendations specified in the United States Pharmacopeia (USP) General Chapter <1116>, *Microbial Evaluations of Cleanrooms and Other Controlled Environments*.

*Microbial Examination:* Once the product has been manufactured, each lot of Pain Ease is tested to USP <61> and USP <62> by an outside, independent laboratory. Lots are not released until the testing is completed and all microbiological results meet acceptance criteria.

USP <61>, *Microbial Examination of Nonsterile Products: Microbial Enumeration Tests* is performed to determine the total aerobic microbial count (TAMC) and total yeast and mold counts (TYMC) present.

USP <62>, *Microbial Examination of Nonsterile Products: Tests for Specified Microorganisms* is performed to test the presence/absence of *Staphylococcus aureus* and *Pseudomonas aeruginosa*.

### **Flammability**

Gebauer's Pain Ease is non-flammable. It can be used in conjunction with ultrasound, x-ray, laser, and cautery equipment. When using cautery equipment special care should be taken to determine that the product has completely evaporated from the surface

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of contact to prevent against possible decomposition due to extreme heat. When product is directly exposed to sources of high temperatures, toxic or corrosive decomposition may occur producing halogens, halogen acids, and possibly carbonyl halides.

### **Clinical Data**

A significant body of clinical data supporting the safety and effectiveness of Gebauer's Pain Ease, as well as other Gebauer vapocoolant products, has been published in a variety of peer-reviewed clinical journals. A comprehensive listing of clinical trial references and abstracts can be reviewed at [www.gebauer.com/resources](http://www.gebauer.com/resources) under Clinical Research.

### **Dosage and Administration**

To apply Gebauer's Pain Ease from the aerosol can, hold the can upright over the treatment area approximately 3 to 7 inches (8 to 18 cm) away from the application site. Press the actuator button firmly, allowing Pain Ease to spray from the can.

*Pre-Injection & Minor Surgical Topical Anesthesia:* Have all necessary equipment ready and prepare the procedure site per facility's protocol. Hold the can upright, 3 to 7 inches (8 to 18 cm) from the procedure site, about a can's length away. Spray steadily 4 to 10 seconds or until the skin begins turning white, whichever comes first. Do not spray longer than 10 seconds. After spraying the site, immediately perform the procedure. The anesthetic effect of Pain Ease lasts about 1 minute.

\*Apply petrolatum to protect the adjacent area for minor surgical procedures.

### *Other Application Methods for Pre-Injection Anesthesia - Cotton*

*Application:* Have necessary equipment ready. Prepare the procedure site per facility's protocol. Spray Pain Ease into a cup, for about 10 seconds, or until 5 ml. of the product has accumulated. Place a cotton ball, cotton swab or gauze into the cup until it is well saturated with Pain Ease, and there is no visible product left in the cup. Cotton may also be directly sprayed for 10 seconds to achieve saturation. Immediately after saturation, apply the cotton to the site. Hold firmly on the site for 5-15 seconds and immediately perform the procedure. Reapply as needed.

Use this application method on intact skin. If the skin is breached use this application method only with STERILE, disposable cotton balls, cotton swabs or gauze.

*Temporary Relief of Minor Sports Injuries:* The pain of bruises, contusions, swelling, minor sprains, cuts, and abrasions may be controlled with Pain Ease. The amount of cooling depends on the dosage. Dosage varies with duration of application. The smallest dose needed to produce the desired effect should be used. The anesthetic effect of Pain Ease lasts about 1 minute. This time interval is usually sufficient to help reduce or relieve the initial trauma of the injury. Hold the can upright 3 to 7 inches (8 to 18 cm) from the target area, about a can's length away. Spray steadily 4 to 10 seconds or until the skin begins turning white,

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whichever comes first. Do not spray longer than 10 seconds. Reapply if necessary.

*Spray and Stretch Technique for Myofascial Pain* (Pain Ease Medium Stream Spray only): Pain Ease Medium Stream Spray may be used as a counterirritant in the management of myofascial pain, restricted motion, and muscle tension. Clinical conditions that may respond to Pain Ease Medium Stream Spray included low back pain (due to tight muscles), acute stiff neck, torticollis, acute bursitis of the shoulder, tight hamstrings, sprained ankle, tight masseter muscles and referred pains due to irritated trigger points. Relief of pain facilitates early mobilization and restoration of muscle function. The spray and stretch technique is a system that involves three stages: Evaluation, Spraying and Stretching. The therapeutic value of the spray and stretch technique is most effective when the practitioner has mastered all of the stages and applies them in the proper sequence.

- 1) **Evaluation:** If the patient has been evaluated to have muscle tension and restricted motion caused by an active, irritated trigger point, then proceed to Step 2.
- 2) **Spraying:**
  - A. Have the patient assume a comfortable position.
  - B. Take precautions to cover the patient's eyes if spraying near the face.
  - C. Hold the can upright. From a distance of 12 to 18 inches (30 to 46 cm, aim the stream

so that it meets the skin at an acute angle lessening the shock of impact.

- D. Direct the spray in parallel sweeps 0.5 to 1 inch (1.5 to 2 cm) apart at the rate of approximately 4 inches per second (10 cm per second).
  - E. Continue until the entire muscle has been covered. The number of sweeps is determined by the size of the muscle. The spray should be applied from the muscle attachment over the trigger point, through and over the reference zone.
- 2) **Stretching:** Passively stretch the muscle during spray application. Gradually increase the force with successive sweeps. As the muscle relaxes, smoothly take up the slack by establishing a new stretch length. It is necessary to reach the full normal length of the muscle to completely inactivate the trigger point and relieve the pain. Rewarm the muscle. If necessary, repeat the procedure. Apply moist heat for 10 to 15 minutes following treatment. For lasting benefit, eliminate any factors that perpetuate the trigger mechanism.

### **Bibliography**

<sup>1</sup> Lehmann JF, Delateur BJ; *Therapeutic Heat and Cold*, 4<sup>th</sup> edition; Baltimore, Williams and Wilkins; 1990.

<sup>2</sup> Merrick MA, Martin KM; *Cold Perception, Surface, Subcutaneous and Intramuscular Temperatures Produced*

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by Gebauer Pain Ease Topical Vapocoolant Spray; *Journal of Athletic Training*, Vol. 47, No. 3; 2012.

<sup>3</sup> Goodheart, Herbert P. MD; Pigmentary Disorders Part 2: Nonvilitiginous Forms of Hypopigmentation, *Dermatology Rounds*, Vol.2, No. 11; Nov. 1999

<sup>4</sup> Rusch GM, Coombs D, and Hardy C; The Acute, Genetic, Developmental, and Inhalation Toxicology of 1,1,1,3,3-Pentafluoropropane (HFC-245fa); *Toxicological Sciences*; 1995.

<sup>5</sup> Talmage SS, Rusch G, Benson R, and Stoll K; *Acute Exposure Guideline Levels (AWGLs) for HFC-134a*; 1998.

<sup>6</sup> Collins MA, Rusch GM, Sato F, Hext PM, and Millischer, R; 1,1,1,2-Tetrafluoroethane: Repeat Exposure Inhalation Toxicity in the Rat, Development Toxicity in the Rabbit, and Genotoxicity in Vitro and in Vivo; *Fundamental and Applied Toxicology*; 1995.

### **Ordering Information**

R<sub>x</sub> only.

The FDA has designated Gebauer's Pain Ease Mist Spray and Medium Spray as Prescription only (Rx) medical devices. This designation means that Pain Ease can be sold to and purchased by any healthcare practitioner who is licensed by the state in which they practice. Healthcare practitioners include doctors, chiropractors, physical therapists, nurses, etc. Any healthcare professional should be able to purchase prescription devices without restriction.

Gebauer's Pain Ease may be purchased by any patient who receives a prescription or "other order" which is defined as an instruction from a healthcare practitioner to use a prescription device. Gebauer's Pain Ease is available in the following configurations:

Gebauer's Pain Ease Mist Spray  
3.9 fl. Oz. (116 ml) Aerosol Can  
U.S. Order No. 0386-0008-02  
1.0 fl. Oz. (30 ml) Aerosol Can  
U.S. Order No. 0386-0008-04

Gebauer's Pain Ease Medium Stream  
3.9 fl. Oz. (116 mL) Aerosol Can  
U.S. Order No. 0386-0008-03  
1.0 fl. Oz. (30 ml) Aerosol Can  
U. S. Order No. 0386-0008-01