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Evidence Table per FDA Draft Guidance Document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Population	# Patients (# ulcers)	Ulcer duration	Provider / Treatment duration / Method of wound size assessment	FDA Draft Guidance Document Recommendations						1° Outcome	2° Outcome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	Antimicrobial treatment: 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.
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					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		
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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					Partial wound closure	Complete wound closure	3 months post-wound closure assessment	Wound size pre- & post-debridement	Antimicrobial treatment: Systemic versus topical	Antimicrobial treatment: 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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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/community	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-debridement	N	N	Time to healing, rate of reduction in ulcer size	

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