EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Ablavar

Procedural steps taken and scientific information after the authorisation

No	Scope	Opinion/ Notification[1] issued on	Commission Decision Issued[2] / amended on	Product Information affected[3]	Summary
IB/0020	C.I.z - Changes (Safety/Efficacy) to Human and Veterinary Medicinal Products - Other variation	15/05/2011	n/a	SPC, Labelling, PL	To update the Summary of Product Information, Labelling and Package Leaflet in order to express the quantitative composition in term of the mass of the active moiety (i.e. 'gadofosveset' and not 'gadofosveset trisodium').
IA/0019	A.2.a - Administrative change - Change in the (invented) name of the medicinal product for Centrally Authorised products	10/01/2011	n/a	SPC, Labelling, PL	
R/0018	Renewal of the marketing authorisation	19/08/2010	25/10/2010	SPC, Annex II, Labelling, PL	
A20/0015	Article 20 Review	19/11/2009	10/06/2010		Please refer to the assessment report published after deletion of commercially confidential information: EMEA/H/0601/A-20/0015.
IA/0017	A.1 - Administrative change - Change in the name and/or address of the MAH	09/03/2010	n/a	SPC, Labelling, PL	
T/0016	Transfer of Marketing Authorisation Holder	04/06/2009	18/06/2009	SPC, Labelling, PL	
II/0014	Change to SPC section 4.8 and compliance	30/05/2008	07/07/2008	SPC, Annex II,	The product information for Vasovist has been amended to

[1] Notifications are issued for type I variations (unless part of a group or a worksharing application). Opinions are issued for all other procedures.
[2] No Commission Decision is issued for type IA and type IB variations or for type II variations and annual re-assessments that do not affect the annexes.
[3] SPC (Summary of Product Characteristics), Annex II, Labelling, PL (Package Leaflet).

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	with QRD template Update of Summary of Product Characteristics, Labelling and Package Leaflet			Labelling, PL	update section 4.8 Undesirable effects of the SPC following the results of four additional clinical studies. Clinical trial experience is now based on more than 1,800 patients and the undesirable effects observed have been updated. Consequently, the following adverse reactions with the frequency 'uncommon' were added: "confusion", "peripheral coldness", "pruritus ani", "vision abnormal", "genital pruritus" and "genital burning sensation".The adverse reaction "swelling face" was added with a frequency rare. The frequency of the following adverse events has been increased from rare to uncommon: "electrolyte imbalance", "feeling hot", "cough", "muscle contractions involuntary", "dyspepsia", "pharyngolaryncheal pain" and "electrocardiogram abnormal". The Package leaflet has been amended accordingly. The product information (SPC, Annex II, labelling and Package Leaflet) were also reformatted to the latest QRD template version 7.2.
II/0012	Change(s) to the manufacturing process for the active substance	21/02/2008	28/02/2008		
II/0013	Change(s) to the test method(s) and/or specifications for the finished product	21/02/2008	28/02/2008		
II/0011	Update of section 4.4 of the SPC with a warning on nephrogenic systemic fibrosis (NSF) associated with gadolinium-containing contrast agents in patients with severe renal impairment, further to a request from the CHMP. The Package Leaflet has been updated accordingly. The list of local representatives has also been updated in the Package Leaflet. Update of Summary of Product Characteristics and Package Leaflet	20/09/2007	23/10/2007	SPC, PL	The MAH applied to update section 4.4 of the SPC with a warning on nephrogenic systemic fibrosis (NSF) associated with gadolinium-containing contrast agents in patients with severe renal impairment, further to a request from the CHMP. The Summary of Product Characteristics was amended as follows: 4.4 Special Warnings and Precautions for use [...] Renal impairment Impaired renal function Since gadofosveset is cleared from the body primarily by urinary excretion, caution should be exercised in patients with impaired renal function (See Section 5.2). Dose adjustment in renal impairment is not necessary. In patients with more severely impaired renal function (clearance < 20 ml/min) who are not supported by routine dialysis, the benefits must be weighed very carefully against the risks. In a clinical trial it was shown that gadofosveset can effectively be

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					removed from the body by dialysis using high flux filters. There have been reports of Nephrogenic Systemic Fibrosis (NSF) associated with use of some gadolinium-containing contrast agents in patients with severe renal impairment (GFR< 30ml/min /1.73 m2). - acute or chronic severe renal impairment (GFR< 30ml/min /1.73 m2) or - acute renal insufficiency of any severity due to the hepato-renal syndrome or in the perioperative liver transplantation period. As there is a possibility that NSF may occur with Vasovist, it should therefore only be used in these patients after careful risk/benefit assessment consideration and if the diagnostic information cannot be obtained by other means. . Haemodialysis has not been established as an effective treatment option for patients with NSF. All patients should be screened, in particular patients over the age of 65, for renal dysfunction by obtaining a history and/or laboratory tests. Haemodialysis shortly after Vasovist administration in patients currently receiving haemodialysis may be useful at removing Vasovist from the body. In a clinical trial it was shown that gadofosveset can effectively be removed from the body by dialysis using high flux filters. There is no evidence to support the initiation of haemodialysis for prevention or treatment of NSF in patients not already undergoing haemodialysis. The Package Leaflet has been updated accordingly. The list of local representatives has also been updated.
II/0008	Quality changes	26/04/2007	04/06/2007	SPC	
II/0007	Quality changes	26/04/2007	03/05/2007		
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IA/0010	01_Change in the name and/or address of	30/03/2007	n/a	SPC, Annex II,	

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	the marketing authorisation holder			Labelling, PL	
II/0006	Update of Summary of Product Characteristics section 4.4 and Package Leaflet Update of Summary of Product Characteristics and Package Leaflet	22/02/2007	14/03/2007	SPC, PL	Upon request of the PhVWP and CHMP the MAH updated section 4.4 of the SPC regarding the risk of nephrogenic systemic fibrosis (NSF) in patients with severe renal failure. The PIL is amended accordingly.
II/0005	Update of or change(s) to the pharmaceutical documentation	18/10/2006	24/10/2006		
II/0004	Update of or change(s) to the pharmaceutical documentation	18/10/2006	24/10/2006		
IA/0003	11_a_Change in batch size of active substance or intermediate - up to 10-fold	10/03/2006	n/a		
II/0002	Change(s) to the manufacturing process for the active substance	23/02/2006	27/02/2006		