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FDA Information for Healthcare Professionals: Phenytoin (Dilantin[®], Phenytek[®]) and Fosphenytoin Sodium (Cerebyx[®]) and Serious Skin Reactions

- FDA has received new preliminary data showing a potential risk for serious skin reactions such as Stevens Johnson Syndrome (SJS) and toxic epidermal necrolysis (TEN) with phenytoin therapy in patients of Asian ancestry carrying the human leukocyte antigen (HLA) allele, HLA-B*1502.¹
- The risk appears to be highest within the first few months of treatment with phenytoin in populations of at-risk ethnicity and genotype.¹
- This warning extends to fosphenytoin since it is a prodrug that is converted to phenytoin.¹
- In December 2007, FDA addressed carbamazepine-induced SJS and TEN in Asian populations associated with the HLA-B*1502 allele.²
 - Carbamazepine labeling advises HLA testing before initiating therapy in patients that may carry the allele and that positive patients not be exposed to carbamazepine.²
- FDA still continues to collect new information regarding the association between phenytoin-induced SJS/TEN and HLA-B*1502.¹
- Per the FDA, as data is preliminary and still being studied, there is no recommendation for HLA testing in at-risk populations considered for therapy with phenytoin.¹
- FDA cautions prescribers on using phenytoin as an alternative antiepileptic agent to carbamazepine in patients whose HLA tests return positive for HLA-B*1502.
- Two published studies found an association between HLA-B*1502 and antiepileptic-induced skin reactions.
 - Man et al. showed that SJS occurred as a result of carbamazepine therapy in Han Chinese subjects with HLA-B*1502.³
 - Locharearnkul et al. showed that SJS occurred as a result of carbamazepine therapy and phenytoin therapy in Thai patients with HLA-B*1502.⁴
- For more information please visit: http://www.fda.gov/cder/drug/InfoSheets/HCP/phenytoin_fosphenytoinHCP.htm.

References

1. FDA. http://www.fda.gov/cder/drug/InfoSheets/HCP/phenytoin_fosphenytoinHCP.htm . (Accessed November 24, 2008).
2. FDA. <http://www.fda.gov/cder/drug/InfoSheets/HCP/carbamazepineHCP.htm> . (Accessed November 24, 2008).
3. Man CB, Kwan P, Baum L, Yu E, Lau KM, Cheng AS, Ng MH. Association between HLA-B*1502 allele and drug-induced cutaneous reactions in Han Chinese. *Epilepsia* 2007; 48(5):1015-1018.
4. Locharearnkul C, Loplumler J, Limotai C, Korkij W, et al. Carbamazepine and phenytoin induced Stevens - Johnson syndrome is associated with the HLA-B*1502 allele in Thai population. *Epilepsia*, Early Online Publication July 14, 2008:1-5.

ACTIONS

- **Facility Director (or physician designee):** Forward this document to the Facility Chief of Staff (COS) and report completion of actions to the VISN Director.
- **Facility COS:** Forward this document to all appropriate providers who prescribe these medications (e.g., **primary care and mental health providers, neurologists, neurosurgeons, and ER physicians**, 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. Report completion of actions to the Facility Director.
- **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).
- **VISN Directors:** Within 10 business days of receipt (due 12/17/2008), communicate to PBM/VAMedSAFE that all actions have been completed via the Feedback tool: http://vaww.national.cmop.va.gov/PBM/visn_drug_recalls_alerts/default.aspx.