Maternal and Fetal Adverse Event Terminology (MFAET) v1.1, 2022

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Guidance on the uset**b**£MFAETseverity grading criteria

Adverse Events

An adverse event (AE)] • ^ uniQward medical occurrence in a patient or dinical trial participant administered a medicinal product and which does not necessarily have a causal relationship with this \check{s} CE \check{s} \mathring{u} . Ea \check{s} _AE is reviewed to determine (1) whether it meets the definition o (Z • CE) $\mu • [$

- x Results in death
- x Is life-threatening
- x Requires inpatient hospitalisation or results in prolongation of existing hospitalisation
- x Results in persistent or significa3(ten)6(n)4(i)22(f)-6(i∞.ic)7(a3(ten)6(n)4EC000012547 0 842 549o</MCID 7/Lang (en-GB)>> BD.2 Tf 1 0 0 1 217.83 425

If an AEfulfils the criteria for more than one grade of severity, the highest applicable grade should be used.

Not all grades are appropriate for all AEs. A single dash (-) indicates that grade is not defined for a given AE

Several fetal AEs only include definitions for grades 2 (moderate) and 4 (life-threatening). This is because current methods of investigating the fetus and predicting short- and long-term prognosis are often not sufficient to differentiate between mild and moderate events and between severe and life-threatening events.

Death resulting from any AE is graded as 5.

Maternal thromboembolic events during pregnancy and the puerperium should be identified by the appropriate MedDRA Lowest Level Term (LLT Venous thrombosis in pregnand)LT Postpartum venoushtrombosis or LLT Obstetrical pulmonary embolism) and graded according to the CTCAE criteria for **Z**Z OE } u } o] À v š [X

Neonatal Adverse Events

Neonatal AEs should be graded using the International Neonatal Consortium (INC)

Maternal and Fetal Adverse Events

Some AEs have the potential to differentially affect the pregnant woman and the fetus (haemorrhage in pregnancy, preterm premature rupture of membranes, chorioamnionitis and anaemia of pregnancy). It is not possible to have separate AE terms for the mother and the fetus within the structure of MedDRA, so these events should be reported using a single MedDRA term, with maternal and fetal severity gradings recorded within the trial records.

Maternal AEsot included in these criteria

Maternal procedural complications, such as pain and infection, should be identified by the appropriate MedDRA Lowest Level Term and graded according to CTCAE criteria.

Maternal diverse event	Grade 1 (mild)	Grade 2 (moderate)	Grade 3 (severe)	Grade 4 (lifthreatening)
Preterm premature	-	Preterm premature	-	-
rupture of membranes:		rupture of membranes		
maternal				
MedDRA LLT: Preterm				
premature rupture of				
membranes				
Definition: The runture of n	nembranes before labour and	d hefore 37 weeks of gestatic	an	
Premature labour		Symptoms of premature	ות 	_
Tremature labour	_	labour	_	_
MedDRA LLT: Premature		laboai		
labour				
	I	I	I	1
Definition: Symptoms of lab	oour before 37 weeks of gest	ation, with or without preter	m delivery	
Chorioamnionitis:	Histological, biochemical	Maternal fever of 38-40	Oinically or pathologically	Clinically or pathologically
maternal	or microbiological	°C(100.4-104.0 °F) and:	diagnosed	diagnosed
	evidence of	maternal leukocytosis	chorioamnionitis and	chorioamnionitis and:
MedDRA LLT:	chorioamnionitis from	(>15,000 cells/mm ³); fetal	fever >40 °C(104.0 °F) for	fever >40 °C(104.0 °F) for
Chorioamnionitis	placental or amniotic fluid	tachycardia (>160bpm);	<24 hours	>24 hours; septic shock;
	examination in the	maternal tachycardia		coagulopathy; adult
	absence of dinical signs in			respiratory distress
	the fetus or mother	amniotic fluid; uterine		syndrome;
		tenderness between		
		contractions		
Definition: Inflammation of	the chorion, amnion, and/or	· nlacenta		
	the Gibrion, aminon, and/or	piactila		

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Maternal daverse event	Grade 1(mild)	Grade 2 (moderate)	Grade 3 (severe)	Grade 4 (lifthreatening)
Puerperal infection	-	Genital tract infection in	Genital tract infection	
		the absence of severe or		
MedDRA LLT: Puerperal		life-threatening		
infection		symptoms, oral antibiotics		
		indicated		

FETAL ADVERSE EVENTS

Fetal averse event	Grade 1 (mild)	Grade 2 (moderate)	Grade 3 (severe)	Grade 4 (lifthreatening)
Fetal fluid collection	-	New onset isolated	New onset accumulation	New onset accumulation
MedDRA LLT: Fetal		pericardial, pleural, or peritoneal fluid collection	of fluid in at least two fetal compartments	of fluid in at least two fetal compartments
compartment fluid collection		or skin oedema, which is not life-threatening	(hydrops) which resolves spontaneously	(hydrops) which is sustained; life-threatening
				isolated pericardial, pleural, or peritoneal fluid collection

Definition: The collection of non-haemorrhagic fluid in one or more fetal compartment (pericardial space, pleural space, peritoneal cavity, and/or skin oedema)

Fetalbradycardia

MedDRA LLT: Fetal

bradycadyiti

Fetal alverse event Grade 1 (mild) Grade 2 (moderate) Grade 3 (severe) Grade 4 (liftehreatening)
Fetal tachyamythmia Resolves spontaneously

MedDRA LLT: Fetal tachyarrhythmia

Fetal alverse event	Grade 1 (mild)	Grade 2 (moderate)	Grade 3 (severe)	Grade 4 (lifthreatening)
Fetal brain scan	-	An abnormality of	-	Haemorrhage; ischaemia;
abnormal		uncertain neurological		an abnormality likely to
		significance which does		lead to permanent
MedDRA ШТ: Brain scan		not fulfil the criteria for		disability; an abnormality
abnormal		Level 4 (life-threatening)		requiring a substantive
				change in management
				including changing the
				course of an
				interventional procedure
				or necessitating delivery
Definition: A newly identifie	ed change on fetal brain imag	ging, outside the scope of nor	mal brain development	
Fetal movement	-	-	-	A complete and sustained
disorders				loss of fetal movement
				induding breathing,
MedDRA LLT: Fetal				swallowing, and limb
movement disorder				movements; sustained
				fetal hypertonia or
				abnormal fetal posture
				suggestive of neurological
				damage

Fetal averse event	Grade 1 (mild)	Grade 2 (moderate)	Grade 3 (severe)	Grade 4 (lifthreatening)
Fetal gastrointestinal	-	Hyperechogenic dilated	Imaging appearance	-
tract imaging abnormal		bowel	highly suggestive of bowel	
			necrosis or perforation	
MedDRA LLT: Fetal				
gastrointestinal tract				
imaging abnormal				
	,	'	,	'

Definition: New abnormality in the appearance of the fetal gastrointestinal tract on imaging

Fetal

Fetal a versævent	Grade 1 (mild)	Grade 2 (moderate)	Grade 3 (severe)	Grade 4 (lifthreatening)
Preterm premature	Membrane separation	Confirmed rupture of	Confirmed rupture of	Confirmed rupture of
rupture of membranes:	without confirmed	membranes between	membranes with	membranes with
fetal	rupture of membranes;	32+0 and 33+6 weeks of	persistently reduced	persistently reduced
	inter-twin membrane	gestation	amniotic fluid, as	amniotic fluid, as
MedDRA LLT: Preterm	disruption not leading to		identified by a deepest	identified by a deepest
premature rupture of	amniotic fluid leakage		vertical pool of less than 2	vertical pool of less than 2
membranes			cm on ultrasound scan,	cm on ultrasound scan, <
			between 22 and 32 weeks	22 weeks of gestation
			of gestation	
· ·	nembranes before labour and	d before 37 weeks of gestation	on	
Chorioamnionitis: fetal	-	Clinically or pathologically diagnosed	-	Clinically or pathologically diagnosed
MedDRA LLT:		chorioamnionitis with		chorioamnionitis with
Chorioamnionitis		fetal tachycardia >160		pathological
		beats/min but without a		cardiotocograph;
		pathological		Clinically or pathological
		cardiotocograph		