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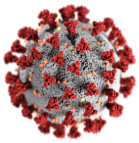
vACCine covid-19  monitoring readinESS

EVENT DEFINITION FORM

Event: Erythema multiforme
Outcome/covariate: outcome
Version: 1
Status: final

Contributing authors

authors	Role	Date
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Miriam Sturkenboom	Review of definition & codes	14-08-2020
Leila Belbachir	Medical review	August 22, 2020
Caitlin Dodd	Algorithm proposal	03-09-2020
Carlos Durán	Rev. narrow/possible assignment	28-03-2021
Miriam Sturkenboom	Inclusion of codes used for final ACCESS reports	23-08-2021

1. Event definition

Erythema multiforme (EM) is an acute, self-limited disease that is typically associated with hypersensitivity reactions to viruses, as well as drugs. It is characterized by targetoid erythematous lesions with predominant acral localization and can be subdivided into isolated cutaneous and combined mucocutaneous forms.[1]

Erythema multiforme is defined by the morphology of the individual lesions and the pattern of distribution. In 1993, an international consensus defined five severe bullous skin reactions including erythema multiforme based on morphological criteria.[2,3] This definition of erythema multiforme is summarized in Table 1. Erythema multiforme was only included in its major form called erythema multiforme major.

By definition in EM, the detachment of the skin affects < 10% body surface area (BSA) and localized typical and/ raised atypical targets are present. Typical targets are defined as lesions less than 3 cm in diameter and characterized by three different concentric zones. Raised atypical targets normally contain only two zones. In typical and raised atypical targets, the center zone might show bullae formation as a sign of epidermal involvement.[1,2]Clinically, EM patterns can be classified into EM with and EM without mucosal involvement.[1] EM has been further subdivided into EM minus (involvement of ≤1 mucosal site) and EM maj or (involvement of ≥ 2 mucosal sites) by some authors.[1]

Table 1. Consensus classification of Erythema multiforme (modified from [2])

Criterion	Erythema multiforme major
Skin detachment (BSA affected)	< 10%
Target lesions	Typical and/or atypical
Raised lesions	Yes
Distribution	Predominantly affects the extremities; in children, frequently affects the trunk
Progression to TEN	No

Abbreviations: BSA, body surface area; TEN, toxic epidermal necrolysis

2. Synonyms / lay terms for the event

- Dermatostomatitis, Erythema Multiforme Type
- Erythema Multiforme Bullosum
- Erythema Polymorphe, Erythema Multiforme Type
- Febrile Mucocutaneous Syndrome
- Herpes Iris, Erythema Multiforme Type
- Polymorphic erythema

3. Laboratory tests that are specific for event

None

4. Diagnostic tests that are specific for event

Histopathological analysis including direct immunofluorescence is performed to confirm the diagnosis as well as to differentiate between EM and autoimmune mucocutaneous diseases.[1]

5. Drugs that are used to treat event

Generally, treatment of EM is symptomatic and guided by clinical severity.

- Agents shown to be potentially effective are thalidomide, immunoglobulins and azathioprine.[3]
- Mycophenolate mofetil for recurrent EM major.[3]
- Topical corticosteroids can be used for mild cases.[3]
- Systemic corticosteroids, for children there is some evidence that its use could reduce the duration and severity of symptoms.

6. Procedures used specific for event treatment

None

7. Setting (outpatient specialist, in-hospital, GP, emergency room) where condition will be most frequently /reliably diagnosed

Outpatient specialist or GP

8. Diagnosis codes or algorithms used in different papers to extract the events in Europe/USA: seek literature for papers that have studied this event, and see how they extracted/measured the event.

- **Strom et al.[4]**

ICD-9-CM code 695.1 (erythema multiforme-EM)

- **Smith et al.[5]**

Erythema multiforme ICD-9-CM 695.1, 695.10, 695.11, 695.12

- **Hao et al.[6]**

ICD-9 code 695.10 or ICD-10 code L51.9 for EM

- **Strom et al.[7]**

Erythema multiforme (ICD-9-CM code 695.1)

- **ICD10**

L51

9. Proposed codes by Codemapper

Coding system	Code	Code name	Concept	Concept name	Algorithm
ICD10/CM	L51	Erythema multiforme	C0014742	Erythema Multiforme	Narrow
ICD10/CM	L51.9	Erythema multiforme major NOS	C3241919	Erythema Multiforme Major	Narrow
ICD10/CM	L51.9	Herpes iris	C0263323	Herpes iris	Narrow
ICD9CM	695.1	Erythema multiforme	C0014742	Erythema Multiforme	Narrow
ICD9CM	695.10	Erythema multiforme, unspecified	C0014742	Erythema Multiforme	Narrow
ICD9CM	695.11	Erythema multiforme minor	C0857751	Erythema multiforme minor	Narrow
ICD9CM	695.12	Erythema multiforme major	C3241919	Erythema Multiforme Major	Narrow
ICD9CM	695.13	Stevens-Johnson syndrome	C0038325	Stevens-Johnson Syndrome	Narrow
ICD9CM	695.15	Toxic epidermal necrolysis	C0014518	Toxic Epidermal Necrolysis	Narrow
ICPC2P	A12005	Stevens Johnson syndrome	C0038325	Stevens-Johnson Syndrome	Narrow
ICPC2P	S99007	Erythema;multiforme	C0014742	Erythema Multiforme	Narrow
ICPC2P	S99032	Stevens Johnson syndrome	C0038325	Stevens-Johnson Syndrome	Narrow
RCD2	M151.	Erythema multiforme	C0014742	Erythema Multiforme	Narrow
RCD2	M1517	Stevens-Johnson syndrome	C0038325	Stevens-Johnson Syndrome	Narrow
RCD2	M1518	Toxic epidermal necrolysis	C0014518	Toxic Epidermal Necrolysis	Narrow
RCD2	M151z	Erythema multiforme NOS	C0014742	Erythema Multiforme	Narrow
SCTSPA	23067006	necrólisis epidérmica tóxica de Lyell, tipo subepidérmico	C0014518	Toxic Epidermal Necrolysis	Narrow
SCTSPA	28664002	herpes iris	C0263323	Herpes iris	Narrow
SCTSPA	36715001	eritema polimorfo	C0014742	Erythema Multiforme	Narrow
SCTSPA	73442001	síndrome de Stevens-Johnson	C0038325	Stevens-Johnson Syndrome	Narrow
SCTSPA	200928007	eritema multiforme, SAI	C0014742	Erythema Multiforme	Narrow
SCTSPA	768962006	síndrome de Lyell	C0014518	Toxic Epidermal Necrolysis	Narrow
SCTSPA	123571000119104	eritema multiforme menor	C0857751	Erythema multiforme minor	Narrow
SNOMEDCT_US	23067006	Lyell's syndrome	C0014518	Toxic Epidermal Necrolysis	Narrow
SNOMEDCT_US	28664002	Herpes iris	C0263323	Herpes iris	Narrow
SNOMEDCT_US	36715001	Erythema multiforme	C0014742	Erythema Multiforme	Narrow
SNOMEDCT_US	36715001	Erythema multiforme			narrow
SNOMEDCT_US	73442001	Stevens-Johnson syndrome	C0038325	Stevens-Johnson Syndrome	Narrow
SNOMEDCT_US	156362004	Antibiotic necrolysis	C0014518	Toxic Epidermal Necrolysis	Narrow
SNOMEDCT_US	156362004	Erythema multiforme	C0014742	Erythema Multiforme	Narrow
SNOMEDCT_US	156362004	Stevens-Johnson synd.	C0038325	Stevens-Johnson Syndrome	Narrow

SNOMEDCT_US	200919006	Erythema multiforme	C0014742	Erythema Multiforme	Narrow
SNOMEDCT_US	200919006	Leyell's syndrome	C0014518	Toxic Epidermal Necrolysis	Narrow
SNOMEDCT_US	200928007	Erythema multiforme NOS	C0014742	Erythema Multiforme	Narrow
SNOMEDCT_US	238818000	Nonbullous erythema multiforme			narrow
SNOMEDCT_US	238819008	Bullous erythema multiforme	C0038325	Stevens-Johnson Syndrome	Narrow
SNOMEDCT_US	267848009	Antibiotic necrolysis	C0014518	Toxic Epidermal Necrolysis	Narrow
SNOMEDCT_US	267848009	Erythema multiforme	C0014742	Erythema Multiforme	Narrow
SNOMEDCT_US	267848009	Stevens-Johnson synd.	C0038325	Stevens-Johnson Syndrome	Narrow
SNOMEDCT_US	768946000	Stevens-Johnson syndrome, toxic epidermal necrolysis spectrum			Narrow
SNOMEDCT_US	768962006	Lyell syndrome	C0014518	Toxic Epidermal Necrolysis	Narrow
SNOMEDCT_US	123571000119104	Erythema multiforme minor	C0857751	Erythema multiforme minor	Narrow
SNOMEDCT_US	123571000119104	Erythema multiforme minor	C0857751	Erythema multiforme minor	Narrow

10. Algorithm proposal

Broad algorithm:

- Concept sets (Erythema_multiforme, Herpes_iris, EM_minor)
- Index date = first occurrence of a code in the concept sets (Erythema_multiforme, Herpes_iris, EM_minor)

Narrow algorithm:

- Concept set Erythema_multiforme
- Index date = first occurrence of a code in the concept set Erythema_multiforme

11. Background rates

Search terms employed to extract background rates for erythema multiforme were: -
(¨Erythema multiforme¨[Mesh]) AND ("incidence"[tw]) NOT (Comment[ptyp] OR Editorial[ptyp] OR News[ptyp] OR Newspaper Article[ptyp]) NOT ("animals"[Mesh] NOT "humans"[Mesh]) AND English[lang]
Between 2010-2020

- No specific background rates have been retrieved for erythema multiforme.

1. Lerch M, Mainetti C, Terziroli Beretta-Piccoli B, Harr T. Current Perspectives on Erythema Multiforme. Clinic Rev Allerg Immunol 2018;54(1):177–84.

2. Bastuji-Garin S, Rzany B, Stern RS, Shear NH, Naldi L, Roujeau JC. Clinical classification of cases of toxic epidermal necrolysis, Stevens-Johnson syndrome, and erythema multiforme. Arch Dermatol 1993;129(1):92–6.

3. Grünwald P, Mockenhaupt M, Panzer R, Emmert S. Erythema multiforme, Stevens-Johnson syndrome/toxic epidermal necrolysis – diagnosis and treatment. JDDG: Journal der Deutschen Dermatologischen Gesellschaft 2020;18(6):547–53.

4. Strom BL, Carson JL, Halpern AC, Schinnar R, Snyder ES, Stolley PD, et al. Using a claims database to investigate drug-induced Stevens-Johnson syndrome. Stat Med 1991;10(4):565–76.

5. Smith MY, Sabidó-Espin M, Trochanov A, Samuelson M, Guedes S, Corvino FA, et al. Postmarketing Safety Profile of Subcutaneous Interferon Beta-1a Given 3 Times Weekly: A Retrospective Administrative Claims Analysis. JMCP 2015;21(8):650–60.

6. Hao M, Zang P, Miller M, Cutler L, Worswick S. Herpes associated erythema multiforme: A retrospective study. The American Journal of Emergency Medicine 2020;S0735675720304435.

7. Strom BL, Carson JL, Halpern AC, Schinnar R, Snyder ES, Shaw M, et al. A Population-Based Study of Stevens-Johnson Syndrome: Incidence and Antecedent Drug Exposures. Arch Dermatol 1991;127(6):831–8.