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

**Kim et al.**

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**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 |