

# Wyoming Drug Utilization Review

## Anorexia

Angela Christensen, PharmD Candidate 2009

Anorexia is present in many disease states such as cancer, anorexia cachexia syndrome, cystic fibrosis, AIDS, and chronic obstructive pulmonary disease (COPD). Anorexia leads to weight loss, tissue wasting, poor performance, and death.<sup>1,2</sup> Most studies researching anorexia have been in cancer patients, cachexia, and in long term care facilities.

hormonal or absorption dysfunctions. One mechanism is dysfunction of the hypothalamic nucleus. The hypothalamus regulates the signals of energy, adipose levels, and appetite stimulation. Hypothalamus neuropeptide Y (NPY) stimulates feeding behaviors and stimulates other orexigenic (appetite stimulating) compounds. Orexigenic compounds include galanin, melanocortin, orexin, argouti related peptides, and ghrelin. Orexigenic compounds also stimulate behaviors related to appetite. Although controversial, evidence has shown that increased levels of serotonin activity in the brain cause anorexia. A third mechanism is low levels of melanocortin. A fourth mechanism is hypermetabolism of carbohydrates, lipids, proteins, and gastrointestinal dysfunction leading to satiety being reached early.<sup>1,2</sup> Appetite stimulants include glucocorticosteroids, progestins, cyproheptadine, cannabinoids, and newer experimental orexigenic agents.

### *Pathophysiologic Causes*

The first step in helping a patient with anorexia is to identify a pathophysiologic trigger for anorexia that can be treated, for example: severe acute illnesses, pain, depression, medications, GI disorders, hyperthyroidism, bad tasting diets (low salt or low cholesterol), nausea, and vomiting.<sup>1,2,3</sup>

Some medications that cause anorexia include digoxin, theophylline, and antipsychotics.<sup>3</sup>

Increasing nutritional status, eliminating the trigger, parenteral feeding, nutritional supplementation, or stopping the offending medications are ways to help alleviate pathophysiologic anorexia.<sup>3,4</sup>

### *Nonpathophysiologic Causes*

Nonpathophysiologic causes can be attributed to several different mechanisms related to

### *Pharmacologic Treatment*

Pharmacologic appetite stimulants should be used if anorexia does not improve or no pathophysiologic cause can be found.<sup>3,4</sup>

### *Appetite Stimulants*

- Glucocorticosteroids (prednisolone, dexamethasone, and methylprednisolone)
- Progestins (megestrol acetate (MA) and medroxy-progesterone acetate (MPA))
- Cyproheptaine
- Cannabinoids (dronabinol)
- Thalidomide
- Newer orexigenic experimental agents (ghrelin and melanocortin)
- Other medications (branched chained amino acids (BCCA), and eicosapentaenoic acid (EPA))

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## WY-DUR Board Meeting Update

The DUR Board met for its bimonthly business meeting on November 20, 2008. Highlights of this meeting include the following.

1. The Pharmacy Program Manager announced that the transition from ACS to GHS for claims processing is still on track for an April implementation. Further information will be provided as this date approaches.
2. The Board approved the Triptan and ARB criteria as previously published. The final criteria will be posted on the DUR website at [www.uwyo.edu/DUR](http://www.uwyo.edu/DUR).
3. The Board approved the following draft criteria to be released for public comment.

### Claims for Versa Foam products will be approved if:

- Recipient has tried and failed two other vehicles (cream, ointment, etc)
- Recipient is unable to tolerate other vehicles
- Recipient has diagnosis of scalp psoriasis or alopecia areata

### Claims for Atopiclair will be approved if:

- Recipient is under the age of 6.

### Claims for Cymbalta will require prior authorization for:

- Initial doses greater than 60 mg
  - Doses of 120 mg and higher
4. There was significant discussion regarding potential limits on narcotic medications. The following limits were approved to be released for public comment.

### Claims for the following will require prior authorization:

- Acetaminophen doses greater than 4 grams per day (for all acetaminophen-containing products)
- Ibuprofen doses greater than 3200 mg of ibuprofen per day (for all ibuprofen-containing products)
- More than one butorphanol nasal inhaler per month
- Any narcotic utilization in combination with buprenorphine
- More than sixty pentazocine/naloxone tablets per month
- Fentanyl patches applied more frequently than every 72 hours
- Marinol doses above 20 mg per day and for diagnoses except for AIDS and cancer

All proposed prior authorization criteria will be posted for public comment. Comments may be sent by email to [alewis13@uwyo.edu](mailto:alewis13@uwyo.edu) or by mail to: Wyoming Drug Utilization Review Board, Dept. 3375, 1000 E. University Avenue, Laramie, WY 82071. Comments should be received prior to January 20, 2009 for Board review.

The next DUR Board meeting will be held January 29, 2009 in Cheyenne. Topics for discussion will include preferred medications for the ADHD class as well as further discussion of the proposed prior authorization criteria listed above. An agenda will be posted approximately two weeks prior to the meeting.

Happy  
Holidays

## Anorexia

### Mechanism of Action

Each appetite stimulant class focuses on a different mechanism of action. The above theories on the mechanisms of appetite stimulation help to explain how different medications work. Progestins, dronabinol, and glucocorticoids all work to decrease different cytokines that act on the hypothalamus. Progestins are thought to work on inhibiting interleukin, tumor necrosis factor, NPY, and calcium channels.<sup>1,2,5</sup> Dronabinol inhibits interleukin, then prostaglandin synthesis, and may act on receptor CB1.<sup>2</sup> Glucocorticoids work to enhance NPY and inhibit TNF alpha, interleukin, and serotonin.<sup>2,3</sup> High levels of histamine inhibit appetite, so decreasing levels may increase appetite. The mechanism of action of cyproheptadine as an appetite stimulant is to antagonize histamine.<sup>1,2,5</sup> The mechanism of action of BCAA is to compete for serotonin receptors in the brain.<sup>2</sup> EPA works by inhibiting interleukin 6 and proteolysis inducing factor.<sup>6</sup> New agents are looking at inhibiting orexigenic peptides in the body that also act on neuropeptides to increase appetite stimulation. Two of these peptides are ghrelin and melanocortin.<sup>1,7,8</sup>

### Summary of Guidelines

Treatment of weight loss and anorexia should consider appetite stimulants after other methods have been tried, such as treating pathophysiologic problems such as depression, pain or acute illness, stopping the offending medications, or increasing nutritional supplementation.<sup>2,9</sup> MA and thalidomide are the appetite stimulants which have been shown to increase weight.<sup>1,2,5,10</sup> MA has some controversial evidence regarding the effectiveness in increased quality of life for patients.<sup>10</sup> No appetite stimulants have studies available that show decreased outcomes for any diseases. MA and dronabinol have appetite stimulation as a labeled use.<sup>11,12,13</sup> Glucocorticoids, cyproheptadine, and thalidomide are used off-label for appetite stimulation.<sup>13,14,15,16</sup>

### First Line Therapy

Glucocorticoids and MA should be used as first line therapy, because they have the most experience and have shown to improve appetite effectively. Glucocorticoids should be used short term; approximately four weeks as an appetite stimulant.

Glucocorticoids may be chosen over MA due to lower cost. MA should be used when appetite stimulation is needed for a longer period of time.<sup>2,9</sup> Few studies have been done with appetite stimulants in cystic fibrosis and COPD, however MA was shown to be possibly effective.<sup>3,7</sup>

### Second Line Therapy

Cyproheptadine, thalidomide, and newer agents being researched can be used as second line agents when the first line agents fail to increase appetite.<sup>2</sup> Cyproheptadine and dronabinol have shown some effectiveness as appetite stimulants in cancer and cachexia, but more data on the effectiveness is needed.<sup>1,2</sup> Neither of these agents is efficacious in noncancer caused anorexia including cystic fibrosis.<sup>1,6</sup> The role that newer agents might play as appetite stimulants has not been determined. Side effects, contraindications, length of therapy, and other therapies should be considered when choosing an appetite stimulant.

### References

1. Elamin E, Glass M, Camporesi E. Pharmacological approaches to ameliorating catabolic conditions. *Curr Opin Clin Nutr Metab Care*. 2006;9:449-454.
2. Inui A. Cancer anorexia-cachexia syndrome: current issues in research and management. *CA Cancer J Clin*. 2002;52:72-91.
3. Thomas DR, Ashmen W, Morley JE, Evans WJ. Nutritional management in long-term care: Development of a clinical guidelines. Council of Nutritional Strategies in Long-Term Care. *J Gerontol A Biol Sci Med Sci*. 2000;55:725-734.
4. Nelson KA, Walsh D, Hussein M. A phase II study of low-dose megestrol acetate using twice-daily dosing for anorexia in nonhormonally dependent cancer. *Am J Hosp Palliat Care*. 2002;19:205-210.
5. Chinuck R, Fornum H, Baldwin D. Appetite stimulants in cystic fibrosis; a systematic review. *J Hum Nutr Diet*. 2007;20:526-537.
6. Weisburg J, Wanger J, Olson J, et al. Megestrol acetate stimulates weight gain and ventilation in underweight COPD patients. *Chest*. 2002;121:1070-1078.
7. Cummings D, Foster-Schubert K, Overduin J. Ghrelin and energy balance; focus on current controversies. *Curr Drug Targets*. 2005;6:153-169.
8. Strasser F. Appraisal of current and experimental approaches to treatment of cachexia. *Curr Opin Support Palliat Care*. 2007;1:312-316.
9. Loprinzi CL, Boldberg RM, Bumham NL. Cancer-associated anorexia and cachexia. Implications for drug therapy. *Drugs*. 1992;43:499-506.
10. Beller E, Tattersall M, Lumley T, et al. Improved quality of life with megestrol acetate in patients with endocrine insensative cancer: a randomized placebo controlled trial. *Ann Oncol*. 1997;8:277-283.
11. Megestrol acetate. Lexi-Comp. Lexi-Comp Online™. Hudson (OH): Lexi-Comp, Inc.; 2008. Available from: <http://online.lexi.com>. Accessed: November 13, 2008.
12. Megestrol acetate. Drugs Facts and Comparisons. Facts & Comparisons 4.0 Online™. Indy (IN): Wolters Kluwer Health Inc.; 2008. Available from: [www.online.factsandcomparisons.com](http://www.online.factsandcomparisons.com). Accessed: November 13, 2008.
13. Dronabinol. Drugs Facts and Comparisons. Facts & Comparisons 4.0 Online™. Indy (IN): Wolters Kluwer Health Inc.; 2008. Available from: [www.online.factsandcomparisons.com](http://www.online.factsandcomparisons.com). Accessed: November 13, 2008.
14. Prednisolone. Drugs Facts and Comparisons. Facts & Comparisons 4.0 Online™. Indy (IN): Wolters Kluwer Health Inc.; 2008. Available from: [www.online.factsandcomparisons.com](http://www.online.factsandcomparisons.com). Accessed: November 13, 2008.
15. Loprinzi CL. Management of cancer anorexia and cachexia. *Support Care Cancer*. 1995;3:120-122.
16. Cyproheptadine. Facts and Comparisons. Facts & Comparisons 4.0 Online™. Indy (IN): Wolters Kluwer Health Inc.; 2008. Available from: [www.online.factsandcomparisons.com](http://www.online.factsandcomparisons.com).

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December 2008

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(November 2008)

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