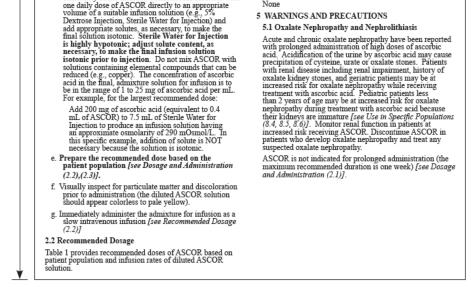
	Top of Page	— 4.	5" ———			
1.	HIGHLIGHTS OF PRESCRIBING INFORMAT These highlights do not include all the informatio to use ASCOR* safely and effectively. See full pre- information for ASCOR. ASCOR (ascorbic acid injection), for intravenous Initial U.S. Approval: 1947 —INDICATIONS AND USAGE ASCOR is vitamin C indicated for the short term (up week) treatment of scurvy in adult and pediatric pati- months and older for whom oral administration is no insufficient or contraindicated. Limitations of Use. ASCOR is not indicated for treatment of vitamin C of that is not associated with signs and symptoms of sc DOSAGE AND ADMINISTRATION • Supplied in a Pharmacy Bulk Package (PBP). Disp single doese to multiple patients in a pharmacy and program; use within 4 hours of puncture (2.1) • Must be diluted prior to use (2.1) • Must be diluted prior to use (2.1) • See Full Prescribing Information for important administration instructions (2.1) • Maximum recommended duration is one week (2.2)	on needed escribing s use p to 1 jents age 5 ot possible, deficiency urvy. pense mixture	None WARNINGS A Oralate nephropathy and has been associated with oxalate nephropathy fold doese of ascorbic acid infi including renal impairmer geriatric patientis, and ped may be at increased risk ( <u>Hemolysis</u> : Patients with dehydrogenase deficiency reduced dose is recommet <u>Laboratory Test Interferer</u> with laboratory tests base including blood and urine	. (500 mg/mL) – MINDICATION: AND PRECAUT Nephrolithiasis: levelopment of a wing prolonged n usion. Patients wing intric patients less 5.1). glucose-6-phospi are at risk of sex aded (5.2). Succesting (Second) EREACTION: tions are pain and DVERSE REAC	Pharmacy Bulk S IONS Ascorbic acid cute or chronic use of high ith renal disease late kidney stones, is than 2 years old hate erere hemolysis; a d may interfere duction reactions, 5.3). S d swelling at the CTIONS, contact	
	Population (2.2)         Recomment           Pediatric patients age 5 months to less than 12 months         50 mg once	nded Doses e daily	or FDA at 1-800-FDA-108 DRUG IN • <u>Antibiotics</u> : Ascorbic acid	8 or <i>www.fda.go</i> NTERACTIONS I may decrease th	w/medwatch. 6	
Fold #2	Pediatric patients age 1 year to less         100 mg one           than 11 years         Adults and pediatric patients age 11         200 mg one           years and older         Specific Populations (2.3, 8.1, 8.2)         200 mg one	ce daily exceed the nmended	erythromycin, kanamycin lincomycin. Bleomycin is acid (7.1). • Amphetamine and Other 1 <u>Aciditation</u> : Ascorbic ac urine and result in decrea: affect excretion and plasm sensitive to urine pH (7.2) • <u>Warfarin</u> : Continue standa See 17 for PATIENT COU	, streptomycin, o inactivated <i>in vi</i> Drugs Affected b cid may cause aci sed amphetamine ta concentrations ). ard monitoring (7	oxycycnne, and two by ascorbic <u>y Urine</u> . diffication of the serum levels and of other drugs 7.3).	
Fold #1	FULL PRESCRIBING INFORMATION: CONT         1 INDICATIONS AND USAGE         2 DOSAGE AND ADMINISTRATION         3 DOSAGE FORMS AND STRENGTHS         4 CONTRAINDICATIONS         5 WARNINGS AND PRECAUTIONS         6 ADVERSE REACTIONS         7 DRUG INTERACTIONS         7.1 Antibiotics         7.2 Amphetamines & Other Drugs Affected by UACIDICATIONS         8 USE IN SPECIFIC POPULATIONS         8.1 Pregnancy         8.2 Lactation         8.4 Pediatric Use         8.5 Geriatric Use         8.6 Renal Impairment		10 OVERDOSAGE 11 DESCRIPTION 12 CLINICAL PHARMAC 12.1 Mechanism of Action 12.3 Pharmacokinetics 13 NONCLINICAL TOXIP 13.1 Carcinogenesis, Mut 16 HOW SUPPLIED/STO 17 PATIENT COUNSELIP *Sections or subsections om information are not listed.	15 COLOGY agenesis, Impairi RAGE AND HA NG INFORMAI	NDLING TON	
14"	FULL PRESCRIBING INFORMATION 1 INDICATIONS AND USAGE ASCOR® is indicated for the short term (up to 1 wee treatment of scurvy in adult and pediatric patients, ai 5 months and older, for whom oral administration is	ek) ge	Table 1: Recommended Rate of Diluted ASCOR :	Dose of ASCOR	and Infusion	
	<ul> <li>possible, insufficient or contraindicated.</li> <li><u>Limitations of Use</u></li> <li>ASCOR is not indicated for the treatment of vitamin deficiency that is not associated with signs and symp scurvy.</li> <li>2 DOSAGE AND ADMINISTRATION</li> </ul>	ı C	Patient Population	ASCOR Once Daily Dose (mg)	Infusion Rate of Diluted ASCOR Solution (mg/minute)	
	2.1 Important Preparation and Administration Instructions • ASCOR vials contain 25,000 mg of ascorbic acia largest recommended single dose is 200 mg. Do	d and the	Pediatric Patients age 5 months to less than 12 months	50	1.3	
	<ul> <li>the entire contents of the vial to a single patient.</li> <li>Do not administer ASCOR as an undiluted intravinjection.</li> </ul>	venous	Pediatric Patients age 1 year to less than 11 years	100	3.3	
	<ul> <li>Minimize exposure to light because ASCOR is lissensitive.</li> <li>ASCOR is supplied as a <b>Pharmacy Bulk Packa</b> (PBP) which is intended for dispensing of single multiple patients in a pharmacy admixture progr.</li> </ul>	ge doses to	Adults and Pediatric Patients 11 years and older	200	33	
	<ul> <li>restricted to the preparation of admixtures for infla. Use only in a suitable ISO Class 5 work area s as a laminar flow hood (or an equivalent cleas compounding area).</li> <li>b. Penetrate each PBP vial closure only one time suitable sterile transfer device or dispensing allows measured dispensing of the contents. that pressure may develop within the vial dustorage, exercise caution when withdrawing. from the vial.</li> <li>c. Once the closure system has been penetrated, all dispensing from the PBP vial within 4 H Each dose must be used immediately. Discumsed portion.</li> <li>d. Prior to administration, ASCOR must be distinguished infusion and the final soft infusion must be isotonic (undiluted the osn of ASCOR is approximately 5,900 mOsmol/) to preparing the admixture for infusion, calc osmolarity of the intended admixture for infusion and and admixture for infusion solution solution (e.g., Dextrose Injection, Sterile Water for Injection, add appropriate solutes as necessary to make the mage of the solution solution (e.g., Dextrose Injection, Sterile Water for Injection).</li> </ul>	fusion: such m air e with a set that Given ring contents complete hours. ard iluted in a ution for nolarity L). Prior ulate the ission. Add opriate 5% n) and	The recommended maxim with ASCOR is seven day symptoms is observed affe until resolution of scorbuit Repeat dosing is not recon than 11 years of age. <b>2.3 Dosage Reductions</b> in Women who are pregnant glucose-6-dehydrogenase- U.S. Recommended Dieta Adequate Intake (AI) leve group and condition [ <i>see I</i> and Use in Specific Popula <b>3 DOSAGE FORMS AND</b> Injection: 25,000 mg /50 n Pharmacy Bulk Package (of solution) <b>4 CONTRAINDICATION</b> None <b>5 WARNINGS AND PRE4</b> <b>5.1 Oxalate Nephropathy</b>	s. If no improve or one week of the c symptoms is of annended in pedia Specific Popula or lactating and J deficiency should deficiency should for ascorbic aci- tarnings and Pre- tations (8.1, 8.2)J. STRENGTHS L (500 mg/mL) clear, colorless to S CAUTIONS	ment in scorbutic atment, retreat bserved. tric patients less ttions vatients with i not exceed the A) or daily d for their age recarding (5.2) supplied as a pale yellow	



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Side One (Front)

5.1 Oxalate Nephropathy and Nephrolithiasis

Notes:

1. Fold in half starting at Fold #1. Repeat for Fold #2

Fold insert such that the product name on Side One is face up and visible. Final fold size is 4.5" x 3.5"

Created by / Date:	McGuff Pharmaceuticals, Ir					
		· ·	or® Ascorbic Acid Injectio DmL Vial, Pharmacy Bul			
Approved by / Date:	Size:	Document #: Part #:	DRW-0037 M381-0073	Rev: 05		
	Sheet:	1 of 2				

#### 5.2 Hemolysis in Patients with Glucose-6-Phosphate Dehydrog enase Deficien

Hemolysis has been reported with administration of ascorbic acid in patients with glucose-6-phosphate dehydrogenase deficiency. Patients with glucose-6-phosphate aenciency. ratients with glucosie-6-phosphate' dehydrogenase deficiency may be at increased risk for severe hemolysis during treatment with ascorbic acid. Monitor hemoglobin and blood count and use a reduced dose of ASCOR in patients with glucose-6-phosphate dehydrogenase deficiency [see Dosage and Administration (2.3)]. Discontinue treatment with ASCOR if hemolysis is suspected and treat as needed.

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#### 5.3 Laboratory Test Interference

Ascorbic acid may interfere with laboratory tests based on oxidation-reduction reactions, including blood and urine glucose testing, nitrite and bilirubin levels, and leucocyte count testing. If possible, laboratory tests based on oxidation-reduction reactions should be delayed until 24 hours after influsion of ASCOR [see Drug Interactions (7.5)].

#### 6 ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail in other sections of the labeling:

Oxalate nephropathy and Nephrolithiasis [see Warnings and Precautions (5.1)].

 Hemolysis in patients with glucose-6-phosphate dehydrogenase deficiency [see Warnings and Precautions (5, 2)] (5.2)]

The following adverse reactions associated with the use of ascorbic acid were identified in the literature. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to estimate their frequency reliably or to establish a causal relationship to drug exposure:

#### Administration site reactions: pain and swelling.

Administration site reactions: pain and sweiling. ASCOR should not be rapidly administered. Rapid intravenous administration (>250 mg/minute) of ASCOR may cause temporary faintness or nausea, lethargy, flushing dizziness, and headache (the recommended infusion rates of diluted ASCOR solution are 1.3 mg/minute (Pediatric Patients age 5 months to less than 12 months), 33 mg/ minute (Pediatric Patients age 1 year to less than 11 years) and 33 mg/minute (Adults and Pediatric Patients 11 years and older) [see Docage and Administration (2.2)]).

Acute and chronic oxalate nephropathy have occurred with prolonged administration of high does of ascorbic acid [see Warnings and Precautions (5.1)]. In patients with glucose-6-phosphate dehydrogenase deficiency, severe hemolysis has occurred [see Warnings and Precautions (5.2)]. 7 DRUG INTERACTIONS

#### 7.1 Antibiotics

Ascorbic acid may decrease activities of erythromycin kanamycin, streptomycin, doxycycline, and lincomycin Bleomycin is inactivated *in vitro* by ascorbic acid. If the antibiotic efficacy is suspected to be decreased by concomitant administration of ASCOR, discontinue ASCOR administration.

7.2 Amphetamine & Other Drugs Affected by Urine Acidification

Ascorbic acid may acidify the urine and lower serum concentrations of amphetamine by increasing renal excretion (as reflected by changes in amphetamine urine recovery rates). In case of decreased amphetamine efficacy, discontinue ASCOR administration. Standard monitoring of therapy is warranted.

In addition, acidification of urine by ascorbic acid will alter the excretion of certain drugs affected by the pH of the urine (e.g., fluphenazine) when administered concurrently. It has been reported that concurrent administration of ascorbic acid and fluphenazine has resulted in decreased fluphenazine plasma concentrations. Standard monitoring of therapy is warranted.

#### 7.3 Warfarin

4

Limited case reports have suggested interference of ascorbic acid with the anticoagulation effects of warfarin; however, for patients on warfarin therapy treated with ascorbic acid doses up to 1000 mg/day (5 times the largest recommended single dose) for 2 weeks (twice the maximum recommended duration), no effect was observed. Standard monitoring for anti-coagulation therapy should continue during ascorbic acid treatment, as per standard of care.

#### 7.4 Laboratory Test Interference

Because ascorbic acid is a strong reducing agent, it can Because ascoroic acta is a strong reducing agent, it can interfere with numerous laboratory tests based on oxidation-reduction reactions (e.g., glucose, nitrite and bilirubin levels, leukocyte count, etc.). Chemical detecting methods based on colorimetric reactions are generally those tests affected. Ascoroic acid may lead to inaccurate results (false negatives) obtained for checking blood or urinary glucose levels, nitrite, bilirubin, and leukocytes if tested during or within 24 hours after infusion [see Warnings and Precautions (5.3)]. 8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy Risk Summary

There are no available data on use of ASCOR in pregnant women to inform a drug-associated risk of adverse developmental outcomes; however, use of ascorbic acid (vitamin C) has been used during pregnancy for several decades and no adverse developmental outcomes are reported in the published literature [see Data]. There are dose adjustments for ascorbic acid (vitamin C) use during pregnancy [see Clinical Considerations].

Animal reproduction studies have not been conducted with ASCOR.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

#### Clinical Considerations

Dose Adjustments During Pregnancy and Post-Partum Period

Follow the U.S. Recommended Dietary Allowances (RDA) for pregnant women when considering use of ASCOR for treatment of scurvy [see Dosage and Administration (2.3)].

Data

#### Human Data

There are no available data on use of ASCOR or another

Recommended Dietary Allowances (RDA) for lactating women when considering use of ASCOR for treatment of scurvy [see Dosage and Administration (2.3)]. 8.4 Pediatric Use

### ASCOR is indicated for the short term (up to 1 week)

ASCOR is indicated for the short term (up to 1 week) treatment of scurvy in pediatric patients age 5 months and older for whom oral administration is not possible, insufficient or contraindicated. The safety profile of ascorbic acid in pediatric patients is similar to adults; however, pediatric patients less than 2 years of age may be at higher risk of oxalate nephropathy following ascorbic acid administration due to age-related decreased glomerular filtration *[see Warnings and Precautions (5.1)]*. ASCOR is not indicated for use in pediatric patients less

#### nths of age than 5 m 8.5 Geriatric Use

Glomerular filtration rate is known to decrease with age and as such may increase risk for oxalate nephropathy following ascorbic acid administration in elderly population [see Warnings and Precautions (5.1)].

#### 8.6 Renal Impairment

3.0 Kenal impairment ASCOR should be used with caution in scorbutic patients with a history of or risk of developing renal oxalate stones evidence of renal impairment or other issues (e.g., patients on dialysis, patients with diabetic nephropathy, and renal transplant recipients). These patients may be at increased risk of developing acute or chronic oxalate nephropathy following high dose ascorbic acid administration [see Warning and Precautions (5.1)].

## 10 OVERDOSAGE

Overdose with ascorbic acid may cause nausea, vomiting, diarnhea, facial flushing, rash, headache, fatigue or disturbed sleep. If overdose of ASCOR occurs, immediately discontinue administration and treat symptoms and signs of overdose, avoiding additional intake of ascorbic acid.

### 11 DESCRIPTION

A SCOR (ascorbic acid injection) for intravenous use is a colorless to pale yellow, preservative-free, hypertonic, sterile, non-pyrogenic solution of ascorbic acid. ASCOR must be dhitted with an appropriate infusion solution (e.g. 5% Dextrose Injection, USP; Sterile Water for Injection, USP) [see Dosage and Administration (2.1)].

The chemical name of Ascorbic Acid is L-ascorbic acid. The molecular formula is  $C_6H_8O_6$ . It has the following structural formula:



Each ASCOR, 50 mL, Pharmacy Bulk Package vial contains 25,000 mg ascorbic acid, equivalent to 28,125 mg sodium

ascoroate. Each mL of ASCOR contains 500 mg of ascorbic acid (equivalent to 562.5 mg of sodium ascorbate which amout to 85 mg sodium/mL of ASCOR), 130 mg of Sodium bicarbonate, and 0.25 mg of edetate disodium. Sodium hydroxide is added for pH adjustment (pH range 5.6-6.6). If contains no bacteriostatic or antimicrobial agent.

#### 12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The exact mechanism of action of ascorbic acid for the treatment of symptoms and signs of scurvy (a disorder caused by severe deficiency in vitamin C) is unknown, however, administration of ascorbic acid in patients with scurvy is thought to restore the body pool of ascorbic acid. 12.3 Pharmacokinetics

In a single pharmacokinetic study, healthy male and female adults (n=8) were given a single intravenous dose of 1000 mg ascorbic acid (5 times the largest recommended single dose) inflused over a 30 minute period. The mean peak exposure to ascorbic acid was 436.2  $\mu$ M and occurred at the end of the 30 minute influsion.

#### Distribution

Ascorbic acid is distributed widely in the body, with large concentrations found in the liver, leukocytes, platelets, glandular tissues, and lens of the eye. Based on data from oral exposure, ascorbic acid is known to be distributed into breast milk and crosses the placental barrier.

#### Elimination

When the body is saturated with ascorbic acid, the plasma concentration will be about the same as that of the renal threshold, if further amounts are then administered, most of it is excreted in the urine. When body tissues are not saturated and plasma concentration is low, administration of ascorbic acid results in little or no renal excretion. The mean+SD (N=3) half-life observed in the single dose PK study, as described above, was 7.4±1.4 h. Metabolism

## A major route of metabolism of ascorbic acid involves its conversion to urinary oxalate, presumably through intermediate formation of its oxidized product, dehydroascorbic acid.

Excretion

There is a renal threshold for ascorbic acid (vitamin C); the vitamin is excreted by the kidney in large amounts only when the plasma concentration exceeds this threshold, which is approximately 1.4 mg/100 mL.

## 13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity, mutagenicity, and fertility studies have not been performed with ASCOR.

#### 16 HOW SUPPLIED/STORAGE AND HANDLING ASCOR for intravenous use is a colorless to pale yellow

olution supplied as: NDC 67157-101-50 One 25,000 mg/50 mL (500 mg/mL)

NDC 67157-101-51 Tray pack of twenty five 25,000 mg/50 mL (500 mg/mL) Pharmacy Bulk Package viale

vials

## Store in a refrigerator at 2° to 8°C (36° to 46°F).

Protect from light. This product contains no preservative. See Dosage and Administration (2.1) for detailed instructions on preparation, dilution, and administration of ASCOR. Excursions to ambient conditions for up to 30 days during storage or shipping are acceptable.

There are no available data on use of ASCOR or another ascorbic acid injection in pregnant women. However, a published meta-analysis of randomized studies evaluating a large number of pregnant women who took oral ascorbic acid (vitamin C) (through diet and supplementation) at dosses ranging from 500 to 1000 mg/day (2.5 to 5 times the recommended daily intravenous dose, respectively) [see Dosage and Administration (2.3)] between the 9th and 16th weeks of pregnancy showed no increased risk of adverse pregnancy outcomes such as miscarriage, preterm premature rupture of membranes, preterm delivery or pregnancy induced hypertension when compared to placebo. These data cannot definitively establish or exclude the absence of a risk with ascorbic acid (vitamin exclude the absence of a risk with ascorbic acid (vitamin C) during pregnancy.

#### 8.2 Lactation

#### Risk Summarv

There are no data on the presence of ascorbic acid (vitamin C) in human milk following intravenous dosing in lactating women. Ascorbic acid (vitamin C) is present in human milk after maternal oral intake. Maternal oral intake of ascorbic acid (vitamin C) exceeding the U.S. Recommended Dietary Allowances (RDA) for lactation does not influence the ascorbic acid (vitamin C) content in breast milk or the estimated daily amount received by breastfed infants. There are no data on the effect of ascorbic acid (vitamin C) on milk production or the breastfed infant. The devalopmental -nended milk production or the breastfed infant. The developmental and health benefits of breastfeding should be considered along with the mother's clinical need for ASCOR and any potential adverse effects on the breastfed child from ASCOR or from the underlying maternal condition. Follow the U.S.

#### 17 PATIENT COUNSELING INFORMATION

- Inform patients that treatment with ASCOR may increase their risk of oxalate nephropathy [see Warnings and Procentions (5.1)] Precautions (5.1)].
- · Inform patients that treatment with ASCOR may impact laboratory results, including blood and urine glucose tests, up to 24 hours after infusion [see Warnings and Precautions (5.3)].
- Inform patients with glucose-6-phosphate dehydrogenase deficiency that treatment with ASCOR may increase their risk of hemolysis [see Warnings and Precautions (5.2)].

Manufactured By:

McGuff Pharmaceuticals, Inc., Santa Ana, CA 92704 M381-0073

Bottom of Page

Side Two (Back)

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			or® Ascorbic Acid Injection, JmL Vial, Pharmacy Bulk F		
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	Sheet:	2 of 2			

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	HIGHLIGHTS OF PRESCRIBING IN ORMATION			
	These highlights do not include all the information needed to use ASCOR* safely and effectively. See full prescribing		MS AND STREM	1
	information for ASCOR. ASCOR (ascorbic acid injection), for incravenous use	Injection: 25,000 mg/50 m Package		
	Initial U.S. Approval: 1947	None CONTR	AINDICATIONS	,
1.	ASCOR is vitamin C indicated for the short term (up to 1	WARNINGS     Oxalate nephropathy and	AND PRECAUT Nephrolithiasis: A	
	week) treatment of scurvy in adult and pediatric patients age 5 months and older for whom oral administration is not possible, insufficient or contraindicated.	has been associated with oxalate nephropathy foll	development of a owing prolonged u	cute or chronic ise of high
	Limitations of Use.	doses of ascorbic acid in including renal impairm geriatric patients, land pe	ent, history of oxal	ate kidney stones,
	ASCOR is not indicated for treatment of vitamin C deficiency that is not associated with signs and symptoms of scurvy. ————————————————————————————————————	may be at increased risk • <u>Hemolysis</u> : Patients with	(5.1). 1 glucose-6-phosph	ate
	<ul> <li>Supplied in a Pharmacy Bulk Package (FBP). Dispense single doses to multiple patients in a pharmacy admixture</li> </ul>	dehydrogenase deficienc reduced dose is recomm	énded (5.2).	
	program, use within 4 hours of puncture (2.1) • Must be diluted prior to use (2.1)	<ul> <li><u>Laboratory Test Interfere</u> with laboratory tests bas including blood and urin</li> </ul>	ed on oxidation-re	duction reactions,
	Administer as a slow intravenous infusion (2.1)		SE REACTIONS	
	<ul> <li>See Full Prescribing Information for important administration instructions (2.1)</li> </ul>	Most common adverse rea site of infusion (6)	-	-
	Maximum recommended duration is one week (2.2)	To report SUSPECTED McGuff Pharmaceuticals	s, Inc., toll free at	1-800-603-4795
	Population (2.2) Recommended Doses	or FDA at 1-800-FDA-10 ————————————————————————————————————	INTERACTIONS	I
	Pediatric patients age 5 months to less than 12 months	<ul> <li>Antibiotics: Ascorbic ac erythromycin, kanamyci lineonycin, Blackwini</li> </ul>	n, streptomycin, do	oxycycline, and
	Pediatric patients age 1 year to less 100 mg once daily than 11 years	lincomycin. Bleomycin acid (7.1).		-
	Adults and pediatric patients age 11 200 mg once daily	<ul> <li>Amphetamine and Other Acidification: Aseorbic a urine and result in decre</li> </ul>	acid may cause aci ased amphetamine	dification of the serum levels and
	years and older Specific Populations (2.3, 8.1, 8.2)	affect excretion and plas sensitive to urine pH (7.	2).	-
	Pregnant women, lactating women, Should not exceed the	• <u>Warfarin</u> : Continue stan	-	
	patients with glucose-6-phosphate dehydrogenase deficiency (RDA)	See 17 for PATIENT CO		
		1		Revised: 01/2024
	FULL PRESCRIBING INFORMATION: CONTENTS*	10 OVERDOSAGE		
	1 INDICATIONS AND USAGE 2 DOSAGE AND ADMINISTRATION	11 DESCRIPTION 12 CLINICAL PHARMA	COLOGY	
	3 DOSAGE FORMS AND STRENGTHS 4 CONTRAINDICATIONS	12.1 Mechanism of Action 12.3 Pharmacokinetics	ons	
	5 WARNINGS AND PRECAUTIONS	13 NONCLINICAL TOX		
	6 ADVERSE REACTIONS 7 DRUG INTERACTIONS	13.1 Carcinogenesis, Mu 16 HOW SUPPLIED/ST		
	7.1. Antibiotics 7.2. Amphetamines & Other Drugs Affected by Urine	17 PATIENT COUNSEL *Sections or subsections or		1
	Acidification 7.3. Warfarin	information are not listed.		
	7.4. Laboratory Test Procedures			
	8 USE IN SPECIFIC POPULATIONS 8.1 Pregnancy			
	8.2 Lactation 8.4 Pediatric Use			
	8.5 Geriatric Use			
Fold #3	8.6 Renal Impairment			
<b>↓</b>	FULL PRESCRIBING INFORMATION 1 INDICATIONS AND USAGE			
14"	ASCOR® is indicated for the short term (up to 1 week) treatment of scurvy in adult and pediatric patients, age	Table 1: Recommended Rate of Diluted ASCOF		and Infusion
2.	5 months and older, for whom oral administration is not possible, insufficient or contraindicated.	Patient Population	ASCOR	Infusion Rate
	Limitations of Use ASCOR is not indicated for the treatment of vitamin C	T attent T optimitor	Once Daily Dose	of Diluted ASCOR
	deficiency that is not associated with signs and symptoms of scurvy.		(mg)	Solution (mg/minute)
	2 DOSAGE AND ADMINISTRATION 2.1 Important Preparation and Administration	Pediatric Patients age 5	50	1.3
	Instructions <ul> <li>ASCOR vials contain 25,000 mg of astorbic acid and the</li> </ul>	months to less than 12 months		
	largest recommended single dose is 200 mg. Do not give the entire contents of the vial to a single patient.	Pediatric Patients age 1 year to less than 11	100	3.3
	Do not administer ASCOR as an undiluted intravenous injection.	years		
	<ul> <li>Minimize exposure to light because A9COR is light sensitive.</li> </ul>	Adults and Pediatic Patients 11 years and	200	33
	<ul> <li>ASCOR is supplied as a Pharmacy Bulk Package (PBP) which is intended for dispensing of single doses to multiple nationation in pharmacy admiring a program and is</li> </ul>	older		
	nultiple patients in a pharmacy admixture program and is restricted to the preparation of admixtures for infusion: a. Use only in a suitable ISO Class 5 work area such	The recommended maxin with ASCOR is seven da	num duration of da ys. If no improven	aly treatment nent in scorbutic
	as a laminar flow hood (or an equivalent clean air compounding area).	with ASCOR is seven da symptoms is observed af until resolution of scorbu	ter one week of tre tic symptoms is ob	atment, retreat served.
	b. Penetrate each PBP vial closure only one time with a suitable sterile transfer device or dispensing set that	Repeat dosing is not reco than 11 years of age.	-	-
	allows measured dispensing of the contents. Given that pressure may develop within the vial during storage, exercise caution when withdrawing contents	2.3 Dosage Reductions Women who are pregnan		
	from the vial. c. Once the closure system has been penetrated, complete	Women who are pregnan glucose-6-dehydrogenas U.S. Recommended Diet Adequate Intake (D.D.)	e deficiency should ary Allowance (RI	not exceed the DA) or daily
	all dispensing from the PBP vial within 4 hours. Each dose must be used immediately. Discard	Adequate Intake (AI) lev group and condition [see and Use in Specifi <mark>c</mark> Popu	Warnings and Pre lations (8.1, 8.2)1.	cautions (5.2)
	unused portion. d. Prior to administration, ASCOR must be diluted in a switchle infusion solution and the final solution for	3 DOSAGE FORMS AN	D STRENGTHS	supplied as a
	suitable infusion solution and the final solution for infusion must be isotonic (undituted the osmolarity of ASCOR is approximately 5,900 mOsmol/L). Prior	Injection: 25,000 ing /50 Pharmacy Bulk Package solution)	(clear, colorless to	pale yellow
	to preparing the admixture for infusion, calculate the osmolarity of the intended admixture for infusion. Add one daily dose of ASCOR directly to an appropriate	4 CONTRAINDIGATIO None	NS	
	volume of a suitable infusion solution (e.g., 5% Dextrose Injection, Sterile Water for Injection) and	5 WARNINGS AND PRI		iada
	add appropriate solutes, as necessary, to make the final solution isotonic. Sterile Water for Injection is highly hypotonic: adjust solute content, as	5.1 Oxalate Nephropatl Acute and chronic oxalat with prolonged administr		
	is highly hypotonic; adjust solute content, as necessary, to make the final infusion solution	with prolonged administr	auon or nigh dose	s of ascoroic

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	<ul> <li>final sichtion isotonic:</li> <li>is highly hypotonic; a necessary, to make the isotonic prior to injec solutions containing el reduced (e.g., copper), acid in the final, admux be in the range of 1 to For example, for the la Add 200 mg of ascor mL of ASCOR to 7. Injection to produce an approximate osma this specific example necessary because the</li> <li>Prepare the recommen patient population fss (2.2), (2.3)].</li> <li>f. Visually inspect for part prior to administration should appear colorles g. Immediately administer slow intravenous infus (2.2)]</li> <li>2.2 Recommended Dosage</li> </ul>	ee Dosage and Administration ticulate matter and discoloration (the diluted ASCOR solution is to pale yellow). r the admixture for infusion as a ion [see Recommended Dosage ded doses of ASCOR based on ion rates of diluted ASCOR	Acute and chronic oxalate nep with prolonged administration acid. Acidification of the urin precipitation of cycleine, urate with renal disease uncluding re oxalate kidney stones, and ger increased risk for bxalate nep treatment with ascorbic acid. than 2 years of age may be at i nephropathy during treatment their kidneys are immature [se (8.4, 8.5, 8.6)]. Monitor renal increased risk receiving ASCC patients who develop oxalate 1 suspected oxalate hephropathy ASCOR is not indicated for pr maximum recommended dural and Administration (2.1)].	hropathy have been reported of high doses of ascorbic e by ascorbic acid may cause or oxalate stones. Patients mal impairment, history of lattic patients may be at iropathy while receiving Pechatric patients less increased risk for oxalate with ascorbic acid because with ascorbic acid because <i>us Use in Specific Populations</i> function in patients at R. Discontinue ASCOR in hephropathy and treat any t.			
Notes:				Created by / Date:	Ma	Cuff Dharmanauticala	Inc
<ol> <li>Fold in thirds starting at Forfor Fold #2.</li> <li>Fold in half starting at Fold Fold insert such that the 2 Side One is face up and visite final fold size is 1.5" x 7"</li> </ol>	d #3. d barcode on			Approved by / Date:	Title: Pacl	CGuff Pharmaceuticals kage Insert, Ascor® Ascorbic Acid Injee (500mg/mL), 50mL Vial, Pharmacy E Document #: DRW-0037 Part #: M381-0073 1 of 2	ction,

#### 5.2 Hemolysis in Patients with Glucose-6-Phosphate Dehydrog enase Deficien

Hemolysis has been reported with administration of ascorbic acid in patients with glucose-6-phosphate dehydrogenase deficiency. Patients with glucose-6-phosphate aenciency. ratients with glucosie-6-phosphate' dehydrogenase deficiency may be at increased risk for severe hemolysis during treatment with ascorbic acid. Monitor hemoglobin and blood count and use a reduced dose of ASCOR in patients with glucose-6-phosphate dehydrogenase deficiency [see Dosage and Administration (2.3)]. Discontinue treatment with ASCOR if hemolysis is suspected and treat as needed.

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#### 5.3 Laboratory Test Interference

Ascorbic acid may interfere with laboratory tests based on oxidation-reduction reactions, including blood and urine glucose testing, nitrite and bilirubin levels, and leucocyte count testing. If possible, laboratory tests based on oxidation-reduction reactions should be delayed until 24 hours after influsion of ASCOR [see Drug Interactions (7.5)].

#### 6 ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail in other sections of the labeling:

Oxalate nephropathy and Nephrolithiasis [see Warnings and Precautions (5.1)].

 Hemolysis in patients with glucose-6-phosphate dehydrogenase deficiency [see Warnings and Precautions (5, 2)] (5.2)]

The following adverse reactions associated with the use of ascorbic acid were identified in the literature. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to estimate their frequency reliably or to establish a causal relationship to drug exposure:

#### Administration site reactions: pain and swelling.

Administration site reactions: pain and sweiling. ASCOR should not be rapidly administered. Rapid intravenous administration (>250 mg/minute) of ASCOR may cause temporary faintness or nausea, lethargy, flushing dizziness, and headache (the recommended infusion rates of diluted ASCOR solution are 1.3 mg/minute (Pediatric Patients age 5 months to less than 12 months), 33 mg/ minute (Pediatric Patients age 1 year to less than 11 years) and 33 mg/minute (Adults and Pediatric Patients 11 years and older) [see Docage and Administration (2.2)]).

Acute and chronic oxalate nephropathy have occurred with prolonged administration of high does of ascorbic acid [see Warnings and Precautions (5.1)]. In patients with glucose-6-phosphate dehydrogenase deficiency, severe hemolysis has occurred [see Warnings and Precautions (5.2)]. 7 DRUG INTERACTIONS

#### 7.1 Antibiotics

Ascorbic acid may decrease activities of erythromycin kanamycin, streptomycin, doxycycline, and lincomycin Bleomycin is inactivated *in vitro* by ascorbic acid. If the antibiotic efficacy is suspected to be decreased by concomitant administration of ASCOR, discontinue ASCOR administration.

7.2 Amphetamine & Other Drugs Affected by Urine Acidification

Ascorbic acid may acidify the urine and lower serum concentrations of amphetamine by increasing renal excretion (as reflected by changes in amphetamine urine recovery rates). In case of decreased amphetamine efficacy, discontinue ASCOR administration. Standard monitoring of therapy is warranted.

In addition, acidification of urine by ascorbic acid will alter the excretion of certain drugs affected by the pH of the urine (e.g., fluphenazine) when administered concurrently. It has been reported that concurrent administration of ascorbic acid and fluphenazine has resulted in decreased fluphenazine plasma concentrations. Standard monitoring of therapy is warranted.

#### 7.3 Warfarin

4

Limited case reports have suggested interference of ascorbic acid with the anticoagulation effects of warfarin; however, for patients on warfarin therapy treated with ascorbic acid doses up to 1000 mg/day (5 times the largest recommended single dose) for 2 weeks (twice the maximum recommended duration), no effect was observed. Standard monitoring for anti-coagulation therapy should continue during ascorbic acid treatment, as per standard of care.

#### 7.4 Laboratory Test Interference

Because ascorbic acid is a strong reducing agent, it can Because ascoroic acta is a strong reducing agent, it can interfere with numerous laboratory tests based on oxidation-reduction reactions (e.g., glucose, nitrite and bilirubin levels, leukocyte count, etc.). Chemical detecting methods based on colorimetric reactions are generally those tests affected. Ascoroic acid may lead to inaccurate results (false negatives) obtained for checking blood or urinary glucose levels, nitrite, bilirubin, and leukocytes if tested during or within 24 hours after infusion [see Warnings and Precautions (5.3)]. 8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy Risk Summary

There are no available data on use of ASCOR in pregnant women to inform a drug-associated risk of adverse developmental outcomes; however, use of ascorbic acid (vitamin C) has been used during pregnancy for several decades and no adverse developmental outcomes are reported in the published literature [see Data]. There are dose adjustments for ascorbic acid (vitamin C) use during pregnancy [see Clinical Considerations].

Animal reproduction studies have not been conducted with ASCOR.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

#### Clinical Considerations

Dose Adjustments During Pregnancy and Post-Partum Period

Follow the U.S. Recommended Dietary Allowances (RDA) for pregnant women when considering use of ASCOR for treatment of scurvy [see Dosage and Administration (2.3)].

Data

#### Human Data

There are no available data on use of ASCOR or another

Recommended Dietary Allowances (RDA) for lactating women when considering use of ASCOR for treatment of scurvy [see Dosage and Administration (2.3)]. 8.4 Pediatric Use

### ASCOR is indicated for the short term (up to 1 week)

ASCOR is indicated for the short term (up to 1 week) treatment of scurvy in pediatric patients age 5 months and older for whom oral administration is not possible, insufficient or contraindicated. The safety profile of ascorbic acid in pediatric patients is similar to adults; however, pediatric patients less than 2 years of age may be at higher risk of oxalate nephropathy following ascorbic acid administration due to age-related decreased glomerular filtration *[see Warnings and Precautions (5.1)]*. ASCOR is not indicated for use in pediatric patients less

#### nths of age than 5 m 8.5 Geriatric Use

Glomerular filtration rate is known to decrease with age and as such may increase risk for oxalate nephropathy following ascorbic acid administration in elderly population [see Warnings and Precautions (5.1)].

#### 8.6 Renal Impairment

3.0 Kenal impairment ASCOR should be used with caution in scorbutic patients with a history of or risk of developing renal oxalate stones evidence of renal impairment or other issues (e.g., patients on dialysis, patients with diabetic nephropathy, and renal transplant recipients). These patients may be at increased risk of developing acute or chronic oxalate nephropathy following high dose ascorbic acid administration [see Warning and Precautions (5.1)].

## 10 OVERDOSAGE

Overdose with ascorbic acid may cause nausea, vomiting, diarnhea, facial flushing, rash, headache, fatigue or disturbed sleep. If overdose of ASCOR occurs, immediately discontinue administration and treat symptoms and signs of overdose, avoiding additional intake of ascorbic acid.

### 11 DESCRIPTION

A SCOR (ascorbic acid injection) for intravenous use is a colorless to pale yellow, preservative-free, hypertonic, sterile, non-pyrogenic solution of ascorbic acid. ASCOR must be dhitted with an appropriate infusion solution (e.g. 5% Dextrose Injection, USP; Sterile Water for Injection, USP) [see Dosage and Administration (2.1)].

The chemical name of Ascorbic Acid is L-ascorbic acid. The molecular formula is  $C_6H_8O_6$ . It has the following structural formula:



Each ASCOR, 50 mL, Pharmacy Bulk Package vial contains 25,000 mg ascorbic acid, equivalent to 28,125 mg sodium

ascoroate. Each mL of ASCOR contains 500 mg of ascorbic acid (equivalent to 562.5 mg of sodium ascorbate which amout to 85 mg sodium/mL of ASCOR), 130 mg of Sodium bicarbonate, and 0.25 mg of edetate disodium. Sodium hydroxide is added for pH adjustment (pH range 5.6-6.6). If contains no bacteriostatic or antimicrobial agent.

#### 12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The exact mechanism of action of ascorbic acid for the treatment of symptoms and signs of scurvy (a disorder caused by severe deficiency in vitamin C) is unknown, however, administration of ascorbic acid in patients with scurvy is thought to restore the body pool of ascorbic acid. 12.3 Pharmacokinetics

In a single pharmacokinetic study, healthy male and female adults (n=8) were given a single intravenous dose of 1000 mg ascorbic acid (5 times the largest recommended single dose) inflused over a 30 minute period. The mean peak exposure to ascorbic acid was 436.2  $\mu$ M and occurred at the end of the 30 minute influsion.

#### Distribution

Ascorbic acid is distributed widely in the body, with large concentrations found in the liver, leukocytes, platelets, glandular tissues, and lens of the eye. Based on data from oral exposure, ascorbic acid is known to be distributed into breast milk and crosses the placental barrier.

#### Elimination

When the body is saturated with ascorbic acid, the plasma concentration will be about the same as that of the renal threshold, if further amounts are then administered, most of it is excreted in the urine. When body tissues are not saturated and plasma concentration is low, administration of ascorbic acid results in little or no renal excretion. The mean+SD (N=3) half-life observed in the single dose PK study, as described above, was 7.4±1.4 h. Metabolism

## A major route of metabolism of ascorbic acid involves its conversion to urinary oxalate, presumably through intermediate formation of its oxidized product, dehydroascorbic acid.

Excretion

There is a renal threshold for ascorbic acid (vitamin C); the vitamin is excreted by the kidney in large amounts only when the plasma concentration exceeds this threshold, which is approximately 1.4 mg/100 mL.

## 13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity, mutagenicity, and fertility studies have not been performed with ASCOR.

#### 16 HOW SUPPLIED/STORAGE AND HANDLING ASCOR for intravenous use is a colorless to pale yellow

olution supplied as: NDC 67157-101-50 One 25,000 mg/50 mL (500 mg/mL)

NDC 67157-101-51 Tray pack of twenty five 25,000 mg/50 mL (500 mg/mL) Pharmacy Bulk Package viale

vials

## Store in a refrigerator at 2° to 8°C (36° to 46°F).

Protect from light. This product contains no preservative. See Dosage and Administration (2.1) for detailed instructions on preparation, dilution, and administration of ASCOR. Excursions to ambient conditions for up to 30 days during storage or shipping are acceptable.

There are no available data on use of ASCOR or another ascorbic acid injection in pregnant women. However, a published meta-analysis of randomized studies evaluating a large number of pregnant women who took oral ascorbic acid (vitamin C) (through diet and supplementation) at dosses ranging from 500 to 1000 mg/day (2.5 to 5 times the recommended daily intravenous dose, respectively) [see Dosage and Administration (2.3)] between the 9th and 16th weeks of pregnancy showed no increased risk of adverse pregnancy outcomes such as miscarriage, preterm premature rupture of membranes, preterm delivery or pregnancy induced hypertension when compared to placebo. These data cannot definitively establish or exclude the absence of a risk with ascorbic acid (vitamin exclude the absence of a risk with ascorbic acid (vitamin C) during pregnancy.

#### 8.2 Lactation

#### Risk Summarv

There are no data on the presence of ascorbic acid (vitamin C) in human milk following intravenous dosing in lactating women. Ascorbic acid (vitamin C) is present in human milk after maternal oral intake. Maternal oral intake of ascorbic acid (vitamin C) exceeding the U.S. Recommended Dietary Allowances (RDA) for lactation does not influence the ascorbic acid (vitamin C) content in breast milk or the estimated daily amount received by breastfed infants. There are no data on the effect of ascorbic acid (vitamin C) on milk production or the breastfed infant. The devalopmental -nended milk production or the breastfed infant. The developmental and health benefits of breastfeding should be considered along with the mother's clinical need for ASCOR and any potential adverse effects on the breastfed child from ASCOR or from the underlying maternal condition. Follow the U.S.

#### 17 PATIENT COUNSELING INFORMATION

- Inform patients that treatment with ASCOR may increase their risk of oxalate nephropathy [see Warnings and Procentions (5.1)] Precautions (5.1)].
- · Inform patients that treatment with ASCOR may impact laboratory results, including blood and urine glucose tests, up to 24 hours after infusion [see Warnings and Precautions (5.3)].
- Inform patients with glucose-6-phosphate dehydrogenase deficiency that treatment with ASCOR may increase their risk of hemolysis [see Warnings and Precautions (5.2)].

Manufactured By:

McGuff Pharmaceuticals, Inc., Santa Ana, CA 92704 M381-0073

Bottom of Page

Side Two (Back)

Created by / Date:	McGuff Pharmaceuticals, Inc.				
			or® Ascorbic Acid Injection, JmL Vial, Pharmacy Bulk F		
Approved by / Date:	Size:	Document #: Part #:	DRW-0037 M381-0073	Rev: 05	
	Sheet:	2 of 2			

	Top of Page	6"		
1				
	HIGHLIGHTS OF PRESCRIBING INFORMATION	DOSAGE FORM	IS AND STRENGT	ня ———
	These highlights do not include all the information needed to use ASCOR <sup>®</sup> safely and effectively. See full prescribing information for ASCOR.	Injection: 25,000 mg/50 mL (500 mg/n	nL) – Pharmacy Bulk	
	ASCOR (ascorbic acid injection), for intravenous use	CONTRA None	INDICATIONS -	
	Initial U.S. Approval: 1947	WARNINGS A	ND PRECAUTION	
Fold	INDICATIONS AND USAGE ASCOR is vitamin C indicated for the short term (up to 1 week) treatment of scurvy	<ul> <li><u>Oxalate nephropathy and Nephrolithi</u> development of acute or chronic oxal high doses of ascorbic acid infusion.</li> </ul>	asis: Ascorbic acid h ate nephropathy follo	as been associated with wing prolonged use of
	in adult and pediatric patients age 5 months and older for whom oral administration - is not possible; maufficient or contraindicated:	<ul> <li>high doses of ascorbic acid infusion.</li> <li>impairment, history of exalide kidney patients less than 2 years old may be</li> </ul>	Patients with renal d	isease including renal ents, and pediatric
	Limitations of Use ASCOR is not indicated for treatment of vitamin C deficiency that is not associated	<ul> <li><u>Hemolysis</u>: Patients with glucose-6-p</li> </ul>	hosphate dehydroger	nase deficiency are at
	with signs and symptoms of scurvy.	risk of severe hemolysis; a reduced d • Laboratory Test Interference: Ascorb		
	DOSAGE AND ADMINISTRATION     Supplied in a Pharmacy Bulk Package (PBP). Dispense single doses to multiple	based on oxidation-reduction reaction (5.3).		
	<ul> <li>Supplied in a Pharmacy Bulk Package (PBP). Dispense single doses to multiple patients in a pharmacy admixture program; use within 4 hours of puncture (2.1)</li> <li>Must be diluted prior to use (2.1)</li> </ul>		E REACTIONS -	
	Administer as a slow intravenous infusion (2.1)	Most common adverse reactions are pa To report SUSPECTED ADVERSE 1	-	
	<ul> <li>See Full Prescribing Information for important administration instructions (2.1)</li> <li>Maximum recommended duration is one week (2.2)</li> </ul>	To report SUSPECTED ADVERSE I Pharmaceuticals, Inc., toll free at 1-8 or www.fda.gov/medwatch.	00-603-4795 or FD.	A at 1-800-FDA-1088
		7	TERACTIONS -	- ai-
Fold	Population (2.2) Recommended Doses	<ul> <li><u>Antibiotics</u>: Ascorbic acid may decre kanamycin, streptomycin, doxycyclin m vino by ascorbic acid (7.1).</li> </ul>	ase the activities of e ie, and lincomycin. B	rythromycin, leomycin is inactivated
	Pediatric patients age 5 months to less than 12 months	<ul> <li>Amphetamine and Other Drugs Affect</li> </ul>	ted by Urine Acidific	ation: Ascorbic acid
	Pediatric patients age 1 year to less 100 mg once daily than 11 years	may cause acidification of the urine a levels and affect excretion and plasm urine pH (7.2).		
	Adults and pediatric patients age 11 200 mg once daily	<u>Warfarin</u> : Continue standard monitor	ing (7.3).	
	years and older	See 17 for PATIENT COUNSELING	INFORMATION	
	Specific Populations (2.3, 8.1, 8.2)	4		Revised: 01/2024
	Pregnant women, lactating women, patients with glucose-6-phosphate believe the former of the second			
Fold	dehydrogenase deficiency	]		
	FULL PRESCRIBING INFORMATION: CONTENTS*	10 OVERDOSAGE		
	1 INDICATIONS AND USAGE	11 DESCRIPTION		
	2 DOSAGE AND ADMINISTRATION 3 DOSAGE FORMS AND STRENGTHS	12 CLINICAL PHARMACOLOGY 12.1 Mechanism of Actions		
	4 CONTRAINDICATIONS	12.3 Pharmacokinetics		
	5 WARNINGS AND PRECAUTIONS 6 ADVERSE REACTIONS	13 NONCLINICAL TOXICOLOGY 13.1 Carcinogenesis, Mutagenesis, J		tv.
	7 DRUG INTERACTIONS	16 HOW SUPPLIED/STORAGE A	•	.y
	7.1. Antibiotics	17 PATIENT COUNSELING INFO *Sections or subsections omitted from		nformation are not listed
Fold	7.2. Amphetamines & Other Drugs Affected by Urine Acidification 7.3. Warfarin	sections or subsections onlined from	are ran presentoing i	mormation are not listed.
	7.4. Laboratory Test Procedures 8 USE IN SPECIFIC POPULATIONS			
	8 USE IN SPECIFIC FOFULATIONS 8.1 Pregnancy			
I	8.2 Lactation 8.4 Pediatric Use			
75"	8.5 Geriatric Use			
12.7	8.6 Renal Impairment			
	FULL PRESCRIBING INFORMATION	Table 1: Recommended Dose of A ASCOR Solution	SCOR and Infusion	Rate of Diluted
Fold	1 INDICATIONS AND USAGE ASCOR® is indicated for the short term (up to 1 week) treatment of scurvy in adult		100000.0	THE PLAN
	ASCOR® is indicated for the short term (up to 1 week) treatment of scurvy in adult - and-pediatate-patients, age 5 months and older; for-whom oral administration-is-not- possible, insufficient or contrainicated.	Patient Population	ASCOR Once Daily Dose	Infusion Rate of Diluted ASCOR
	Limitations of Use		(mg)	Solution (mg/minute)
	ASCOR is not indicated for the treatment of vitamin C deficiency that is not associated with signs and symptoms of scurvy.	Pediatric Patients age 5 months to	50	1.3
	2 DOSAGE AND ADMINISTRATION 2.1 Important Preparation and Administration Instructions	less than 12 months		
	ASCOR vials contain 25,000 mg of ascorbic acid and the largest recommended	Pediatric Patients age 1 year to less than 11 years	100	3.3
	single dose is 200 mg. Do not give the entire contents of the vial to a single patient.	Adults and Pediatric Patients 11	200	33
	<ul> <li>Do not administer ASCOR as an undiluted intravenous injection.</li> <li>Minimize exposure to light because ASCOR is light sensitive.</li> </ul>	years and older		
Fold	<ul> <li>ASCOR is supplied as a Pharmacy Bulk Package (PBP) which is intended for dispensing of single doses to multiple patients in a pharmacy admixture program</li> </ul>	The recommended maximum duration	on of daily treatment	with ASCOR is seven
	and is restricted to the preparation of admixtures for infusion:	treatment, retreat until resolution of	ie-symptome is observ	ved-after one week of
	<ul> <li>a. Use only in a suitable ISO Class 5 work area such as a laminar flow hood (or an equivalent clean air compounding area).</li> </ul>	2 3 Dosage Reductions in Specific		ess than 11 years of age.
	b. Penetrate each PBP vial closure only one time with a suitable sterile transfer device or dispensing set that allows measured dispensing of the contents.			lucose-6-dehydrogenase
	Given that pressure may develop within the vial during storage, exercise caution when withdrawing contents from the vial.	Women who are pregnant or lactatin deficiency should not exceed the U.3 or daily Adequate Intake (AI) level condition <i>[see Warnings and Precau</i>	or ascorbic acid for t for ascorbic acid for t	heir age group and
	c. Once the closure system has been penetrated, complete all dispensing from the PBP vial within 4 hours. Each dose must be used immediately.	(8.1, 8.2)].		pooque i opinations
	Discard unused portion. d. Prior to administration, ASCOR must be diluted in a suitable infusion	3 DOSAGE FORMS AND STREN Injection: 25,000 mg /50 mL (500 m	g/mL) supplied as a l	Pharmacy Bulk Package
	solution and the final solution for infusion must be isotonic (undiluted the osmolarity of ASCOR is approximately 5,900 mOsmol/L). Prior	(clear, colorless to pale yellow solut 4 CONTRAINDICATIONS	ion)	
Fold	to preparing the admixture for influsion, calculate the osmolarity of the intended admixture for influsion. Add one daily dose of ASCOR directly to an emerginate understanding of a simple admixture activity of the admixture of a simple admixture	None		
	to an appropriate volume of a suitable influsion solution (e.g., 5% Dextrose Injection, Sterile Water for Injection) and add appropriate soluties, as processary to make the final solution isotonic. Sterile Water for Injection	5. WARNINGS AND PRECAUTIO 5.1 Oxalate Nephropathy and Nep		
	nécessary, to make the final solution isotonic. Sferile Water for Injection is highly hypotonic; adjust solute content, as necessary, to make the final infusion solution isotonic prior to injection. Do not mix ASCOR	Acute and chronic oxalate nephropa administration of high doses of asco		d with prolonged
	with solutions containing elemental compounds that can be reduced (e.g., copper). The concentration of ascorbic acid in the final, admixture solution	administration of high doses of asco ascorbic acid may cause precipitatio	roic acid. Acidificati n of cysteine, urate o	on of the urine by r oxalate stones. Patients
	for infusion is to be in the range of 1 to 25 mg of ascorbic acid per mL. For example, for the largest recommended dose:		eased risk for oxalate	nephropathy while
1		receiving nearment with ascoroic ac	m. remaine patients	icos man 2 years of age
	Add 200 mg of ascorbic acid (equivalent to 0.4 mL of ASCOR) to 7.5 mL of Sterile Water for Injection to produce an infusion solution having	receiving treatment with ascorbic ac may be at increased risk for oxalate acid because their kidneys are imma	ture Isee Use in Spec	ific Populations (8.4.
	mL of Sterile Water for Injection to produce an infusion solution having an approximate osmolarity of 290 mOsmol/L. In this specific example,	acid because their kidneys are imma 8.5, 8.6)]. Monitor renal function in	ture [see Use in Spec patients at increased	ific Populations (8.4, risk receiving ASCOR.
	<ul> <li>mL of Sterile Water for Injection to produce an infusion solution having an approximate osmolarity of 290 mOsmol/L. In this specific example, addition of solute is NOT necessary because the solution is isotonic.</li> <li>e. Prepare the recommended dose based on the patient population [see</li> </ul>	acid because their kidneys are imma <i>8.5, 8.6)]</i> . Monitor renal function in Discontinue ASCOR in patients who suspected oxalate nephropathy.	ture [see Use in Spec patients at increased develop oxalate nep	<i>ific Populations (8.4,</i> nisk receiving ASCOR. hropathy and treat any
Fold	mL of Sterile Water for Injection to produce an infusion solution having an approximate osmolarity of 290 mOsmol/L. In this specific example, addition of solute is NOT necessary because the solution is isotonic.	acid because their kidneys are imma 8.5, 8.6)]. Monitor renal function in Discontinue ASCOR in patients who	ture [see Use in Spec patients at increased o develop oxalate nep ed administration (th [see Dosage and Ad	ific Populations (8.4, risk receiving ASCOR. hropathy and treat any e maximum ministration (2.1)].

Fold	<li>f. Visually inspect for particulate matter and discoloration prior to administration (the diluted ASCOR solution should appear colorless to pale vellow).</li>	5.2 Hemolysis in Patients with Glucose-6-Phosphate Dehydrogenase Deficiency	
	<ul> <li>g. Immediately administer the admixture for infusion as a slow intravenous infusion [<i>see Recommended Dosage</i> (2.2)]</li> <li>2.2 Recommended Dosage Table 1 provides recommended doses of ASCOR based on patient population and infusion rates of diluted ASCOR solution.</li> </ul>	Hemolysis has been reported with administration of ascorbic acid in patients with glucose-6-phosphate dehydrogenase deficiency. Patients with glucose-6-phosphate dehydrogenase deficiency may be at increased risk for severe hemolysis during treatment with ascorbic acid. Monitor hemoglobin and blood count and use a reduced dose of ASCOR in patients with glucose-6-phosphate dehydrogenase deficiency <i>Isee Dosage and Administration (2.3)</i> . Discontinue treatment with ASCOR if hemolysis is suspected and treat as needed. <b>5.3 Laboratory Test Interference</b> Ascorbic acid may interfere with laboratory tests based on oxidation-reduction reactions, including blood and urine glucose testing, initie and bilirubin levels, and leucocyte count testing. If possible, laboratory tests based on oxidation-reduction reactions should be delayed until 24 hours after infusion of ASCOR <i>Isee Drug Interactions (7.5)</i> ].	
	Bottom of Page		

Side One (Front)

Notes:

- 1. Fold insert such that the product name and 2d barcode on Side One is face up and visible. Final fold size is 1.416" x 6"
- 2. Glue dots are applied to the interior surface of the top flap of the insert

Created by / Date:	Мс	McGuff Pharmaceuticals, Inc.				
		· ·	or® Ascorbic Acid Injection 0mL Vial, Pharmacy Bulk			
Approved by / Date:	Size: Sheet:	Document #: Part #: 1 of 2	DRW-0037 M381-0073	Rev: 05		

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The following adverse reactions are discussed in greater detail in other sections of the labeling:

 Oxalate nephropathy and Nephrolithiasis [see Warnings and Precautions (5.1)]. Hemolysis in patients with glucose-6-phosphate dehydrogenase deficiency [see Warnings and Precautions (5.2)].

The following adverse reactions associated with the use of ascorbic acid were identified in the literature. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to estimate their frequency reliably or to establish a causal relationship to drug exposure:

#### Administration site reactions: pain and swelling.

Administration sine reactions, pain and sweining. ASCOR should not be rapidly administered. Rapid intravenous administration (~250 mg/minute) of ASCOR may cause temporary faintness or nausea, lethargy, flushing, dizziness, and headache (the recommended influsion rates of diluted ASCOR solution are 1.3 mg/minute (Pediatric Patients age 5 months to less than 12 months), 3.3 mg/minute (Pediatric Patients age 1 year to less than 11 years) and 33 mg/minute (Adults and Pediatric Patients 11 years and older) [see Doscoge and Administration (2.2)]).

# Acute and chronic oxalate nephropathy have occurred with prolonged administration of high doses of accorbic acid *Isee Warnings and Precautions* (5.1)). In patients with glucose-6-phosphate dehydrogenase deficiency, severe hemolysis has occurred *Isee Warnings and Precautions* (5.2)].

7 DRUG INTERACTIONS

## 7.1 Antibiotics

Ascorbic acid may decrease activities of erythromycin, kanamycin, streptomycin, doxycycline, and lincomycin. Bleomycin is inactivated *in vitro* by ascorbic acid. If the antibiotic efficacy is suspected to be decreased by concomitant administration of ASCOR, discontinue ASCOR administration.

#### 7.2 Amphetamine & Other Drugs Affected by Urine Acidification

Ascorbic acid may acidify the urine and lower serum concentrations of amphetamine by increasing renal excretion (as reflected by changes in amphetamine urine recovery rates). In case of decreased amphetamine efficacy, discontinue ASCOR administration. Standard monitoring of therapy is warranted.

In addition, acidification of urine by ascorbic acid will alter the excretion of certain drugs affected by the pH of the urine (e.g., fluphenazine) when administered concurrently. It has been reported that concurrent administration of ascorbic acid and fluphenazine has resulted in decreased fluphenazine plasma concentrations. Standard monitoring of therapy is warranted.

#### 7.3 Warfarin

Limited case reports have suggested interference of ascorbic acid with the anticoagulation effects of warfarin; however, for patients on warfarin therapy treated with ascorbic acid doses up to 1000 mg/day (5 times the largest recommended single dose) for 2 weeks (twice the maximum recommended duration), no effect was observed. Standard monitoring for anti-coagulation therapy should continue during ascorbic acid treatment, as per standard of care. 7.4 Laboratory Test Interference

Because acorbic acid is a strong reducing agent, it can interfere with numerous laboratory tests based on oxidation-reduction reactions (e.g., glucose, nitrite and bilirubin levels, leukocyte count, etc.). Chemical detecting methods based on colorimetric reactions are generally those tests affected. Ascorbic acid may lead to inaccurate results (false negatives) obtained for checking blood or urinary glucose levels, mitrite, bilirubin, and leukocytes if tested during or within 24 hours after infusion [see Warnings and Precautions (5.3)].

### 8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no available data on use of ASCOR in pregnant women to inform a drug-associated risk of adverse developmental outcomes; however, use of ascorbic acid (vitamin C) has been used during pregnancy for several decades and no adverse developmental outcomes are reported in the published literature [see Data]. There are dose adjustments for ascorbic acid (vitamin C) use during pregnancy [see Clinical Considerations].

#### Animal reproduction studies have not been conducted with ASCOR.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

#### Clinical Considerations

Dose Adjustments During Pregnancy and Post-Partum Period Follow the U.S. Recommended Dietary Allowances (RDA) for pregnant women when considering use of ASCOR for treatment of scurvy [see Dosage and Administration (2.3)].

#### Data Human Data

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Human Data There are no available data on use of ASCOR or another ascorbic acid injection in pregnant women. However, a published meta-analysis of randomized studies evaluating a large number of pregnant women who took oral ascorbic acid (vitamin C) (htrough diet and supplementation) at doses ranging from 500 to 1000 mg/day (2.5 to 5 times the recommended daily intravenous dose, respectively) [see Dosage and Administration (2.3)] between the 9th and 16th weeks of pregnancy showed no increased risk of adverse pregnancy outcomes such as miscarriage, preterm premature rupture of membranes, pretern delivery or pregnancy induced hypertension when compared to placebo. These data cannot definitively establish or exclude the absence of a risk with ascorbic acid (vitamin C) during pregnancy.

### 8.2 Lactation

Risk Summarv

Risk Summary. There are no data on the presence of ascorbic acid (vitamin C) in human milk following intravenous dosing in lactating women. Ascorbic acid (vitamin C) is present in human milk after maternal oral intake. Maternal oral intake of ascorbic acid (vitamin C) exceeding the U.S. Recommended Dietary Allowances (RDA) for lactation does not influence the ascorbic acid (vitamin C) content in breast milk or the estimated daily amount received by breastfed infants. There are no data on the effect of ascorbic acid (vitamin C) on milk production or the breastfed infant. The developmental and health benefits of breastfeding should be considered along with the mother's clinical need for ASCOR and any potential adverse effects on the breastfed child from ASCOR or from the underlying maternal condition. Follow the U.S. Recommended Dietary Allowances (RDA) for lactating women when considering use of ASCOR for treatment of scurvy [*See Dosage and Administration (2.3)*].

#### 8.4 Pediatric Use

A remain Use ASCOR is indicated for the short term (up to 1 week) treatment of scurvy in pediatric patients age 5 months and older for whom oral administration is not possible, insufficient or contraindicated. The safety profile of ascorbic acid in pediatric patients is similar to adults; however, pediatric patients less than 2 year of age may be at higher risk of oxalate nephropathy following ascorbic acid administration due to age-related decreased glomerular filtration [see Warnings and Precautions (5.1)].

ASCOR is not indicated for use in pediatric patients less than 5 months of age 8.5 Geriatric Use

Glomerular filtration rate is known to decrease with age and as such may increase risk for oxalate nephropathy following ascorbic acid administration in elderly population [see Warnings and Precautions (5.1)].

8.6 Renal Impairment

#### 11 DESCRIPTION

- ASCOR (ascorbic acid injection) for intravenous use is a colorless to pale yellow, preservative-free, hypertonic, sterile, non-pyrogenic solution of ascorbic acid. ASCOR must be dulited with an appropriate infusion solution (e.g., 5% Dextrose Injection, USP; Sterile Water for Injection, USP) [see Dosage and Administration dulity] Injecta (2.1)].
- The chemical name of Ascorbic Acid is L-ascorbic acid. The molecular formula is  $C_{o}H_{*}O_{o}$ . It has the following structural formula:



Each ASCOR, 50 mL, Pharmacy Bulk Package vial contains 25,000 mg as corbic acid, equivalent to 28,125 mg sodium as corbate.

Each mL of ASCOR contains 500 mg of ascorbic acid (equivalent to 562.5 mg of sodium ascorbate which amounts to 65 mg sodium/mL of ASCOR), 130 mg of Sodium bicarbonate, and 0.25 mg of edetate disodium. Sodium hydroxide is added for pH adjustment (pH range 5.6-6.6). It contains no bacteriostatic or minimicrobia search antimicrobial agent.

#### 12 CLINICAL PHARMACOLOGY 12.1 Mechanism of Action

The exact mechanism of action of ascorbic acid for the treatment of symptoms and signs of scurvy (a disorder caused by severe deficiency in vitamin C) is unknown; however, administration of ascorbic acid in patients with scurvy is thought to restore the body pool of ascorbic acid.

#### 12.3 Pharmacokinetics

In a single pharmacokinetic study, healthy male and female adults (n=8) were given a single intravenous dose of 1000 mg ascorbic acid (5 times the largest recommended single dose) infused over a 30 minute period. The mean peak exposure to ascorbic acid was 436.2 µM and occurred at the end of the 30 minute infusion.

#### Distribution

Ascorbic acid is distributed widely in the body, with large concentrations found in the liver, leukocytes, platelets, glandular tissues, and lens of the eye. Based on data from oral exposure, ascorbic acid is known to be distributed into breast milk and crosses the placental barrier. Elimination

When the body is saturated with ascorbic acid, the plasma concentration will be about the same as that of the renal threshold; if further amounts are then administered, most of it is excreted in the urine. When body tissues are not auminisered, most of it is excreted in ite unite: when outly usuals are how assumed and plasma concentration is low, administration of ascorbic acid results in little or no renal excretion. The mean+SD (N=3) half-life observed in the single dose PK study, as described above, was 7.4±1.4 h. Metabolism

A major route of metabolism of ascorbic acid involves its conversion to urinary oxalate, presumably through intermediate formation of its oxidized product, dehydroascorbic acid. Excretion

There is a renal threshold for ascorbic acid (vitamin C); the vitamin is excreted by the kidney in large amounts only when the plasma concentration exceeds this threshold, which is approximately 1.4 mg/100 mL.

#### 13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility Carcinogenicity, mutagenicity, and fertility studies have not been performed with ASCOR.

16 HOW SUPPLIED/STORAGE AND HANDLING

- ASCOR for intravenous use is a colorless to pale yellow solution supplied as: NDC 67157-101-50 One 25,000 mg/50 mL (500 mg/mL) Pharmacy Bulk Package vial
- NDC 67157-101-51 Tray pack of twenty five 25,000 mg/50 mL (500 mg/mL) Pharmacy Bulk Package vials
- Store in a refrigerator at 2° to 8°C (36° to 46°F).

Protect from light. This product contains no preservative. See Dosage and Administration (2.1) for detailed instructions on preparation, dilution, and administration of ASCOR. Excursions to ambient conditions for up to 30 days during storage or shipping are acceptable

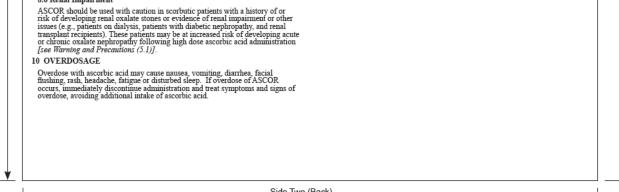
17 PATIENT COUNSELING INFORMATION

- Inform patients that treatment with ASCOR may increase their risk of oxalate nephropathy [see Warnings and Precautions (5.1)].
- Inform patients that treatment with ASCOR may impact laboratory results, including blood and urine glucose tests, up to 24 hours after infusion [see Warnings and Precautions (5.3)].
- Inform patients with glucose-6-phosphate dehydrogenase deficiency that treatment with ASCOR may increase their risk of hemolysis [see Warnings and Precautions (5.2)].

#### Manufactured By:

McGuff Pharmaceuticals, Inc., Santa Ana, CA 92704 M381-0073

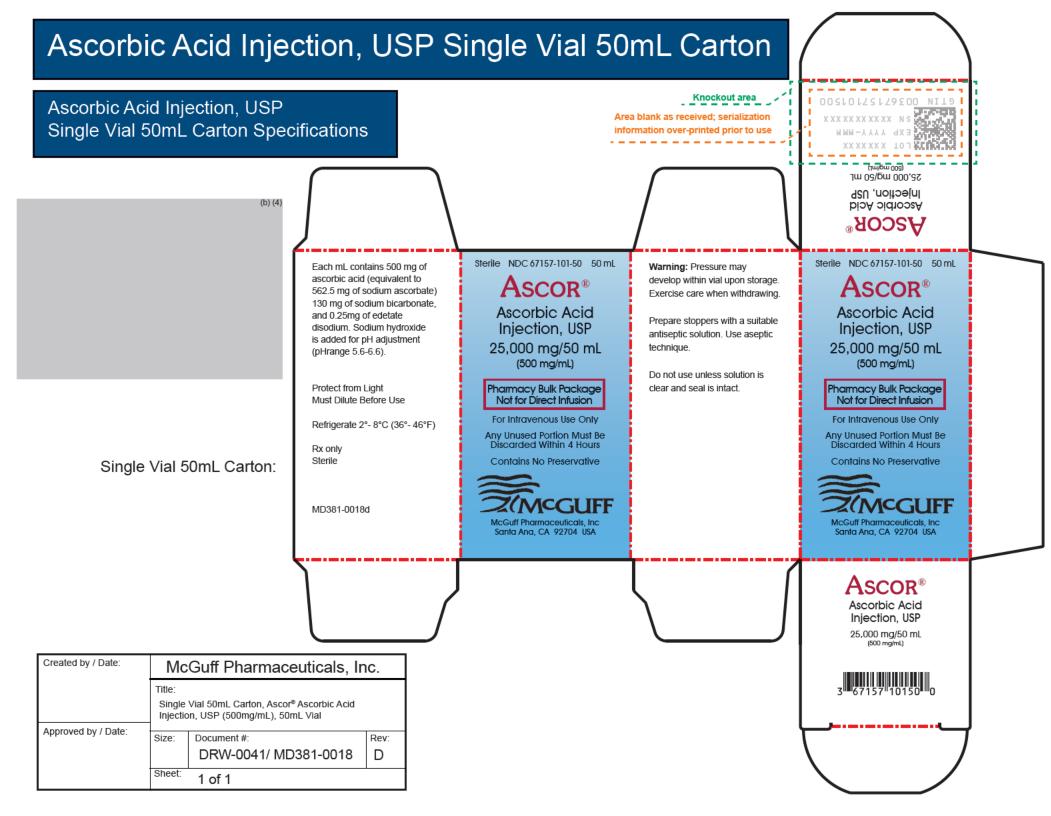
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# Ascorbic Acid Injection, USP Vial Label



## Ascorbic Acid Injection, USP Vial Label Specifications



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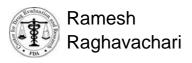
# Ascorbic Acid Injection, USP 25 Tray Pack Label



# Ascorbic Acid Injection, USP 25 Tray Pack Label Specifications

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