

**Clinical trial results:****An Open-Label Extension Study of the Safety and Efficacy of Ferumoxytol for the Episodic Treatment of Iron Deficiency Anemia in Pediatric Subjects with Chronic Kidney Disease****Summary**

EudraCT number	2010-019550-40
Trial protocol	DE GB HU ES RO LT BG
Global end of trial date	24 April 2015

**Results information**

Result version number	v1 (current)
This version publication date	13 December 2017
First version publication date	13 December 2017

**Trial information****Trial identification**

Sponsor protocol code	AMAG-FER-CKD-253
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**Additional study identifiers**

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01264679
WHO universal trial number (UTN)	-

Notes:

**Sponsors**

Sponsor organisation name	AMAG Pharmaceuticals, Inc.
Sponsor organisation address	1100 Winter Street, Waltham , United States, 02451
Public contact	Medical Information, AMAG Pharmaceuticals, Inc., +1 877-411-2510, amag@druginfo.com
Scientific contact	Medical Information, AMAG Pharmaceuticals, Inc., +1 877-411-2510, amag@druginfo.com

Notes:

**Paediatric regulatory details**

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000373-PIP02-09
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

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**Results analysis stage**

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Analysis stage	Final
Date of interim/final analysis	24 April 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 April 2015
Global end of trial reached?	Yes
Global end of trial date	24 April 2015
Was the trial ended prematurely?	Yes

Notes:

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**General information about the trial**

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Main objective of the trial:

Study AMAG-FER-CKD-253 is an extension study of the combined AMAG-FER-CKD-251 (2010-019387) and AMAG-FER-CKD-252 (2010-019388) studies to evaluate the efficacy and safety of episodic treatment of iron deficiency anemia (IDA) with ferumoxytol.

Study AMAG-FER-CKD-251 was a study evaluating the efficacy and safety of intravenous (IV) ferumoxytol in pediatric participants with dialysis-dependent chronic kidney disease (CKD). Study AMAG-FER-CKD-252 was a study evaluating the efficacy and safety of IV ferumoxytol in pediatric participants with nondialysis-dependent chronic kidney disease. Due to significant challenges with enrollment for both studies, Study AMAG-FER-CKD-252 was combined with Study AMAG-FER-CKD-251 and enrollment continued under Study AMAG-FER-CKD-251 and then led the Sponsor to discontinue the combined AMAG-FER-CKD-251 and AMAG-FER-CKD-252 studies and the AMAG-FER-CKD-253 study as designed.

Protection of trial subjects:

This study was conducted according to international standards of Good Clinical Practice, International Conference on Harmonization (ICH), United States Food and Drug Administration regulations, applicable government regulations, and institutional research policies and procedures. AMAG will also continue to support the principles of the Declaration of Helsinki.

All participants were to remain in the clinic for 1 hour following each IV injection of ferumoxytol, with frequent monitoring of vital signs and close observation for adverse events.

Background therapy:

There was no background therapy administered across all participant groups.

Evidence for comparator: -

Actual start date of recruitment	27 December 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

Country: Number of subjects enrolled	United States: 1
Country: Number of subjects enrolled	Mexico: 1
Country: Number of subjects enrolled	Peru: 3
Country: Number of subjects enrolled	Poland: 1
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	Germany: 1
Worldwide total number of subjects	8
EEA total number of subjects	3

Notes:

<b>Subjects enrolled per age group</b>	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	8
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

The study population will consist of pediatric participants (6 months to <18 years of age) with IDA defined as hemoglobin <12.0 grams/deciliter (g/dL) and with either transferrin saturation (TSAT)  $\leq$ 40% or ferritin <100 nanograms/milliliter (ng/mL) and CKD.

### Pre-assignment

Screening details:

Screening was to take place within 2 weeks of the start of the study. Screening assessments included review of inclusion/exclusion criteria, signature of informed consent, medical history, vital signs measurement, physical examination, clinical laboratory assessments including iron panel, and start of adverse events capture.

### Period 1

Period 1 title	Overall period (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

### Arms

Arm title	Ferumoxytol
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Arm description:

When a participant had persistent or recurrent IDA (defined as hemoglobin <12.0 g/dL and with either TSAT  $\leq$ 40% or ferritin <100 ng/mL), the participant began a 7-week treatment. Participants received 2 IV injections of ferumoxytol 7.0 mg iron (Fe)/kilogram (kg) (maximum of 510 mg/dose), the first dose administered on Day 1 and the second on Days 3 through 9 of the Treatment Period.

Arm type	Experimental
Investigational medicinal product name	Ferumoxytol
Investigational medicinal product code	
Other name	Feraheme
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ferumoxytol for IV injection: Each 20 mL single-use vial contains 17 mL of ferumoxytol that consists of iron, at a concentration of 30 mg Fe/mL, and mannitol, at a concentration of 44 mg/mL, in a black to reddish brown sterile, aqueous, colloidal, isotonic solution. The product contains no preservatives. Osmolality: 270-330 milliosmoles/kg; pH: 6-8.

Administration was 2 IV injections of ferumoxytol 7.0 mg Fe/kg (maximum of 510 mg/dose), the first dose administered on Day 1 and the second on Days 3 through 9 of the Treatment Period.

Number of subjects in period 1 <sup>[1]</sup>	Ferumoxytol
Started	7
Received at Least One Dose of Study Drug	7
Completed	3
Not completed	4
Physician decision	1
Sponsor's Suspension of Dosing	2

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**Notes:**

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: One participant was enrolled in the study, but withdrew consent prior to receiving any study drug.

## Baseline characteristics

### Reporting groups

Reporting group title	Ferumoxytol
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Reporting group description:

When a participant had persistent or recurrent IDA (defined as hemoglobin <12.0 g/dL and with either TSAT ≤40% or ferritin <100 ng/mL), the participant began a 7-week treatment. Participants received 2 IV injections of ferumoxytol 7.0 mg iron (Fe)/kilogram (kg) (maximum of 510 mg/dose), the first dose administered on Day 1 and the second on Days 3 through 9 of the Treatment Period.

Reporting group values	Ferumoxytol	Total	
Number of subjects	7	7	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	7	7	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
The birth date is missing for 1 of the 7 pediatric participants. Therefore, arithmetic mean and standard deviation for Age continuous are based on 6 participants.			
Units: years			
arithmetic mean	15.3		
standard deviation	± 1.51	-	
Gender categorical			
Units: Subjects			
Female	4	4	
Male	3	3	

## End points

### End points reporting groups

Reporting group title	Ferumoxytol
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Reporting group description:

When a participant had persistent or recurrent IDA (defined as hemoglobin <12.0 g/dL and with either TSAT ≤40% or ferritin <100 ng/mL), the participant began a 7-week treatment. Participants received 2 IV injections of ferumoxytol 7.0 mg iron (Fe)/kilogram (kg) (maximum of 510 mg/dose), the first dose administered on Day 1 and the second on Days 3 through 9 of the Treatment Period.

Subject analysis set title	Intent-to-Treat (ITT)
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Subject analysis set type	Intention-to-treat
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Subject analysis set description:

The ITT Population included all randomized participants who had received at least 1 dose of study drug. Sample data were collected, but not run through any analysis to obtain end point data. As such, summary of the data set is not possible.

### Primary: Mean Change in Hemoglobin From Baseline to Week 5

End point title	Mean Change in Hemoglobin From Baseline to Week 5 <sup>[1]</sup>
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End point description:

Mean changes in hemoglobin following the first course of ferumoxytol from Baseline to Week 5 were to be presented. Despite efforts to complete the studies as designed, several factors contributed to significant challenges in enrollment and led the Sponsor to discontinue the combined AMAG-FER-CKD-251 and AMAG-FER-CKD-252 studies, and the AMAG-FER-CKD-253 study. Blood samples were collected, but not run through an analysis to obtain end point data. As such, the data set for this primary end point cannot be summarized nor can the statistical analysis, as described in the protocol, be provided in a way that will provide any significant data based upon the limited study datasets.

End point type	Primary
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End point timeframe:

Baseline, Week 5

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Sample data were collected, but not run through any analysis to obtain end point data. As such, summary and statistical analysis of the data set is not possible.

<b>End point values</b>	Ferumoxytol			
Subject group type	Reporting group			
Number of subjects analysed	0 <sup>[2]</sup>			
Units: participants				

Notes:

[2] - Sample data were collected, but not run through any analysis to obtain end point data.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Proportion Of Participants With An Increase In Hemoglobin From Baseline To Week 5 And To Week 7

End point title	Proportion Of Participants With An Increase In Hemoglobin From Baseline To Week 5 And To Week 7
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End point description:

The proportion of participants with an increase hemoglobin to ≥1.0 g/dL or to ≥12.0 g/dL during the period from Baseline to Week 5 and to Week 7 following each course of ferumoxytol was to be presented. However, despite efforts to complete the studies as designed, several factors contributed to significant challenges in enrollment and led the Sponsor to discontinue the combined AMAG-FER-CKD-

251 and AMAG-FER-CKD-252 studies, and the AMAG-FER-CKD-253 study. Blood samples were collected, but not run through an analysis to obtain end point data. As such, the data set for this secondary end point cannot be summarized in a way that will provide any significant data based upon the limited study datasets.

End point type	Secondary
End point timeframe:	
Baseline, Week 5 and Week 7	

<b>End point values</b>	Ferumoxytol			
Subject group type	Reporting group			
Number of subjects analysed	0 <sup>[3]</sup>			
Units: participant				

Notes:

[3] - As only 7 participants received study drug, efficacy parameters were not analyzed.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Mean Change In TSAT From Baseline To Week 5 And To Week 7

End point title	Mean Change In TSAT From Baseline To Week 5 And To Week 7
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End point description:

Mean changes in TSAT following the first course of ferumoxytol from Baseline to Week 5 and to Week 7 were to be presented. However, despite efforts to complete the studies as designed, several factors contributed to significant challenges in enrollment and led the Sponsor to discontinue the combined AMAG-FER-CKD-251 and AMAG-FER-CKD-252 studies, and the AMAG-FER-CKD-253 study. Blood samples were collected, but not run through an analysis to obtain end point data. As such, the data set for this secondary end point cannot be summarized in a way that will provide any significant data based upon the limited study datasets.

End point type	Secondary
End point timeframe:	
Baseline, Week 5 and Week 7	

<b>End point values</b>	Ferumoxytol			
Subject group type	Reporting group			
Number of subjects analysed	0 <sup>[4]</sup>			
Units: percent				
arithmetic mean (standard deviation)	( )			

Notes:

[4] - As only 7 participants received study drug, efficacy parameters were not analyzed.

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Randomization up to 24 months

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	13.0
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### Reporting groups

Reporting group title	Ferumoxytol
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Reporting group description:

When a participant has persistent or recurrent iron deficiency anemia (IDA) (defined as hemoglobin <12.0 g/dL and with either TSAT ≤40% or ferritin <100 ng/mL), the participant will begin a 7-week treatment. Participants will receive 2 IV injections of ferumoxytol 7.0 mg iron (Fe) per kilogram (kg) (maximum of 510 mg/dose), the first dose administered on Day 1 and the second on Days 3 through 9 of the Treatment Period.

<b>Serious adverse events</b>	Ferumoxytol		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 7 (42.86%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Ligament rupture			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Device breakage			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			

Renal failure chronic			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

<b>Non-serious adverse events</b>	Ferumoxytol		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 7 (100.00%)		
Injury, poisoning and procedural complications			
Procedural nausea			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Procedural vomiting			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Ureteric anastomosis complication			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Vascular disorders			
Air embolism			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Hypertension			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Cardiac disorders			
Congestive cardiomyopathy			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Ventricular flutter			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Blood and lymphatic system disorders			

Nephrogenic anaemia subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
General disorders and administration site conditions Oedema peripheral subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)  Gastritis subjects affected / exposed occurrences (all)  Nausea subjects affected / exposed occurrences (all)  Peritoneal lesion subjects affected / exposed occurrences (all)  Dental caries subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1  1 / 7 (14.29%) 1		
Psychiatric disorders Depression subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 3		
Renal and urinary disorders Anuria subjects affected / exposed occurrences (all)  Bladder spasm	2 / 7 (28.57%) 2		

<p>subjects affected / exposed occurrences (all)</p> <p>Renal colic subjects affected / exposed occurrences (all)</p>	<p>1 / 7 (14.29%) 1</p> <p>1 / 7 (14.29%) 1</p>		
<p>Musculoskeletal and connective tissue disorders</p> <p>Joint swelling subjects affected / exposed occurrences (all)</p>	<p>1 / 7 (14.29%) 1</p>		
<p>Infections and infestations</p> <p>Device related infection subjects affected / exposed occurrences (all)</p> <p>Influenza subjects affected / exposed occurrences (all)</p> <p>Nasopharyngitis subjects affected / exposed occurrences (all)</p> <p>Oral herpes subjects affected / exposed occurrences (all)</p> <p>Pharyngitis subjects affected / exposed occurrences (all)</p> <p>Urinary tract infection subjects affected / exposed occurrences (all)</p>	<p>1 / 7 (14.29%) 1</p> <p>1 / 7 (14.29%) 1</p> <p>2 / 7 (28.57%) 8</p> <p>1 / 7 (14.29%) 1</p> <p>2 / 7 (28.57%) 2</p> <p>1 / 7 (14.29%) 1</p>		
<p>Metabolism and nutrition disorders</p> <p>Hyperkalaemia subjects affected / exposed occurrences (all)</p> <p>Hypocalcaemia subjects affected / exposed occurrences (all)</p>	<p>1 / 7 (14.29%) 1</p> <p>1 / 7 (14.29%) 1</p>		



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

While sample data were collected, it was not run through any analysis to obtain the necessary end point data. As such, summary of the data set is not possible.

Notes: