**The relative value of anti-obesity medications compared to similar therapies**

**Kim et al.**

**Supplementary Materials Table of Contents:**

Table S1. Initial therapeutic areas identified as potential comparisons to obesity

Table S2. Deprioritized therapeutic areas using a high-level rationale

Table S3.Dimensions used for further analysis and prioritization of nine remaining therapeutic areas

Table S4. PICOS criteria for the therapeutic area analogues assessed in the targeted literature review

Table S5. Search strategy: smoking cessation (as of 23 June 2021)

Table S6. Search strategy: daytime sleepiness (as of 23 June 2021)

Table S7. Search strategy: migraine (as of 23 June 2021)

Table S8. Search strategy: fibromyalgia (as of 23 June 2021)

Table S9. Most common comorbidities and financial impact for each condition

Table S10. Clinical outcomes and patient-reported endpoints

**Table S1.** Initial therapeutic areas identified as potential comparisons to obesity

|  |  |  |
| --- | --- | --- |
| Attention-deficit/hyperactivity disorder | Dental care | Interstitial lung disease |
| Allergies | Dermatology | Mental health |
| Anti-hypertensives | Diabetes | Migraine |
| Anticoagulants | Fibromyalgia | Multiple Sclerosis |
| Antivirals | Gastrointestinal | Oncology |
| Asthma / Chronic Obstructive Pulmonary Disease (respiratory) | Heart failure | Pain |
| Autoimmune and inflammatory | Hypoactive Sexual Desire Disorder  | Smoking cessation |
| Daytime sleepiness | Hypercholesteremia | Vaccines (human papillomavirus) |
|  |  | Vision care |

Note: Twenty-five therapeutic areas were selected and screened based on pre-aligned criteria including healthcare cost spending, relevance to obesity (i.e., prevalence), type of indication, and duration of treatment.

**Table S2.** Deprioritized therapeutic areas using a high-level rationale

| **Therapeutic area** | **Rationale for exclusion** |
| --- | --- |
| Attention-deficit/hyperactivity disorder | A high number of generics in the therapy area |
| Anti-hypertensives | A high number of generics in the therapy area |
| Allergies | A high number of generics in the therapy area |
| Anticoagulants | Disease area characterized by acute episodes |
| Antivirals | Disease area characterized by acute episodes |
| Autoimmune and inflammatory | Highly commoditized market, high rebates, negative payer perceptions |
| Dental care | Falls outside medical/pharmacy budget as treatment focuses on procedures rather than medication |
| Diabetes | Overlap with existing portfolio |
| Heart failure | Disease area characterized by acute episodes |
| Hypercholesteremia | Highly genericized market; overlap with existing portfolio  |
| Interstitial lung disease | High short-term morbidity/mortality disease area  |
| Mental health | A high number of generics in the therapy area |
| Multiple sclerosis | High short-term morbidity disease area  |
| Oncology | High short-term mortality disease area |
| Pain | Heterogenous therapy area (fibromyalgia is included in select list) |
| Vision care | Falls outside medical/pharmacy budget as treatment focuses on procedures rather than medication |

**Table S3.** Dimensions used for further analysis and prioritization of nine remaining therapeutic areas

| **Dimension** | **Description** | **Metric** | **Relevance** |
| --- | --- | --- | --- |
| Population size | Annual size of the patient population, based on the incidence in the US and recent growth trends | Millions of patients | Provides an idea of the disease's magnitude in the US |
| Reimbursement history | Health plans' coverage evolution of relevant products on each disease, including changes on the management approach for the disease | Time from launch to meeting percentage threshold of plans to cover | Shows the likelihood of coverage/active management of the disease |
| Cost evolution | Cost variations in response to entry of innovative treatments or other relevant events in the disease area | 10-year CAGR in costs | Shows the price elasticity of the therapeutic area when a critical event takes place |
| Type of therapies | Summary of the therapies available in the area | Number of products by mechanism of action, routes of administration, presence of generics | Reflects how similar, in terms of therapies, each disease is compared to obesity |
| Benefit to patients | Evolution of benefits provided to patients | Percentage of the change in efficacy / reduction of critical cases in a 10-year period | Shows the impact of innovation/new therapies on the disease area |
| Barriers | List of barriers in each disease area to a new product entry, coverage, or uptake | High barriers, medium barriers, low barriers | Shows the challenges for new products in each therapeutic area and reflects potential barriers to get coverage in the disease area |
| Lifestyle indication | 'Lifestyle Medicine' is an established branch of medicine reflecting on lifestyle's contribution to health in addition to non-pharmacological intervention in the treatment and management of lifestyle diseases, such as exercise in diabetes mellitus and weight management in obesity  | Yes, is a lifestyle medicine; no, is not a lifestyle medicine | Reflects lifestyle decisions, not necessarily covered by common coverage, as it is a good analogue for obesity |

**Abbreviations:** CAGR, compound annual growth rate

**Table S4.** PICOS criteria for the therapeutic area analogues assessed in the targeted literature review

| **PICOS Criteria** | **Definition** |
| --- | --- |
| Population  | Adults treated for the four therapeutic categories of smoking cessation, daytime sleepiness, migraines, and fibromyalgia |
| Intervention | All pharmacological treatments approved in the US excluding over the counter treatments, alternative medicines, and physical therapy |
| Comparator  | Standard of care, none, or any other pharmacologic treatment |
| Outcomes | Direct medical costs, indirect costs, health care resource use, cost drivers, and other clinical outcomes |
| Study Design | Real-world studies (secondary database, registry, claims, observational), modeling, and cost-effectiveness studies |

**Abbreviations:** US, United States

**Table S5.** Search strategy: smoking cessation (as of 23 June 2021)

|  |  |  |  |
| --- | --- | --- | --- |
| **#** | **Concept – product(s)** | **Searches** | **Results** |
| 1 | Chantix –title/abstract, keywords | Varenicline/ or (varenicline or Chantix or N07BA03).ab,ti,kw. or ((nicotine or tobacco or smok\* or cigarette) adj (quit\* or stop\* or cessa\*)).ab,ti,kw. or (smoking-cessation).ab,ti,kw. | N/A |
| **#** | **Concept – outcomes** | **Searches** | **Results** |
| 2 | Economics/costs – title/abstract, keywords• Direct medical costs • Health care resource use• Indirect costs  • Cost drivers  | (cost\* or expens\* or economic\* or pharmacoeconomic\* or utilization).ab,ti,kw. or (productiv\* or absentee\* or "missed day\*" or resource\*).ab,ti,kw. | N/A |
| 3 | Mental health – title/abstract, keywords | (((mental or psychological) adj (health)).ab,ti,kw. or ((mental or psychological or cognitive or depression or anxiety) and (question\* or scale or inventory)).ab,ti,kw.) and (cost\* or econ\* or impact).mp. | N/A |
| 4 | Combine outcome strings | 2 or 3 | N/A |
| **#** | **Concept – study design** | **Searches** | **Results** |
| 5 | Real-world studies and modeling and cost-effectiveness studies – title/abstract, publication | (observational or longitudinal or prospective\* or retrospective\* or registry or registries).ab,ti,pt. or ('population based' or 'real world' or 'claims data' or 'claims analysis' or modeling).ab,ti. or (database\* and analysis).ab,ti. | N/A |
| **#** | **Concept – combine terms and set limits** | **Searches** | **Results** |
| 6 | Combine smoking cessation, outcomes, and study design | 1 and 4 and 5 | 1,940 |
| 7 | Limit to English language | limit 6 to English language | 1,900 |
| 8 | Limit to last 15 years | limit 7 to yr="2006 -Current" | 1,669 |
| 9 | Number to screen | Remove duplicates from MEDLINE and Embase | 1,101 |

**Table S6.** Search strategy: daytime sleepiness (as of 23 June 2021)

|  |  |  |  |
| --- | --- | --- | --- |
| **#** | **Concept – product(s)** | **Searches** | **Results** |
| 1 | Provigil, Provigil – title/abstract, keywords | modafinil/ or (modafinil or Provigil or N06BA07 or armodafinil or Provigil).ab,ti,kw. or ((((excessive or daytime or inadequate) and (sleep\* or drows\* or somnolence)) or (hypersomnia)) and (treat\* or therap\* or pharm\* or medica\*)).ab,ti,kw. | N/A |
| **#** | **Concept – outcomes** | **Searches** | **Results** |
| 2 | Economics/costs – title/abstract, keywords• Direct medical costs • Health care resource use• Indirect costs  • Cost drivers  | (cost\* or expens\* or economic\* or pharmacoeconomic\* or utilization).ab,ti,kw. or (productiv\* or absentee\* or "missed day\*" or resource\*).ab,ti,kw. | N/A |
| 3 | Mental health – title/abstract, keywords | (((mental or psychological) adj (health)).ab,ti,kw. or ((mental or psychological or cognitive or depression or anxiety) and (question\* or scale or inventory)).ab,ti,kw.) and (cost\* or econ\* or impact).mp. | N/A |
| 4 | Combine outcome strings | 2 or 3 | N/A |
| **#** | **Concept – study design** | **Searches** | **Results** |
| 5 | Real-world studies and modeling and cost-effectiveness studies – title/abstract, publication | (observational or longitudinal or prospective\* or retrospective\* or registry or registries).ab,ti,pt. or ('population based' or 'real world' or 'claims data' or 'claims analysis' or modeling).ab,ti. or (database\* and analysis).ab,ti. | N/A |
| **#** | **Concept – combine terms and set limits** | **Searches** | **Results** |
| 6 | Combine smoking cessation, outcomes, and study design | 1 and 4 and 5 | 577 |
| 7 | Limit to the English language | limit 6 to the English language | 566 |
| 8 | Limit to last 15 years | limit 7 to yr="2006 -Current" | 522 |
| 9 | Number to screen | Remove duplicates from MEDLINE and Embase | 395 |

**Table S7.** Search strategy: migraine (as of 23 June 2021)

|  |  |  |  |
| --- | --- | --- | --- |
| **#** | **Concept – product(s)** | **Searches** | **Results** |
| 1 | Aimovig, Emgality, Ajovy – title/abstract, keywords | (erenumab\* or Aimovig or N02CD0\* or galcanezumab\* or Emgality or fremanezumab or Ajovy).ab,ti,kw or (migraine\* and (treat\* or pharm\* or therap\*)).ab,ti,kw. | N/A |
| **#** | **Concept – outcomes** | **Searches** | **Results** |
| 2 | Economics/costs – title/abstract, keywords• Direct medical costs • Health care resource use• Indirect costs  • Cost drivers  | (cost\* or expens\* or economic\* or pharmacoeconomic\* or utilization).ab,ti,kw. or (productiv\* or absentee\* or "missed day\*" or resource\*).ab,ti,kw. | N/A |
| 3 | Mental health – title/abstract, keywords | (((mental or psychological) adj (health)).ab,ti,kw. or ((mental or psychological or cognitive or depression or anxiety) and (questionn\* or scale or inventory)).ab,ti,kw.) and (cost\* or econ\* or impact).mp. | N/A |
| 4 | Combine outcome strings | 2 or 3 | N/A |
| **#** | **Concept – study design** | **Searches** | **Results** |
| 5 | Real-world studies and modeling and cost-effectiveness studies – title/abstract, publication | (observational or longitudinal or prospective\* or retrospective\* or registry or registries).ab,ti,pt. or ('population based' or 'real world' or 'claims data' or 'claims analysis' or modeling).ab,ti. or (database\* and analysis).ab,ti. | N/A |
| **#** | **Concept – combine terms and set limits** | **Searches** | **Results** |
| 6 | Combine migraine, outcomes, and study design | 1 and 4 and 5 | 1,270 |
| 7 | Limit to the English language | limit 6 to the English language | 1,236 |
| 8 | Limit to last five years | limit 7 to last five years | 1,075 |
| 9 | Number to screen | Remove duplicates from MEDLINE and Embase | 778 |

**Table S8.** Search strategy: fibromyalgia (as of 23 June 2021)

|  |  |  |  |
| --- | --- | --- | --- |
| **#** | **Concept – product(s)** | **Searches** | **Results** |
| 1 | Lyrica, Savella – title/abstract, keywords | (pregabalin or Lyrica or N03AX1\* or milnacipran or Savella).ab,ti,kw or ((fibromyalgia\* or fibrositis) and (treat\* or pharm\* or therap\* or medica\*)).ab,ti,kw. | N/A |
| **#** | **Concept – outcomes** | **Searches** | **Results** |
| 2 | Economics/costs – title/abstract, keywords• Direct medical costs • Health care resource use• Indirect costs  • Cost drivers  | (cost\* or expens\* or economic\* or pharmacoeconomic\* or utilization).ab,ti,kw. or (productiv\* or absentee\* or "missed day\*" or resource\*).ab,ti,kw. | N/A |
| 3 | Mental health – title/abstract, keywords | (((mental or psychological) adj (health)).ab,ti,kw. or ((mental or psychological or cognitive or depression or anxiety) and (questionn\* or scale or inventory)).ab,ti,kw.) and (cost\* or econ\* or impact).mp. | N/A |
| 4 | Combine outcome strings | 2 or 3 | N/A |
| **#** | **Concept – study design** | **Searches** | **Results** |
| 5 | Real-world studies and modeling and cost-effectiveness studies – title/abstract, publication | (observational or longitudinal or prospective\* or retrospective\* or registry or registries).ab,ti,pt. or ('population based' or 'real world' or 'claims data' or 'claims analysis' or modeling).ab,ti. or (database\* and analysis).ab,ti. | N/A |
| **#** | **Concept – combine terms and set limits** | **Searches** | **Results** |
| 6 | Combine migraine, outcomes, and study design | 1 and 4 and 5 | 1,051 |
| 7 | Limit to the English language | limit 6 to the English language | 1,016 |
| 8 | Limit to last five years | limit 7 to last five years | 962 |
| 9 | Number to screen | Remove duplicates from MEDLINE and Embase | 682 |

**Table S9.** Most common comorbidities and financial impact for each condition

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Obesity** | **Smoking** | **Daytime Sleepiness** | **Migraine** | **Fibromyalgia** |
| Cardiovascular  | **$$$** | **$$$** |  |  |  |
| Cancer  | **$$$** | **$$$** |  |  |  |
| Stroke  | **$$$** | **$$$** |  | **$$$** |  |
| Pulmonary embolism | **$$$** | **$$$** |  |  |  |
| Kidney failure  | **$$** |  |  |  |  |
| Sleep apnea  | **$$** | **$$** | **$$** |  |  |
| Coronary artery disease | **$$** |  |  |  |  |
| Respiratory  | **$$** | **$$** | **$$** |  |  |
| Osteoarthritis | **$$** |  |  | **$$** |  |
| Pain  | **$$** |  | **$$** | **$$** | **$$** |
| Non-alcoholic fatty liver disease (NAFLD) | **$** |  |  |  |  |
| Dyslipidemia | **$** |  |  |  |  |
| Gastroesophageal reflux disease (GERD) | **$** |  |  |  |  |
| Depression | **$** | **$** | **$** | **$** |  |
| Hypertension | **$** |  |  | **$** | **$** |
| Urinary stress | **$** |  |  |  |  |
| Diabetes | **$** |  |  |  |  |
| Anxiety |  | **$** | **$** | **$** |  |
| Endometriosis  |  |  |  |  |  |
| Epilepsy |  |  |  | **$** |  |
| Irritable bowel syndrome (IBS) |  |  |  | **$** |  |
| Osteoporosis  |  |  |  | **$$** |  |

Note: $ correlates with the cost of the comorbidity relative to each other.1 $: low: moderate $$$: high

**Table S10.** Clinical outcomes and patient-reported endpoints

|  | **Obesity** (subcutaneous semaglutide 2.4 mg) | **Smoking cessation** (varenicline) | **Daytime sleepiness** (modafinil) | **Migraines** (erenumab) | **Fibromyalgia** (pregabalin) |
| --- | --- | --- | --- | --- | --- |
| **Clinical endpoints** | * Weight-loss
* Blood pressure
* Decrease in cholesterol
* Blood-sugar
 | * Angina pectoris
 | * Sleep latency
 | * Migraine events
 | * Percent of patients with improved symptoms
 |
| **Patient-reported endpoints** | * Physical functioning score
* Work and mobility score
 | * Time to relapse
* Depression
* Anxiety
 | * Maintenance of Wakefulness (7-point scale)
 | * Migraine responder days
 | * Fibromyalgia severity
* Pain visual analogue scale
 |