

of dicyclomine hydrochloride [see Warnings and Precautions (5.1)], the blood concentrations of drug were 200, 220, and 505 ng/mL.

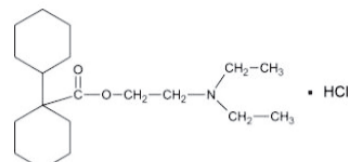
It is not known if dicyclomine hydrochloride is dialyzable. Treatment should consist of gastric lavage, emetics, and activated charcoal. Sedatives (e.g., short-acting barbiturates, benzodiazepines) may be used for management of overt signs of excitement. If indicated, an appropriate parenteral cholinergic agent may be used as an antidote.

11 DESCRIPTION

Dicyclomine is an antispasmodic and anticholinergic (antimuscarinic) agent available in the following dosage form:

Dicyclomine Hydrochloride Injection, USP is a sterile, pyrogen-free, aqueous solution for intramuscular injection (NOT FOR INTRAVENOUS USE). Each mL contains 10 mg dicyclomine hydrochloride USP in sterile water for injection, made isotonic with sodium chloride.

Dicyclomine hydrochloride is [bicyclohexyl]-1-carboxylic acid, 2-(diethylamino) ethyl ester, hydrochloride, with a molecular formula of C₁₉H₃₅NO₂ · HCl and the following structural formula:



Molecular weight: 345.95

Dicyclomine hydrochloride occurs as a fine, white, crystalline, practically odorless powder with a bitter taste. It is soluble in water, freely soluble in alcohol and chloroform, and very slightly soluble in ether.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Dicyclomine relieves smooth muscle spasm of the gastrointestinal tract. Animal studies indicate that this action is achieved via a dual mechanism:

- a specific anticholinergic effect (antimuscarinic) at the acetylcholine-receptor sites with approximately 1/8 the milligram potency of atropine (in vitro, guinea pig ileum); and
- a direct effect upon smooth muscle (musculotropic) as evidenced by dicyclomine's antagonism of bradykinin- and histamine-induced spasms of the isolated guinea pig ileum.

Atropine did not affect responses to these two agonists. In vivo studies in cats and dogs showed dicyclomine to be equally potent against acetylcholine (ACh)- or barium chloride (BaCl₂)-induced intestinal spasm while atropine was at least 200 times more potent against effects of ACh than BaCl₂. Tests for mydriatic effects in mice showed that dicyclomine was approximately 1/500 as potent as atropine; antisialagogue tests in rabbits showed dicyclomine to be 1/300 as potent as atropine.

12.2 Pharmacodynamics

Dicyclomine hydrochloride can inhibit the secretion of saliva and sweat, decrease gastrointestinal secretions and motility, cause drowsiness, dilate the pupils, increase heart rate, and depress motor function.

12.3 Pharmacokinetics

Absorption and Distribution

In man, dicyclomine is rapidly absorbed after oral administration, reaching peak values within 60 to 90 minutes. Mean volume of distribution for a 20 mg oral dose is approximately 3.65 L/kg suggesting extensive distribution in tissues.

Elimination

The metabolism of dicyclomine was not studied. The principal route of excretion is via the urine (79.5% of the dose). Excretion also occurs in the feces, but to a lesser extent (8.4%). Mean half-life of plasma elimination in one study was determined to be approximately 1.8 hours when plasma concentrations were measured for 9 hours after a single dose. In subsequent studies, plasma concentrations were followed for up to 24 hours after a single dose, showing a secondary phase of elimination with a somewhat longer half-life.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term animal studies have not been conducted to evaluate the carcinogenic potential of dicyclomine. In studies in rats at doses of up to 100 mg/kg/day, dicyclomine produced no deleterious effects on breeding, conception, or parturition.

14 CLINICAL STUDIES

In controlled clinical trials involving over 100 patients who received drug, 82% of patients treated for functional bowel/irritable bowel syndrome with dicyclomine hydrochloride at initial doses of 160 mg daily (40 mg four times daily) demonstrated a favorable clinical response compared with 55% treated with placebo (p<0.05).

16 HOW SUPPLIED/STORAGE AND HANDLING

Dicyclomine Hydrochloride Injection, USP, 20 mg/2 mL (10 mg/mL), (for Intramuscular use only, NOT FOR Intravenous USE) is supplied as follows:

NDC 31722-963-32: 5 x 2 mL Single Dose Vials

Store at 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature].

Protect from freezing.

17 PATIENT COUNSELING INFORMATION

17.1 Inadvertent Intravenous Administration

Dicyclomine injection is for intramuscular administration only. Do not administer by any other route. Inadvertent administration may result in thrombosis or thrombophlebitis, and injection site reactions such as pain, edema, skin color change and even reflex sympathetic dystrophy syndrome [see Adverse Reactions (6.2)].

17.2 Use in Infants

Inform parents and caregivers not to administer dicyclomine in infants less than 6 months of age [see Use in Specific Populations (8.4)].

17.3 Use in Nursing Mothers

Advise lactating women that dicyclomine should not be used while breastfeeding their infants [see Use in Specific Populations (8.3, 8.4)].




17.4 Peripheral and Central Nervous System

In the presence of a high environmental temperature, heat prostration can occur with dicyclomine hydrochloride use (fever and heat stroke due to decreased sweating). If symptoms occur, the drug should be discontinued and a physician contacted. Dicyclomine hydrochloride may produce drowsiness or blurred vision. The patient should be warned not to engage in activities requiring mental alertness, such as operating a motor vehicle or other machinery or to perform hazardous work while taking dicyclomine [see Warnings and Precautions (5.3)].



Manufactured for
Camber Pharmaceuticals, Inc.
Piscataway, NJ 08854

INS-0006 R4

 Nosco complete packaging individual solutions™		NOSCO GRAPHIC SERVICES 651 S. M. L. King Jr. Avenue, Waukegan, IL 60085 Phone: 847.336.4200 Fax: 847.360.4924 Serving Nosco Facilities in Illinois, Texas, Pennsylvania and New York.	Proof A 8/23/2019
Product Information Item: INS-0006-R4 Eval: X3731585 Cust: GRAND RIVER ASEPTIC MANUFACTURING, INC. Size: +19.25 x +9.7813	Specified Colors  Black  Head to Head <small>Item Group: EVS-ENC</small>	Approved By Name _____ Date _____ <input type="checkbox"/> OK to Print <input type="checkbox"/> New Proof Required We must have signed proof before we can begin production. This proof is to show size, copy placement and color break. Spot/PMS colors will be matched on press to: PMS Book, 4 Color Process Digital Color Guide, Extended Gamut Digital Color Guide and/or approved color standards. 4 Color Process proofs are verified to G7 standards and approved for color match.	

WebScan TruCheck™ USB Verification Report

Software Version: 3.03.58, Unit Serial: TC-829-0519-006

Verified: Wed 21-Aug-2019 06:23:50 AM, Last Calibrated: Tue 20-Aug-2019 04:14:58 PM

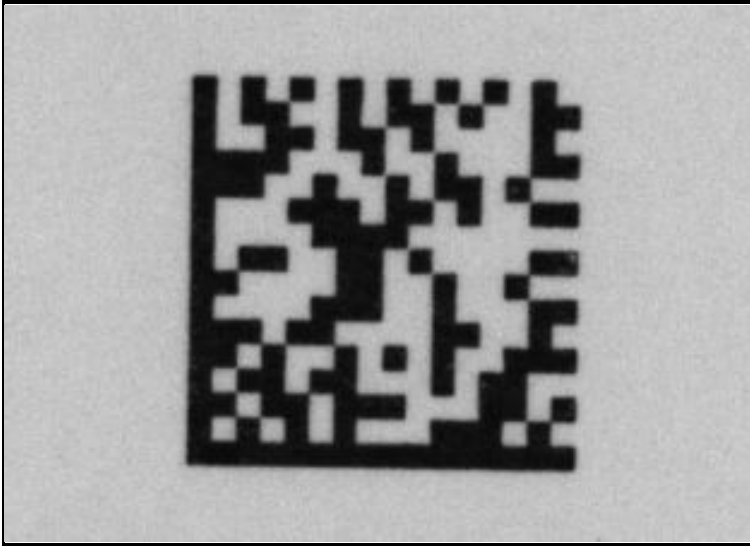
Report Summary

Data	INS-0006-R4
Unicode Data	INS-0006-R4
Symbology	DataMatrix
Company Name	Nosco Inc

Verification Grades

Standard	Grade	Aperture	Wavelength	Lighting	Formal Grade
ISO29158 (AIM-DPM)	A (4.0)	15	660	45Q	DPM 4.0/15/660/45Q

Image



General Characteristics

Matrix Size	16x16 (Data: 14x14)
Horizontal BWG	4%
Vertical BWG	3%
Encoded characters	11
Total Codewords	24
Data Codewords	12
Error Correction Budget	12
Errors Corrected	0
Error Capacity Used	0
Error Correction Type	ECC 200
Image	Black on white
Nominal X Dim	18.2 mil
Contrast Uniformity	83 at module(14,13)
MRD	81% (85% - 4%)
Stability	87%

ASCII Values

073 078 083 045 048 048 048 054 045 082 052

ISO 29158 Quality Parameters

Parameter	Value	Grade	RI/Rd (100/10)	Result
1. Unused Error Correction (UEC)	100%	A		PASS
2. Cell Contrast (CC)	90%	A	RI/Rd (100/10)	PASS
3a. Cell Modulation (CMOD)		A		PASS
3b. Reflectance Margin (RM)		A		PASS
4. Axial Nonuniformity (ANU)	0%	A		PASS
5. Grid Nonuniformity (GNU)	4%	A		PASS
6. Fixed Pattern Damage (FPD)	4.0	A		PASS
7. Left 'L' Side (LLS)		A		PASS
8. Bottom 'L' Side (BLS)		A		PASS
9. Left Quiet Zone (LQZ)		A		PASS
10. Bottom Quiet Zone (BQZ)		A		PASS
11. Top Quiet Zone (TQZ)		A		PASS
12. Right Quiet Zone (RQZ)		A		PASS
13. Top Transition Ratio (TTR)	0%	A		PASS
14. Right Transition Ratio (RTR)	0%	A		PASS
15. Top Clock Track (TCT)		A		PASS
16. Right Clock Track (RCT)		A		PASS
17. Distributed Damage Grade (DDG)	4.0	A		PASS
18. DECODE		A		PASS
19. Minimum Reflectance (MR)	83%	A		PASS

Data Matrix Codewords

4A 4F 54 2E 82 88 2E 53 35 81 FB 93 A2 0A D0 91 F0 CB DD
46 5A 08 1E 8F
* = Fixed by Error Correction

Encodation Analysis

Codeword	Mode	Result
4A	ASCII	I
4F	ASCII	N
54	ASCII	S
2E	ASCII	-
82	ASCII	00
88	ASCII	06
2E	ASCII	-
53	ASCII	R
35	ASCII	4
81	ASCII	ASCII PAD
FB	ASCII	ASCII PAD
93	ASCII	ASCII PAD
A2, 0A, D0, 91, F0, CB, DD, 46, 5A, 08, 1E, 8F	ECC	

WebScan TruCheck™ USB Verification Report

Software Version: 3.03.58, Unit Serial: TC-829-0519-006

Verified: Wed 21-Aug-2019 06:24:01 AM, Last Calibrated: Tue 20-Aug-2019 04:14:58 PM

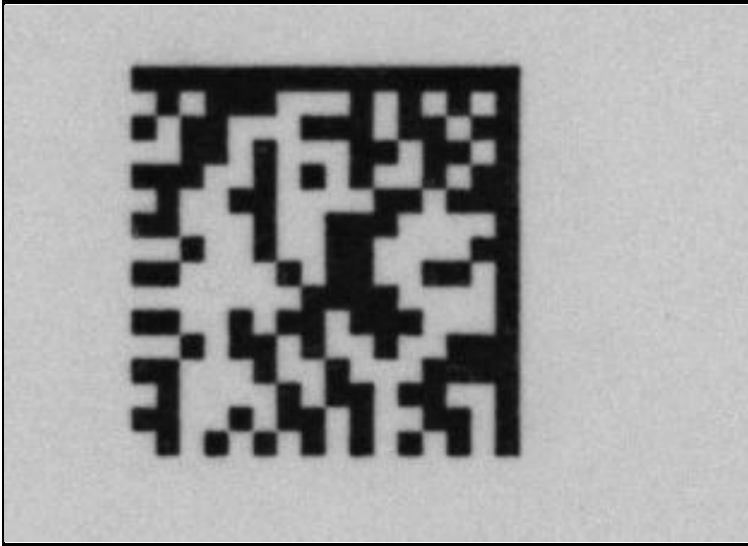
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MRD	80% (86% - 6%)
Stability	81%

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3a. Cell Modulation (CMOD)		A		PASS
3b. Reflectance Margin (RM)		A		PASS
4. Axial Nonuniformity (ANU)	0%	A		PASS
5. Grid Nonuniformity (GNU)	3%	A		PASS
6. Fixed Pattern Damage (FPD)	4.0	A		PASS
7. Left 'L' Side (LLS)		A		PASS
8. Bottom 'L' Side (BLS)		A		PASS
9. Left Quiet Zone (LQZ)		A		PASS
10. Bottom Quiet Zone (BQZ)		A		PASS
11. Top Quiet Zone (TQZ)		A		PASS
12. Right Quiet Zone (RQZ)		A		PASS
13. Top Transition Ratio (TTR)	0%	A		PASS
14. Right Transition Ratio (RTR)	0%	A		PASS
15. Top Clock Track (TCT)		A		PASS
16. Right Clock Track (RCT)		A		PASS
17. Distributed Damage Grade (DDG)	4.0	A		PASS
18. DECODE		A		PASS
19. Minimum Reflectance (MR)	83%	A		PASS

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2E	ASCII	-
82	ASCII	00
88	ASCII	06
2E	ASCII	-
53	ASCII	R
35	ASCII	4
81	ASCII	ASCII PAD
FB	ASCII	ASCII PAD
93	ASCII	ASCII PAD
A2, 0A, D0, 91, F0, CB, DD, 46, 5A, 08, 1E, 8F	ECC	

