

# A Comparison Of The Costs For Treating Central Precocious Puberty During The First Year With Monthly Leuprolide Acetate Injectable And Histrelin Acetate Implant

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## BACKGROUND

Puberty results when secretion of gonadotropin releasing hormone (GnRH) is initiated and the hypothalamic-pituitary-gonadal axis is activated.<sup>1</sup> During puberty, the brain produces GnRH through a complex process. GnRH causes increases in other hormones like luteinizing hormone (LH) and follicle stimulating hormone (FSH). It is these hormones that cause the ovaries to produce estrogen and the testicles to produce testosterone. The onset of puberty is marked by breast development in girls and testicular enlargement in boys.

Central precocious puberty (CPP) refers to premature activation of the hypothalamic-pituitary-gonadal axis. CPP has traditionally been defined as physical signs of sexual development before age 8 years in white girls, age 7.5 years in black and Hispanic girls, and 9 years in boys<sup>2</sup>. Precocious puberty is listed as a rare disease by the Office of Rare Diseases<sup>3</sup>.

Clinical concerns when precocious puberty progresses include early menarche in girls, short adult stature due to early epiphyseal fusion and adverse psychological outcomes in both sexes<sup>4</sup>. CPP is typically treated with GnRH agonists such as leuprolide acetate (Abbott's Lupron Depot-PED) or histrelin acetate (ENDO's Supprelin LA). Leuprolide acetate is weight-base dosed with an IM injection every 4 weeks (Depot-PED is not available in 3-month formulation). When therapy is initiated with leuprolide acetate, the dose is titrated upward until no progression of the condition is noted either clinically and/or by laboratory parameters. Histrelin acetate is a 12-month implant. When comparing the cost of treatment for the two products, it is important to take into account the potential dose escalation that can occur with titration of leuprolide acetate and desired/achieved compliance with therapy.

## OBJECTIVES

Central precocious puberty (CPP) is generally treated with gonadotropin releasing hormone (GnRH) agonists. The objective was to compare the overall costs of first year treatment using the monthly pediatric leuprolide acetate injections and once-a-year histrelin acetate implants.

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## METHODS

Two retrospective cohort studies were conducted using datasets derived from the Thomas Reuter's MarketScan® Multi-State Medicaid Database (2003-2007) and the MarketScan® Commercial Database (2005-2009). A probabilistic patient flow model was developed using estimates for treatment patterns and costs for products, office visits, and monitoring therapy.

Inclusion criteria were:

- 2 claims with target diagnoses occurring 30 or more days apart (259.1 – Precocious sexual development and puberty, 255.2 – Adrenogenital disorders, 256.0 – Hyperestrogenism, 256.1 – Other ovarian hyperfunction, 257.0 – Testicular hyperfunction), and
- Enrollment for 3+ months before first treatment, and
- Treatment with leuprolide acetate for 12 months or more or histrelin acetate or treatment with histrelin implant and eligible for following 12 months.

## RESULTS

- 4,802 Medicaid and 7,391 Commercial beneficiaries age 12 years or younger were identified as diagnosed with CPP.
- 323 Medicaid and 383 Commercial beneficiaries met the inclusion criteria and were treated with leuprolide for 365 days or more.
- 47% of Medicaid and 46% of Commercial patients treated with leuprolide were considered to be compliant with their leuprolide therapy (13+ treatments/year).
- Leuprolide compliant patients had an average of 14.8 and 14.0 treatments per year (Medicaid and Commercial, respectively).
- Leuprolide non-compliant patients had 9.2 and 7.7 treatments per year (Medicaid and Commercial, respectively).
- 200 histrelin acetate patients were identified in the Commercial data set. These patients had an average of 2.8 office visits for monitoring per year.

Cost for treating 100 patients were simulated using existing levels of non-compliance and an assumption that all patients should be compliant.

- Based on current levels of non-compliance, costs for histrelin implants were 2.0% lower in Medicaid and 6.5% higher in Commercial plans.
- When an assumption is made that all patients should be compliant, costs for histrelin implants were 12.9% lower in Medicaid and 12.6% lower in Commercial plans.

MEDICAID MODEL		Estimated Annual Cost of Treatment if all PTs Treated With . . .				
			Lupron	SUPPRELIN LA		
Quality of Care Compliance Assumption	100% compliance with Lupron treatment (All patients receive 13+ treatments in year)	Product costs	\$ 1,770,201	\$ 1,515,188		
		Office visit costs	\$ 79,896	\$ 14,000		
		Implant procedures		\$ 91,400		
		Lab/xray for monitoring	\$ 53,900	\$ 37,500		
		<b>TOTAL COST TO PAYER</b>	<b>\$ 1,903,997</b>	<b>\$ 1,658,088</b>		
	Normal Compliance with Lupron:			Lupron	SUPPRELIN LA	
		Patients with < 13 treatments per year	Product costs	\$ 1,572,921	\$ 1,515,188	
		% of TXd PTs: 53%	Aver. # TXs / year: 9.2	Office visit costs	\$ 70,992	\$ 14,000
		Patients with 13+ treatments per year	Implant procedures		\$ 91,400	
		% of TXd PTs: 47%	Aver. # TXs / year: 14.8	Lab/xray for monitoring	\$ 47,893	\$ 37,500
		<b>TOTAL COST TO PAYER</b>	<b>\$ 1,691,806</b>	<b>\$ 1,658,088</b>		

COMMERCIAL PLAN MODEL		Estimated Annual Cost of Treatment if all PTs Treated With . . .				
			Lupron	SUPPRELIN LA		
Quality of Care Compliance Assumption	100% Compliance with Lupron treatment (All patients receive 13+ treatments in year)	Product costs	\$ 1,749,034	\$ 1,515,188		
		Office visit costs	\$ 83,980	\$ 15,400		
		Implant procedures		\$ 91,400		
		Lab/xray for monitoring	\$ 65,800	\$ 37,500		
		<b>TOTAL COST TO PAYER</b>	<b>\$ 1,898,814</b>	<b>\$ 1,659,488</b>		
	Normal compliance with Lupron:			Lupron	SUPPRELIN LA	
		Patients with < 13 treatments per year	Product costs	\$ 1,434,695	\$ 1,515,188	
		% of TXd PTs: 54%	Aver. # TXs / year: 7.7	Office visit costs	\$ 68,887	\$ 15,400
		Patients with 13+ treatments per year	Implant procedures		\$ 91,400	
		% of TXd PTs: 46%	Aver. # TXs / year: 14.0	Lab/xray for monitoring	\$ 53,974	\$ 37,500
		<b>TOTAL COST TO PAYER</b>	<b>\$ 1,557,556</b>	<b>\$ 1,659,488</b>		

## CONCLUSIONS

With current levels of non-compliance with leuprolide therapy, overall costs for treatment of CPP with histrelin are slightly (2%) less in Medicaid and somewhat (6.5%) higher in Commercial plans. If all patients are assumed to be compliant with leuprolide therapy, overall costs of treatment with histrelin implants are lower in both markets (12.9% and 12.6% for Medicaid and Commercial, respectively). The additional medical costs that may be related to poor outcomes associated with non-compliance were not included in this model.

## REFERENCES

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