

MAXIMA *Pharmaceuticals*

**DIFFUSIMAX[®] and
DIFFUSIMAX[®] KIT**



Product Information

Patient Instructions

Compounding Directions

References



MAXIMA Pharmaceuticals, Inc.

Contents

| | |
|----------------------------------|---|
| Product Information | 2 |
| Patient Instructions | 3 |
| Compounding Directions | 4 |
| References | 9 |

Call Toll Free: 1-888-MAXIMA8 (629-4628)

www.maximapharmaceuticals.com



MAXIMA Pharmaceuticals, Inc.
Edmonton, Canada T6E 6N2

Do Transdermal NSAIDS Work?

Absolutely! Transdermal NSAIDs are both effective and safe. A meta-analysis of 86 randomized, placebo-controlled trials of transdermal NSAIDs included 10,160 patients (Moore RA, et al. British Medical Journal; 1998; 316:333-338). It concluded that

"topical non-steroidal anti-inflammatory drugs are effective in relieving pain in acute and chronic conditions".

In fact, topically applied NSAIDs were just as effective as oral NSAIDs in those studies where comparisons were done. A significant difference, however, was that with transdermal therapy

"local and systemic adverse events... were no different than placebo".

A randomized, placebo-controlled Canadian study of lateral epicondylitis showed that transdermal diclofenac in pluronic lecithin organogel (PLO gel) reduced pain and increased functional status (Burnham R, et al. Clinical J Sports Med; 1998; 8:78-81). Another Canadian study showed that diclofenac in PLO gel was an effective treatment for osteoarthritis (Grace D, et al. J Rheumatol; 1999; 26:2659-2663).

Product Information

DiffusiMAX[®] and DiffusiMAX[®] KIT

DiffusiMAX is the trade name for a unique cosmetic cream base made of pluronic lecithin organogel (PLO gel). It is composed of micelles (or liposomes) that incorporate drug molecules to allow transdermal medication delivery.

Use

Transdermal delivery of medications.

Features

Non-medicated, hypoallergenic, lanolin-free cream base.

Format

- DiffusiMAX is supplied as 100 g or 500 g jars of convenient pre-mixed cream.
- DiffusiMAX Kits are supplied as separate hydrophilic and lipophilic components for making 100 mL, 500 mL or 1000 mL of PLO gel.

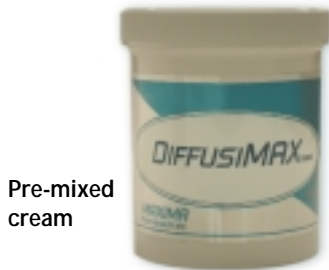
Storage

DiffusiMAX Pre-Mixed Cream

Stable for 12 months at room temperature. Once the container is opened and medications are added, stability may be reduced.

DiffusiMAX Kit Components

- Both DiffusiMAX A and DiffusiMAX B can be stored at room temperature.
- DiffusiMAX B has the unusual property of solidifying at room temperature. It should be refrigerated prior to use to liquify for mixing.
- DiffusiMAX A may solidify if cooled. Warm to room temperature prior to use.



Pre-mixed
cream



Kits to be
compounded

- Both components are stable for 12 months at room temperature if unopened.
- The prepared gel is stored at room temperature and is stable for 12 months. The addition of medications may alter stability.

Contamination

Pluronic lecithin organogel is an organic mixture that supports mold growth. Preservatives are used, but mold may still grow if the gel becomes contaminated. When preparing any product with DiffusiMAX clean all jars, spatulas and equipment with alcohol. Instruct patients on the importance of proper application technique.

Patient Instructions

Counselling Information

- Apply DiffusiMAX cream thinly with clean hands. Allow to air dry before covering with clothing. Wash hands after application. Rinse with cold water if cream gets in the eyes.
- Apply over affected area if used for local effects.
- Apply behind the ears, on the inside of the wrists or over the collarbones if used for systemic effects.
- Apply specified quantity from a syringe (without a needle) when accurate dosing is prescribed for certain medications.
- Store in the original container. Always keep the lid on when not in use.
- DiffusiMAX is hypoallergenic, but skin irritation can occasionally occur. Patients should not be given a drug in DiffusiMAX that they are allergic to when taken orally.

Compounding Directions

DiffusiMAX® KIT

1. Determine if the drug to be used is soluble in DiffusiMAX Compound A (lipophilic phase) or DiffusiMAX Compound B (hydrophilic phase), and determine the appropriate solvent (see Tables).
2. Mix the drug with the solvent to a smooth paste. Whenever possible, use less than 3 mL solvent per 50 mL of cream.
3. Mix this paste with appropriate DiffusiMAX compound.
4. Add the second kit component in the ratio of 1 part A : 3 parts B. The kits are supplied in these proportions. Mix well.
5. The cream will form as the mixture reaches room temperature.
6. For clean-up, wipe equipment, rinse with cold water and then wash with detergent.

Notes

- Pure drug powders rather than crushed tablets should be used whenever possible.
- The use of crushed tablets can lead to granularity due to fillers.
- Compound A may solidify if cooled. Warm to room temperature before use.
Compound B solidifies at room temperature. Refrigerate before use.

DiffusiMAX® Pre-MIXED Cream

1. Determine the appropriate solvent for the drug to be used (see Tables).
2. Mix the drug with the solvent to a smooth paste. Whenever possible, use less than 3 mL solvent per 50 g of cream.
3. Mix this paste with DiffusiMAX cream.
4. For clean-up, wipe equipment, rinse with cold water and then wash with detergent.

Notes

- Pure drug powders rather than crushed tablets should be used whenever possible.
- The use of crushed tablets can lead to granularity due to fillers.
- Cream appearance may be affected by cooling. Mixing will restore consistency.

*Compounding directions and information in the medication tables are recommended for DiffusiMAX® products only.
The use of other PLO formulations may result in an inferior final product.*

TABLE D1**Non-Steroidal Anti-inflammatories in DiffusiMAX®**

| Drug | Solvent | DiffusiMAX Compound | Concentration Range (%) | Typical Concentration (%) | Application Frequency |
|--------------|----------------|----------------------------|--------------------------------|----------------------------------|------------------------------|
| diclofenac | alcohol | A | 2 – 5 | 2 | tid |
| ibuprofen | alcohol | A | 5 – 10 | 5 | tid |
| ketaprofen | alcohol | A | 2 – 10 | 5 | tid |
| indomethacin | alcohol | A | 5 – 10 | 5 | tid |
| naproxen | alcohol | A | 5 – 10 | 5 | tid |

DiffusiMAX Compound = component of DiffusiMAX Kit to be used to solubilize drug
 Alcohol = ethyl alcohol (95%) or isopropyl alcohol (70%)

Application: Over affected body area. Not usually applied in measured aliquots.

This information applies to DiffusiMAX® products only. The use of other PLO formulations may result in an inferior final product. No claims are made as to the safety or efficacy of this product. This information is provided solely at the unsolicited request of physicians and pharmacists. Do not reproduce without permission.

TABLE D2**Muscle Relaxants in DiffusiMAX®**

| Drug | Solvent | DiffusiMAX Compound | Concentration Range (%) | Typical Concentration (%) | Application Frequency |
|-----------------|------------------|----------------------------|--------------------------------|----------------------------------|------------------------------|
| cyclobenzaprine | water | B | 1 – 2 | 2 | bid - qid |
| baclofen | propylene glycol | B | 2 – 5 | 2 | bid - qid |
| bupirone | propylene glycol | B | 2 – 5 | 2 | bid - qid |

DiffusiMAX Compound = component of DiffusiMAX Kit to be used to solubilize drug
 Water = distilled water

Application: Over affected body area. May be applied in measured aliquots using calibrated syringes (without needles).

This information applies to DiffusiMAX® products only. The use of other PLO formulations may result in an inferior final product. No claims are made as to the safety or efficacy of this product. This information is provided solely at the unsolicited request of physicians and pharmacists. Do not reproduce without permission.

TABLE D3

Neuropathy Drugs in DiffusiMAX®

| Drug | Solvent | DiffusiMAX Compound | Concentration Range (%) | Typical Concentration (%) | Application Frequency |
|---------------|------------------|---------------------|-------------------------|---------------------------|-----------------------|
| clonidine | water | B | 0.1 – 0.2 | 0.1 | bid – qid |
| capsaicin | alcohol | A | 0.025 – 0.075 | 0.025 | bid – qid |
| amitriptyline | alcohol | A | 1 – 4 | 2 | bid – qid |
| gabapentin | propylene glycol | B | 4 – 8 | 4 | tid – qid |
| phenytoin | alcohol | A | 2 – 5 | 2 | tid – qid |
| ketamine | alcohol | A | 0.5 – 2 | 1 | tid – qid |

DiffusiMAX Compound = component of DiffusiMAX Kit to be used to solubilize drug

Water = distilled water

Application: Over affected body area. May be applied in measured aliquots using calibrated syringes (without needles).

This information applies to DiffusiMAX® products only. The use of other PLO formulations may result in an inferior final product. No claims are made as to the safety or efficacy of this product. This information is provided solely at the unsolicited request of physicians and pharmacists. Do not reproduce without permission.

TABLE D4

Antiemetics in DiffusiMAX®

| Drug | Solvent | DiffusiMAX Compound | Concentration Range (%) | Typical Concentration (%) | Typical Volume (mL) | Typical Dose (mg) | Application Frequency |
|----------------|------------------|---------------------|-------------------------|---------------------------|---------------------|-------------------|-----------------------|
| dexamethasone | propylene glycol | B | 1 – 5 | 2 | 0.5 | 10 | bid |
| dimenhydrinate | water | B | 2 – 5 | 5 | 1 | 50 | q4 – 6h |
| metaclopramide | water | B | 1 – 5 | 1 | 1 | 10 | q4 – 6h |
| scopolamine | water | B | 0.25 – 0.5 | 0.25 | 0.5 | 0.25 | q8h |

DiffusiMAX Compound = component of DiffusiMAX Kit to be used to solubilize drug

Water = distilled water

Application: For systemic administration. Should be dispensed in calibrated syringes (without needles) so exact amount can be applied. Apply to areas with thin skin, such as behind the ears, the clavicles or the inside of the wrists.

This information applies to DiffusiMAX® products only. The use of other PLO formulations may result in an inferior final product. No claims are made as to the safety or efficacy of this product. This information is provided solely at the unsolicited request of physicians and pharmacists. Do not reproduce without permission.

TABLE D5
Systemic Analgesics in DiffusiMAX®

| Drug | Solvent | DiffusiMAX Compound | Concentration Range (%) | Typical Concentration (%) | Typical Volume (mL) | Typical Dose (mg) | Application Frequency |
|------------------|------------------|---------------------|-------------------------|---------------------------|---------------------|-------------------|-----------------------|
| acetaminophen | propylene glycol | B | 5 – 10 | 6.5 | 10 | 650 | q4 – 6h |
| hydromorphone | water | B | 0.1 – 2 | 1 | 0.5 | 5 | q4 – 6h |
| morphine sulfate | water | B | 0.1 – 2 | 1 | 2 | 20 | q4 – 6h |

DiffusiMAX Compound = component of DiffusiMAX Kit to be used to solubilize drug

Water = distilled water

Application: For systemic administration. Should be dispensed in calibrated syringes (without needles) so exact amount can be applied. Apply to areas with thin skin, such as behind the ears, the clavicles or the inside of the wrists. Dose ranges for narcotics can vary widely depending on tolerance.

This information applies to DiffusiMAX® products only. The use of other PLO formulations may result in an inferior final product. No claims are made as to the safety or efficacy of this product. This information is provided solely at the unsolicited request of physicians and pharmacists. Do not reproduce without permission.

TABLE D6
Systemic Hormones in DiffusiMAX®

| Drug | Solvent | DiffusiMAX Compound | Concentration Range (%) | Typical Concentration (%) | Typical Volume (mL) | Typical Dose (mg) | Application Frequency |
|----------------------|------------------|---------------------|-------------------------|---------------------------|---------------------|-------------------|-----------------------|
| progesterone | propylene glycol | B | 1 – 10 | 3 | 2.5 | 75 | qd |
| testosterone (women) | alcohol | A | 1 – 5 | 1 | 1 | 10 | qd – bid |
| testosterone (men) | alcohol | A | 1 – 5 | 2 | 5 | 100 | qd – bid |

Alcohol = ethyl alcohol (95%) or isopropyl alcohol (70%)

Application: For systemic administration. Should be dispensed in calibrated syringes (without needles) so exact amount can be applied. Apply to areas with thin skin, such as behind the ears, the clavicles or the inside of the wrists.

This information applies to DiffusiMAX® products only. The use of other PLO formulations may result in an inferior final product. No claims are made as to the safety or efficacy of this product. This information is provided solely at the unsolicited request of physicians and pharmacists. Do not reproduce without permission.

References

1. J Microencapsulation 1994; 11:431
Increased drug delivery across skin by PLO gel
2. J Pharm Sci 1992; 81:871
PLO is the best transdermal drug delivery method
3. Eur J Clin Pharm 1994; 47:297
Transdermal NSAID treatment
4. J Pharm Sci 1995; 84:324
PLO is the best method of transdermal NSAID delivery
5. Int J of Pharmaceutical Compounding 1997; 1:190
Pluronic organogel
6. J Intern Med Res 1990; 18:372
Transdermal NSAID treatment
7. Pain 1995; 60:267
Transdermal clonidine
8. Clin Ther 1993; 15:10
Transdermal capsaicin
9. Eur J Rheum Inflamm 1994; 14:21
Topical NSAIDs are as good as oral
10. Brit Med J 1998; 316:333
Meta-analysis showing effectiveness of transdermal NSAIDs
11. Clin J Sports Med 1998; 8:78
Diclofenac in PLO gel for lateral epicondylitis
12. J Rheumatol 1999; 26:2659
Diclofenac in PLO gel for osteoarthritis of the knee

