National Institute for Health and Clinical Excellence

IP244/4 Ultrasound-guided foam sclerotherapy for varicose veins

Consultation Comments table

IPAC date: 13 December 2012

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
1	Consultee 1 NHS Professional	**1**	Agreed	Thank you for your comment.
2	Consultee 2 NHS Professional	**1**	No comment	Thank you for your comment.
3	Consultee 3 Private Sector Professional	**1.1**	There is International evidence that UGFS is more than adequate but a very sucessfull treatment on par with other modalities and superior in the case of recurrent varicose veins. Â	Thank you for your comment. The remit of the Guidance was to evaluate safety and efficacy of ultrasound-guided foam sclerotherapy.
4	Consultee 3 Private Sector Professional	1.2	The rare reports of significant complications can also be attributed to the other forms of varicose vein treatments ie surgery, laser and radiofrequency ablation.	Thank you for your comment. The remit of the Guidance was to evaluate safety and efficacy of ultrasound-guided foam sclerotherapy. The Interventional Procedures programme does not assess the efficacy and safety of comparator interventions.
5	Consultee 4 Private Sector Professional	**1.2**	Serious complications including myocardial infarction, stroke and death have been reported as rare events following varicose vein stripping operations. Â Myocardial infarction and stroke have also been reported following endovenous laser ablation and after endovenous radiofrequency ablation. Â Rare serious adverse events are not confined to treatment by foam sclerotherapy and are not more common following this	Thank you for your comment. The remit of the Guidance was to evaluate safety and efficacy of ultrasound-guided foam sclerotherapy The Interventional Procedures programme does not assess the efficacy and safety of comparator interventions.

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			treatment than any other treatment for varicose veins.	
6	Consultee 4 Private Sector Professional	**1.3**	ERRONEOUS INFO: It is incorrect to say that creating a foam from all sclerosants constitutes off label use. In the UK the sclerosant Fibrovein 1% and 3% (sodium tetradecyl sulphate, STD Pharmaceuticals) is licensed for injection of a foam created by mixing with air using the Tessari technique. Please correct this factual inaccuracy.	Thank you for your comment. At the time the document went out for consultation details on change to the product licence was not available. Section 1.3 of the Guidance has been changed.
7	Consultee 3 Private Sector Professional	**1.3**	Â The statement that creating foam is off-label use is not longer valid as 1% and 3% sodium tetradecyl sulphate, STD Pharmaceuticals) is licensed for injection of foam created using the Tessari method."	Thank you for your comment. Section 1.3 of the Guidance has been changed.
8	Consultee 5 Manufacturer STD Pharmaceutical	**1.3**	We have just gained approval in the UK for new licences for 3% and 1% Fibrovein which has foam as an indication. Foam is thus not off label if Fibrovein 3% or 1% is used according to the Summary of Product Characteristics. Product licence numbers PL00398/0207 and PL00398/0206.	Thank you for your comment. Section 1.3 of the Guidance has been changed.
9	Consultee 1 NHS Professional	**2.1**	Agreed	Thank you for your comment.
10	Consultee 2 NHS Professional	**2.1**	Surgery should be ligation of great and/or small saphenous vein(NB the terms great and small saphenous should replace long and short saphenous throughout the guidance).	Thank you for your comment. The terms long and short saphenous veins will be changed to great and small saphenous veins, respectively.
11	Consultee 2 NHS Professional	**2.1**	Liquid sclerotherapy has a limited place only in treatment of symptomatic varicose veins.	Thank you for your comment. Section 2.1.2 of the Guidance has been amended.
12	Consultee 5 Manufacturer STD Pharmaceutical	**2.1.2**	. Liquid sclerotherapy is rarely used for varicose veins, it is used more for thread veins. When comparing treatments for varicose veins it should be foam sclerotherapy not liquid sclerotherapy that is listed as one of the options.	Thank you for your comment. Section 2.1.2 of the Guidance has been amended.
13	Consultee 3	**2.1.2**	Â Varicose veins do cause significant health problems	Thank you for your comment.

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	Private Sector Professional		as the symptoms described in 2.1.1 cause significant detriment to quality of life and studies have shown considerable improvement following treatment of their varicose veins	Section 2.1.2 of the Guidance has been amended.
14	Consultee 4 Private Sector Professional	**2.1.2**	The statement that treatment for varicose veins is not needed for most patients is not justifiable. Several studies have shown improvements in quality of life following a number of different varicose veins treatments. I agree that if treatment is not provided for varicose veins, serious complications such as leg ulceration only arise in a proportion of such patients."	Thank you for your comment. Section 2.1.2 of the Guidance has been amended.
15	Consultee 1 NHS Professional	**2.2**	Agreed	Thank you for your comment.
16	Consultee 6 NHS Professional	**2.2.2**	Local anaesthesia is usually unnecessary.	Thank you for your comment. Section 2.2.2 of the Guidance has been amended.
17	Consultee 2 NHS Professional	**2.2.2**	Local anaesthesia is not always required; only if ultrasound-guided cannulation of the GSV/SSV. Tributaries and or accessory saphenous systems are cannulated with Butterfly cannulae with a LA.	Thank you for your comment. Section 2.2.2 of the Guidance has been amended.
18	Consultee 4	**2.2.3**	" What does the phrase ?aeration methods? mean? In the UK the only licensed method of preparing sclerosant foam is to use the sclerosant Fibrovein 1% or 3% in combination with air by mixing using a three-way tap. Â I acknowledge that other methods of preparing foam also exist, but the licensed technique remains the most widely used."	Thank you for your comment. Section 2.2.3 of the Guidance has been amended.
19	Consultee 5 Manufacturer STD Pharmaceutical	**2.2.3**	Final sentence. Whilst the final statement is true that various sclerosants may be used to produce foam it should be noted that a) Fibrovein is the only licenced sclerosant in the UK for liquid or foam sclerotherapy. b) Fibrovein is now licenced for foam for the 3% and 1%. Use of any other sclerosant is off label.	Thank you for your comment. Section 2.2.3 of the Guidance has been amended.
20	Consultee 1	**2.3**	Agreed	Thank you for your comment.

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	The Vascular Society			
21	Consultee 2 NHS Professional	**2.3**	Other outcomes can include prevention of phlebitis, prevention of bleeding VV etc.	Thank you for your comment. The Guidance Overview document include the reports of outcomes identified in literature in further detail.
22	Consultee 3 Private Sector Professional	**2.3**	"These RCT trials that you are referencing are quite old and there are many more current studies. It is not usual procedure now to surgically treat the sapheno-femoral junction in combination with UGFS as it is not necessary and could cause neovascularisation. There are many patient series published showing the efficacy of UGFS"	Thank you for your comment. The Randomised Controlled Trials (RCT) included in the overview and guidance were those available at the time. A more recent RCT (Shadid 2012), was identified in the post consultation literature search. The Committee agreed to add this study to the main extraction table of the Guidance Overview document.
23	Consultee 4 Private Sector Professional	**2.3**	"Section 2.3 This section cites some studies, but there is no reference to the papers you are using. Please include this information."	Thank you for your comment. References to the papers mentioned in the Guidance can be found in the efficacy and safety section of the Guidance Overview document.
24	Consultee 1NHS Professional	**2.4**	Agreed	Thank you for your comment.
25	Consultee 5 Manufacturer STD Pharmaceutical	**2.4**	A full list of possible adverse reactions is listed on the SPCs for Fibrovein 3% and 1% along with the expected frequencies.	Thank you for your comment. Section 2.4 lists the safety issues that have been identified in the literature or by Specialist Advisers.
26	Consultee 3 Private Sector Professional	**2.4.4**	"2.4.4 Â This study showed that bubbles were detected not sclerosant foam. Studies show that complications following UGFS is minimal to the number of treatments undertaken worldwide each day"	Thank you for your comment. Section 2.4.4 of the Guidance has been amended.
27	Consultee 4 Private Sector Professional	**2.4.4**	This says that foam embolisation was detected. This is incorrect. Active sclerosant foam has never been shown to embolise although the bubbles of gas or air do commonly pass in to the systemic circulation via a PFO. The study that you cite found bubbles of gas (a mixture of CO2 and oxygen was used to create the foam) in very small numbers in the middle cerebral artery. As you say, this led to no neurological event detectable clinically or using MRI scanning.	Thank you for your comment. Section 2.4.4 of the Guidance has been amended.

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28	Consultee 4 Private Sector Professional	**2.4.10**	Extravasation or injection of foam outside a vein may cause a local adverse reaction but this has rarely been observed. Intra-arterial injection of foam has rarely been reported by causes severe damage to the tissues supplied by the artery."	Thank you for your comment. This is the opinion of Specialist Advisers.
29	Consultee 1 NHS Professional	**2.5**	"The problem of consistent production of foam has been answered by some presented but unpublished work by the manufacturers of Fibrovein (Venous Forum April 2012). The committee may wish to consider the evidence that 20 syringe passages appears to provide a consistent form of foam with reproducible micro-bubble sizes."	Thank you for your comment. The NICE IP Methods Guide highlights that efficacy outcomes from non peer-reviewed studies are not normally presented to the Committee
30	Consultee 7 NHS Professional	**2.5**	"The problem of consistent production of foam has been answered by some presented but unpublished work by the manufacturers of Fibrovein. The committee may wish to consider the evidence that 20 syringe passages appears to provide a consistent form of foam with reproducible micro-bubble sizes. I am please that Foam is now considered appropriate for routine use. EIDO have recently produced a patient information sheet that can be used as part of the consent process."	Thank you for your comment. The NICE IP Methods Guide highlights that efficacy outcomes from non peer-reviewed studies are not normally presented to the Committee. NICE will produce an *Information for the Public v*ersion of the guidance.
31	Consultee 2 NHS Professional	**2.5**	Common preparations and volumes should be highlighted e.g. in my practice I use 3% STS for truncal veins and 1% STS for tributaries- in a 1:4 ratio.	Thank you for your comment. IP Guidance would not normally include such detail.
32	Consultee 3 Private Sector Professional	**2.5**	Sodium tetradecyl sulphate, STD Pharmaceuticals, is licensed for use as a foam sclerosant. The manufacturers have submitted data to the MHRA that show that this technique can be used to prepare a foam of reproducible quality. The MHRA found that the foam	Thank you for your comment. Sections 1.3 and 2.5 of the Guidance have been changed.

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			prepared using this method was of sufficient quality to permit the licensing of sclerosant foam.	
33	Consultee 4 Private Sector Professional	**2.5**	The licensing of Fibrovein 1% and 3% as a foam includes a description of the method to be used in the SPC using two syringes and a three-way tap (Tessari Technique). The manufacturers have submitted data to the MHRA that show that this technique can be used to prepare a foam of reproducible quality. Â In contradiction of your statement, the MHRA found that the foam prepared using this method was of sufficient quality to permit the licensing of sclerosant foam."	Thank you for your comment. Sections 1.3 and 2.5 of the Guidance have been changed.
34	Consultee 5 Manufacturer STD Pharmaceutical	**2.5**	Agree that there is insufficient evidence to draw conclusions on safety and efficacy of different foams made with different methods. However as part of gaining approval for foam on the new licences we did a lot of foam characterisation work that showed that the Tessari method produces foam with consistent properties. The Tessari method was used to make foam in the clinical series using Fibrovein that were reveiwed for safety and efficacy. We were thus able to demonstrate that Fibrovein foam produced using the Tessari method has consistent properties and has a known safety profile and this is the method recommended on the new SmPCs with air:liquid ratios of 3:1 or 4:1.	Thank you for your comment. Sections 1.3 and 2.5 of the Guidance have been changed.
35	Consultee 8 The Vascular Society	**General**	I have been asked to comment upon USGFS by the Vascular Society. However, I began using USGFS in 2006 and undertake about 50 each year. I have conducted the audit recommended by NICE. The audit reported favourably on USGFS and my personal experience is that it is a safe and efficacious procedure.	Thank you for your comment.
36	Consultee 5 Manufacturer STD Pharmaceutical	**Other**	Employee of STD Pharmaceutical [redacted]	Thank you for your comment.

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37	Consultee 6 NHS Professional	**Other**	I am a vascular surgeon who has been using foam sclerotherapy regularly for more than 5 yr. I rarely use local anaesthesia.	Thank you for your comment. Section 2.2.2 of the Guidance has been amended.