DRUG-DRUG INTERACTIONS

Clinical Infectious Diseases

IDSA GUIDELINE

Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis

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Nahid P et al (2016)Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis. Clin Infect Dis. 2016 Oct 1;63(7):e147-e195. *doi: 10.1093/cid/ciw376*. Epub 2016 Aug 10. PMID: 27516382; PMCID: PMC6590850.

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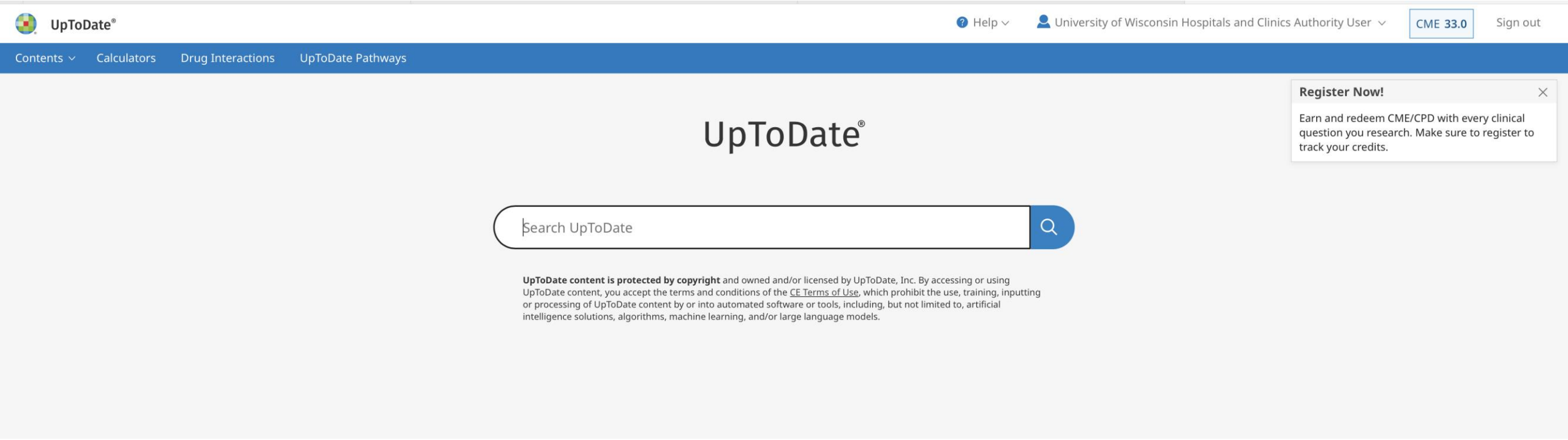

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Drug Interactions

Print

Item(s)

Enter Item Name

Add

✕ **Isoniazid**

✕ **Phenytoin**

Clear

Analyze

Display complete list of interactions for an individual item by clicking item name.

X	Avoid combination	C	Monitor therapy	A	No known interaction
D	Consider therapy modification	B	No action needed	*More about Risk Ratings*	▼

1 Result

Filter Results by Item

View interaction detail by clicking on link(s) below.

C Phenytoin (Fosphenytoin-Phenytoin)
Isoniazid

Title Fosphenytoin-Phenytoin / Isoniazid

Dependencies

- **Phenotype**: This interaction may be of greater magnitude and significance in patients with impaired isoniazid metabolism (ie, those with N-acetyltransferase 2 [NAT2] polymorphisms).

Risk Rating C: Monitor therapy

Summary Isoniazid may increase the serum concentration of Fosphenytoin-Phenytoin. **Severity** Moderate **Reliability Rating** Good

Patient Management Monitor for increased phenytoin concentrations and toxicities if fosphenytoin or phenytoin is combined with isoniazid. Fosphenytoin/phenytoin dose adjustments may be needed.

Fosphenytoin-Phenytoin Interacting Members Fosphenytoin, Phenytoin

Discussion Significant increases in serum phenytoin concentrations, as well as signs and symptoms of toxicity, have been reported in several studies and case reports when isoniazid was added to phenytoin therapy.[1,2,3,4,5,6,7,8,9] This interaction has occurred within days of isoniazid initiation in some cases, and up to several weeks after treatment initiation in others. Additionally, the risk for phenytoin toxicity with this combination appears to be greater in patients with impaired isoniazid metabolism (ie, those with N-acetyltransferase 2 [NAT2] polymorphisms).[6,7,8,9]

Prescribing information for both phenytoin and isoniazid state that isoniazid may increase phenytoin concentrations.[10,11] Monitor phenytoin concentrations when these agents are combined and adjust phenytoin doses as needed.[10,11]

The mechanism of this interaction has not been fully investigated, but isoniazid-mediated inhibition of CYP enzymes responsible for phenytoin metabolism may contribute. It has also been proposed that the higher isoniazid concentrations observed in patients with impaired isoniazid metabolism may lead to greater inhibition of phenytoin metabolism.[8,9,12]

Footnotes

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4. Miller RR, Porter J, Greenblatt DJ. Clinical importance of the interaction of phenytoin and isoniazid: a report from the Boston Collaborative Drug Surveillance Program. *Chest*. 1979;75(3):356-358. [PubMed 421578]

5. Witmer DR, Ritschel WA. Phenytoin-isoniazid interaction: a kinetic approach to management. *Drug Intell Clin Pharm*. 1984;18(6):483-486. [PubMed 6734435]

6. Avasthi R, Jain AP. Phenytoin-isoniazid interaction. *J Assoc Physicians India*. 1989;37(11):728. [PubMed 2517288]

7. Walubo A, Aboo A. Phenytoin toxicity due to concomitant antituberculosis therapy. *S Afr Med J*. 1995;85(11):1175-1176. [PubMed 8597009]

8. Adole PS, Singh A, Kharbanda PS, Sharma S. Phenotypic interaction of simultaneously administered isoniazid and phenytoin in patients with tuberculous meningitis or tuberculoma having seizures. *Eur J Pharmacol*. 2013;714(1-3):157-162. [PubMed 23792142]

9. Adole PS, Kharbanda PS, Sharma S. N-acetyltransferase 2 (NAT2) gene polymorphism as a predisposing factor for phenytoin intoxication in tuberculous meningitis or tuberculoma patients having seizures - A pilot study. *Indian J Med Res*. 2016;143(5):581-590. [PubMed 27488001]

10. Dilantin (phenytoin) [prescribing information]. New York, NY: Pfizer Inc; March 2021.

11. Isoniazid [prescribing information]. Princeton, NJ: Sandoz Inc; April 2019.

12. Adithan C, Subathra A. NAT2 gene polymorphism: covert drug interaction causing phenytoin toxicity. *Indian J Med Res*. 2016;143(5):542-544. [PubMed 27487996]