

Appendix I

Evidence Table per FDA Draft Guidance Document

Venous ulcers

Evidence Table - RCTS of venous ulcers (additional data on 20 selected studies)

Author Year Country	Population	# Patients (# ulcers)	Ulcer duration	Provider / Treatment duration / Method of wound size assessment	FDA Draft Guidance Document Recommendations						1° Outcome	2° Outcome
					Partial wound closure	Complete wound closure	3 months post-wound closure assessment	Wound size pre- & post- debridement	Antimicrobial treatment			
									Systemic versus topical	Pre- versus during study		
Arosio 2001 Italy	Age 62±11 % male Tx: 73 Ctrl: 67 Setting Outpatient clinics	183	3 months	Provider unknown/ Treatment until healing or at 24 weeks/ Computerized planimetry	N	Y	N	ND	ND	ND	Time to healing; complete ulcer epithelialization	Time-course of ulcer-associated pain
Barwell 2004 UK	Age 73 % male 42 Setting Outpatient	500	5 months	Nurse/ 24 weeks/ Not specified	N	Y	Y	ND	ND	ND	Complete epithelialization or ulcer healing rate at 24 weeks	Epithelial breakdown or recurrence rate at 12 months
Coccheri 2002 Italy	Age 63 % male 46 Setting Outpatient	235	66% up to 1 year 34% > 1 year	Provider unknown/ 3 months/ Computerized planimetry	N	Y	N	ND	ND	At study	Complete healing or re- epithelialization	Complete ulcer healing after 3 months & time course of reduction of ulcer area

Mean and standard deviation unless otherwise noted.

¹ Unclear whether complete or partial wound closure.

² Subset of Falanga 2000.

Abbreviations: ABI = ankle/brachial index; Y = yes; N = no; ND = no data

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									Systemic versus topical	Pre- versus during study		
Dale 1999 UK	Age 70 % male 34 Setting Outpatient leg ulcer clinics	200	≥ 2 months	Non-patient provider/ 24 weeks/ Planimetry	N	Y	N	ND	ND	ND	Healing rate; complete ulcer epithelialization	Adverse event
De Sanctis 2002 Italy/UK	Age 64 % male 44 Setting Ambulatory	172	> 2 months	Provider unknown/ 6 months/ Computerized planimetry	N	Y	N	ND	ND	ND	Complete ulcer epithelialization	
Falanga 2000 USA	Age ND % male ND Setting Ambulatory	240	≥ 1months	Provider unknown/ 6 months/ Not specified	N	Y	N	ND	ND	ND	Complete wound closure	Adverse event
Falanga 1999 USA	Age 58 % male 62 Setting Outpatient	129	≥ 2 months	Provider unknown/ 24 weeks/ Computerized planimetry	N	Y	N	ND	ND	ND	Complete healing	Adverse event

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									Systemic versus topical	Pre- versus during study		
Falanga 1999 USA Subset of Falanga 2000	Age 58 % male 61 Setting Ambulatory	120	> 1 year	Provider unknown/ 6 months/ Photograph imaging, tracings	N	Y	Y	ND	ND	ND	Healing defined as formation of epithelium over entire wound surface with no evidence of drainage	
Falanga 1998 USA	Age 60 % male 53 Setting Ambulatory	275	~ 70% > 6 months	Provider unknown/ 6 months/ Computerized planimetry, photograph imaging	Y	Y	Y	ND	S	At study	Wound healing defined as full epithelialization and no drainage	Adverse events
Franks 1999 Moffatt 1999 UK	Age 67 % male 45 Setting Outpatient	232	7.5 weeks	Provider unknown/ 24 weeks/ Not specified	Y	Y	N	ND	ND	ND	Healing of ulcer	QOL for sleep, pain, physical mobility, psycho- social outcomes
Hansson 1998 Sweden	Age 72 % male ND Setting Outpatient clinic	158	ND	Provider unknown/ 12 weeks/ Photograph imaging, tracings	Y	N	N	ND	N	N	Reduction of ulcer size	Cessation of exudation

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Lyon 1998 USA	Age 60 % male 65 Setting Outpatient	164	ND “Chronic”	Non-patient provider/ 12 weeks/ Computerized planimetry	Y	Y	N	ND	ND	ND	Percent of ulcer area healing at study completion	Interval to complete or partial ulcer healing
Meyer 2002 UK	Age ND % male ND Setting Outpatient	112	ND	Nurse/ 26 weeks/ Photograph imaging	N	Y	N	ND	ND	ND	Complete ulcer healing defined as restoration of entirely unbroken skin integrity w/o any purulent discharge after removal of all scabs	Time to healing based on ulcer size

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									Systemic versus topical	Pre- versus during study		
Meyer 2003 UK	Age 66 median % male 56 Setting Outpatient	133	14.8 - 19.8 months	Nurse/ 52 weeks/ Photograph imaging	N	Y	N	ND	ND	ND	Complete ulcer healing defined as restoration of entirely unbroken skin integrity without any purulent discharge after removal of all scabs; time to complete ulcer healing; failure to heal at 52 wks; time to apply bandages; bandages comfort/tolerability; healing costs	
Neander 2003 Germany	Age 70 % male 32 Setting Dermatology clinics	227	> 2 years	Nurse/ 12 months/ Not specified	N	Y ¹	N	ND	ND	ND	Increased erythema levels	

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O'Brien 2003 Ireland	Age 71 % male 34 Setting Outpatient	200	9-11 weeks	Nurse/ 12 weeks/ Photograph imaging	N	Y	N	ND	ND	ND	Complete ulcer healing defined as full epithelialization and no scab present	Cost effectiveness of various treatments
Partsch 2001 Austria, The Netherlands	Age Tx1: 68 Tx2: 71 % male 37.5 Setting Outpatient	112	Median Tx1: 5 weeks Tx2: 4 weeks (range 1- 1040)	Non-patient provider/ 16 weeks/ Computerized planimetry	N	Y	N	ND	ND	ND	Healing defined as complete epithelialisation of all areas of ulceration on the reference limb	QOL
Roztocil 2003 Czech and Slovak Republics	Age 64 % male Tx: 23 Ctrl: 23 Setting Ambulatory	150	≥ 3 months	Provider unknown/ 6 months/ Computerized planimetry, photograph imaging	N	Y	N	ND	Topical	At study	Rate of fully healed ulcers; time to healing	Variation in ulcer surface; appearance of skin in ulcer area; chronic venous insufficiency evolution

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Schulze 2001 UK, Germany	Age 73 (28-97) % male 34 Setting 38% Hospitalized 16% Outpatient 46% Alternative/com munity	113	44 weeks (0.5 – 744)	Non-patient provider/ 2-4 weeks/ Computerized planimetry	N	Y	N	ND	ND	ND	Exudates level; wound healing	User acceptability; treatment costs
Stacey 1997 Australia	Age 31-92 y % male 41 Setting Leg ulcer clinic	133	0.25-504 months	Non-patient provider/ 9 months/ Not specified	Y	Y	N	Pre- debrid ement	N	N	Time to healing, rate of reduction in ulcer size	

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