

# BUDGET IMPACT OF METYRAPONE FOR THE TREATMENT OF CUSHING'S SYNDROME FROM A PAYER PERSPECTIVE IN FRANCE

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## BACKGROUND

- Endogenous Cushing's syndrome (CS) is caused by increased cortisol production by one or both adrenal glands (adrenal CS), or from either elevated pituitary tumour adrenocorticotropic hormone (ACTH) secretion (Cushing disease) or non-pituitary tumour ACTH ectopic secretion, which stimulates excessive cortisol.<sup>1</sup>
- Patients for whom surgery fails or is not an option require medical therapy like steroidogenesis inhibitors (metyrapone, ketoconazole, osilodrostat) to control cortisol levels and reduce associated comorbidities.<sup>2</sup>
- Metyrapone is approved for the treatment of endogenous CS<sup>3</sup>, and results in a rapid and sustained normalisation of cortisol levels, which can improve quality of life for patients with CS.<sup>4,5</sup>
- Metyrapone has a long history of use<sup>6</sup> with a manageable safety profile and low risk of adrenal insufficiency.<sup>7</sup>
- Despite the lack of direct comparison with other steroidogenesis inhibitors, the recent indirect comparison study and its preliminary data (MOSKETEER study) suggest that metyrapone is similarly effective to other steroidogenesis inhibitors (osilodrostat and ketoconazole) with fewer therapy interruptions due to adverse events (AE).<sup>8,9</sup>
- Osilodrostat has recently been approved for the treatment of endogenous CS.<sup>10,11</sup> There are no head-to-head studies for osilodrostat and metyrapone. A recent Health Technology Assessment (HTA) evaluation in the Czech Republic accepted comparable efficacy between osilodrostat and metyrapone (data on file, available upon request).<sup>12</sup>

## OBJECTIVE

- This analysis assesses the budget impact of metyrapone versus osilodrostat for the treatment of endogenous CS from a healthcare system perspective in France.

## METHODS

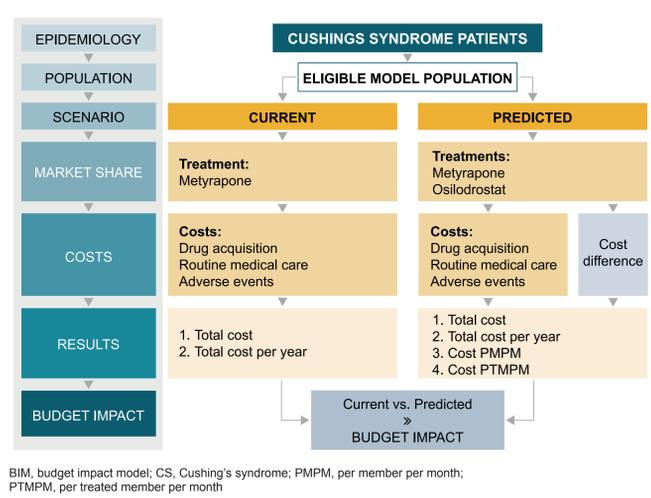
### MODEL STRUCTURE

- A 5-year budget impact model (BIM) was developed to evaluate treatment costs for adult patients diagnosed with CS in France across two scenarios (Figure 1):
  - Scenario 1:** 100% of patients treated with metyrapone vs. 100% of patients treated with osilodrostat
  - Scenario 2:** Osilodrostat adoption gradually increasing from 25% of patients in year 1 to 75% from year 3 onward

### POPULATION

- Patients diagnosed with CS prevalence: 68 per million; annual incidence: 3 per million.<sup>13</sup>

**Figure 1: Structure of BIM assessing the budget impact of metyrapone versus osilodrostat use for patients diagnosed with CS from a payer perspective in France**



BIM, budget impact model; CS, Cushing's syndrome; PMPM, per member per month; PTMPM, per treated member per month

## COSTS

- Drug acquisition (using publicly available prices in France).<sup>14</sup>
- Routine medical care.<sup>15</sup>
- Management of treatment-related adverse events (TRAEs) that occur in >5% of patients.<sup>16-18</sup>

## ASSUMPTIONS

- Daily treatment dose of metyrapone 1,500mg/day in accordance with SmPC.<sup>3,18</sup>
- Osilodrostat dose titrated based on the EMA SmPC starting at 2mg twice daily (BID), up to 5mg BID.<sup>10</sup>
- Assumptions for net drug costs reflect typical rebate levels in France, including those applied to products with a minor clinical added value rating.

## ADVERSE EVENTS (AES) MODELLED (TABLE 1)

- Isolated (i.e. occurring once per year): fatigue, myalgia, arthralgia, hypertension and asthenia.
- Chronic (i.e. recurring, occurring more than once per year): adrenal insufficiency (cost applied annually once diagnosed).

**Table 1: Incidence rates and management costs of AEs associated with metyrapone or osilodrostat use included in the BIM**

Isolated AE*	Incidence per year		Management cost <sup>17</sup> (EU€)
	Metyrapone <sup>18</sup>	Osilodrostat <sup>16</sup>	
Fatigue	0.10	0.4	€100
Myalgia	0.05	0.25	€50
Arthralgia	0.10	0.45	€225
Hypertension	0.10	0.22	€100
Asthenia	0.10	0.23	€100
Chronic adverse event**	Prevalence		Cost per year <sup>19</sup> (EU€)
	Metyrapone <sup>18</sup>	Osilodrostat <sup>16</sup>	
Adrenal insufficiency	0.05	0.26	€5,129

AE, adverse events; BIM, budget impact model  
\*Estimated to occur once per year. \*\*Recurring; estimated to occur more than once per year. Note: Incidence rates are used for isolated AEs expected to occur once per year, while prevalence rates are used for chronic AEs that are ongoing or occur multiple times per year.

## RESULTS

### SCENARIO 1, COST COMPARISON: 100% METYRAPONE VS. 100% OSILODROSTAT

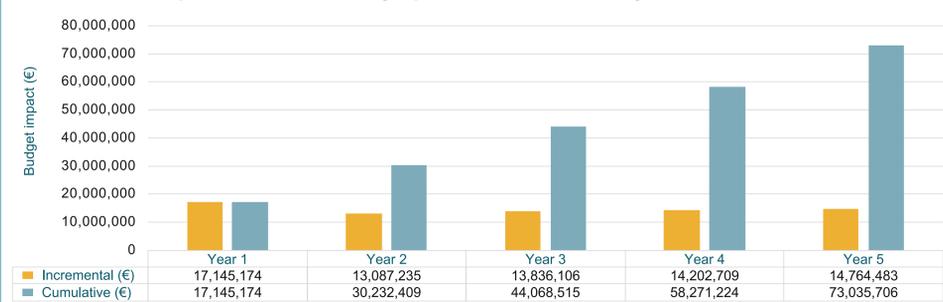
Per patient costs over 5 years:

- In France, the cost of treating a patient with metyrapone (drug acquisition cost only) over 5-years is approximately €46,035, compared with €110,875 for osilodrostat, resulting in a **€64,840 or 58% cost saving**.
- Over 5 years, metyrapone AE management costs per patient are estimated to be approximately **81% lower than with osilodrostat** (€1,338 vs. €6,869 per patient).
- This is predominantly due to the cost of managing adrenal insufficiency, which accounts for approximately €6,665 of the osilodrostat AE management costs over the 5-year period per patient versus €1,280 for metyrapone.

Population level 5-year budget impact:

The net cumulative 5-year budget impact for the whole population, including drug acquisition, disease monitoring and AE management costs is **€73,035,706**, representing a **54% cost saving** with metyrapone versus osilodrostat (Figure 2).

**Figure 2: Scenario 1: Estimated incremental and cumulative net budget impact of 100% osilodrostat compared with 100% metyrapone treatment over 5 years in France**



### SCENARIO 2, BUDGET IMPACT OF GRADUALLY INCREASING THE MARKET SHARE OF OSILODROSTAT FROM 25% IN YEAR 1 TO 75% IN YEAR 3 ONWARDS

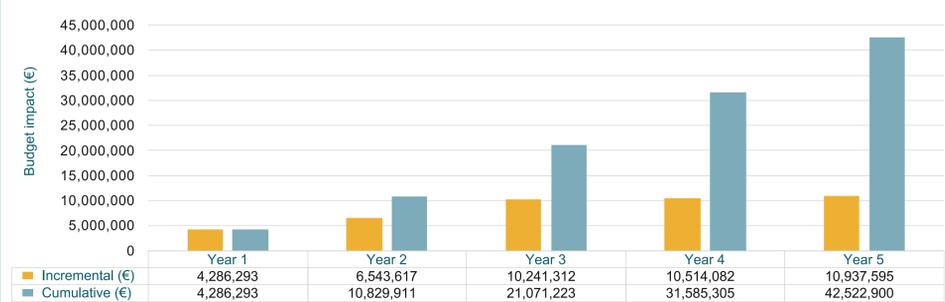
Per patient costs over 5 years:

- The cost per patient over 5 years, including drug acquisition, disease monitoring and AE management costs is €59,130 with 100% metyrapone use. This cost increases to €99,784 over 5 years if osilodrostat market share is increased to 75% by year 3.

Population level 5-year budget impact:

- Introducing osilodrostat for 25% of patients in year 1, 50% in year 2, and 75% in years 3, 4 and 5 would result in a total cost over 5 years of **€103,501,478** compared to €60,978,578 from treating 100% of patients with metyrapone. This represents a **cumulative 5-year incremental budget impact of €42,522,900 (Figure 3)** and a **41% cost-saving** if 100% metyrapone use is maintained instead.

**Figure 3: Scenario 2: Estimated incremental and cumulative net budget impact of osilodrostat (increasing market share from 25% in year 1 to 75% in year 3 onwards) compared with 100% metyrapone treatment over 5 years in France**



## CONCLUSION

- In France, a cost comparison scenario showed that treating all patients with metyrapone instead of osilodrostat results in a **€73,035,706 or 54% cost saving over 5 years**.
- Even a partial shift toward osilodrostat use in patients with CS from 0% to 75% over 5-years would increase the national budget for CS management by 41% to **€103,501,478**.
- There are no direct clinical comparison studies of metyrapone versus osilodrostat. However, a recent HTA assessment report from Czech Republic and evidence from a retrospective multicentre study, MOSKETEER, indicate that metyrapone has comparable efficacy to osilodrostat in reducing 24h urinary free cortisol in patients with CS.<sup>8,12</sup>
- Potential limitations of this analysis include the assumptions made around treatment doses and net drug costs, as well as the frequency of AEs modelled.
- This analysis suggests that metyrapone, when compared to osilodrostat, is a **substantially cost-saving therapy option for endogenous CS in France**.

## DISCLOSURES/FUNDING

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