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Raptiva (efalizumab) and Progressive Multifocal Leukoencephalopathy (PML)

- On February 19, 2009, the Food and Drug Administration (FDA) released a Public Health Advisory regarding use of Raptiva (efalizumab) and the increased risk of PML.[1]
- The European Medicines Agency (EMEA) recommended suspension of the marketing of Raptiva (efalizumab) due to:
  - Modest benefits[2];
  - Other potential serious side effects (i.e., Guillain-Barre and Miller-Fisher syndromes, encephalitis, encephalopathy, meningitis, sepsis, and opportunistic infections) [2];
  - Lack of evidence to identify a group of patients where benefits of treatment with Raptiva (efalizumab) outweigh the risks[2];
  - Lack of safety and effectiveness data on patients immunocompromised from previous treatments and with no other treatment options[2].
- PML cases have been reported between September 2008 and January 2009 in patients 47-75 years of age with moderate to severe plaque psoriasis receiving ongoing treatment with Raptiva (efalizumab) for greater than 3 years. [1, 3]
  - 3 confirmed cases with 2 deaths; [1, 3]
  - 1 possible case resulting in death. [1, 3]
  - None of the above patients were receiving any other immunosuppressive drugs concomitantly. [1]
- Raptiva (efalizumab) was approved by the FDA in 2003 for the treatment of moderate to severe plaque psoriasis. [1]
- Clinical trials at the time of approval did not show any cases of PML (N=2764). [1]
- In October 2008, FDA requested for the manufacturers of Raptiva to:
  - Include a BOXED WARNING in the labeling that describes the risk for life-threatening infections, such as PML; and
  - Establish a Risk Evaluation and Mitigation Strategy (REMS). [1]
- As FDA continues to review the latest information, the agency recommends that healthcare providers:
  - Inform patients using Raptiva (efalizumab) of the potential risk of developing PML. [1]
  - Inform patients there are no known screening tests that can reliably predict PML or medical interventions that can prevent or treat this disease.
  - Monitor and periodically evaluate patients being treated with Raptiva (efalizumab) for the onset of neurologic symptoms. [1]
  - Discontinue Raptiva (efalizumab) if PML is suspected. [1]
  - Educate patients on possible symptoms of PML (i.e., unusual weakness, loss of coordination, changes in vision, difficulty speaking, personality changes) and if these changes occur, to contact their provider and/or seek care immediately. [1]

REFERENCES
1. FDA. http://www.fda.gov/cder/drug/advisory/efalizumab.htm. (Accessed February 19, 2009)
2. EMEA. http://www.emea.europa.eu/humandocs/PDFs/EPAR/raptiva/2085709en.pdf. (Accessed February 19, 2009)
3. EMEA. http://www.emea.europa.eu/humandocs/PDFs/EPAR/raptiva/RaptivaQ&A_1552509en.pdf. (Accessed February 19, 2009)

ACTIONS:

- ***Facility COS:*** *Forward this document to all appropriate providers who prescribe this agent (e.g.,* ***primary care providers, dermatologists, and rheumatologists*** *including contract providers, etc.). In addition, forward to the Associate Chief of Staff (ACOS) for Research and Development (R&D). Forward to other VA employees as deemed appropriate.*
- ***ACOS for R&D:*** *Forward this document to Principal Investigators (PIs) who have authority to practice at the facility and to your respective Institutional Review Board (IRB).*