**Supplemental Appendix**

Table 1: Incident definitions of rarity10

|  |  |  |
| --- | --- | --- |
| **Jurisdiction/Organization** | **Definition** | **Incidence/Prevalence threshold** |
| Health Canada | The drug is intended for the diagnosis, treatment, mitigation or prevention of a life-threatening, seriously debilitating, or serious and chronic disease or condition affecting not more than five in 10 thousand persons in Canada and; the drug is not currently authorized by the Minister or if currently authorized, it will provide a potentially substantial benefit for the patient distinguishable from the existing therapy. | Not specified |
| Ontario | Ontario’s publicly funded drug plan’s working definition of rare disease includes those with an incidence rate of fewer than one in 150,000 live births or new diagnoses per year | <1/150,000 |
| US National Cancer Institute | A rare cancer is one that occurs in fewer than 15 out of 100,000 people each year. Most types of cancer are considered rare, and they are often more difficult to prevent, diagnose, and treat than the more common cancers. Because there are fewer cases, research is difficult. Examples of rare cancers are anal, stomach, and laryngeal cancer. | <15/100,000 |
| Canadian Organization for Rare Diseases (CORD) | A rare disease is a condition affecting fewer than 1 person in 2000 in their lifetime. | <1/2000 |
| Food and Drug Administration (FDA) | A rare disease affects less than 200,000 persons in the United States, or affects more than 200,000 in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for such disease or condition will recovered from sales in the United States of such drug. Determinations under the preceding sentence with respect to any drug shall be made on the basis of the facts and circumstances as of the date the request for designation of the drug under this subsection is made. | <200,000 |
| European Union (EU) | A rare disease is one that affects fewer than 5 in 10 000 people | <5/10,000 |
| **HTA Body** | **Definition** | **Incidence/Prevalence Threshold** |
| CADTH-pCODR | Not defined | Suggested: <5/10,000 but closer to 1/100,000 |
| Institute National d’excellence en Santé et en Services Sociaux (INESSS) | Not defined | Not specified |
| National Institute for Health and Care Excellence (NICE) | A separate review process for “very rare condition” through an HST program; the process largely follows the NICE standard technology appraisal process for the review but has issued guidance on the appraisal of HST, which makes additional consideration for assessing DRDs | Not specified |
| Scottish Medicine Consortium (SMC) | Orphan medicine: Orphan status designed by EMA; i.e., conditions affecting < 2,500 per 5 million or a “medicine to treat an equivalent size of population irrespective of designated orphan status” Ultra-orphan medicine: “used to treat a condition with a prevalence of 1 in 50,000 or less (around 100 people in Scotland)”15 | Orphan status:  <2,5000/5,000,000  Ultra rare:  <1/50,000 |

Table 2: Drugs for rare indications reviewed by the pan Canadian Oncology Drug Review (pCODR)

|  |  |  |  |
| --- | --- | --- | --- |
| Datea | Drug | Disease Site | Indication |
| 18-May-12 | Sunitinib malate | GI | Patients with unresectable locally advanced or metastatic, well-differentiated pancreatic neuroendocrine tumours, whose disease is progressive |
| 17-Sep-12 | Everolimus | GI | Patients with well- or moderately differentiated neuroendocrine tumours of pancreatic origin (pNET) in patients with unresectable, locally advanced or metastatic disease. |
| 16-Sep-13 | Brentuximab vedotin | Hematology | For HL patients after failure of ASCT or after failure of at least two prior therapies in patients who are not ASCT candidates |
| 20-Dec-13 | Brentuximab vedotin | Hematology | For second-line treatment of sALCL patients - i.e. after failure of at least one prior multi-agent chemotherapy regimen |
| 27-Jan-14 | Vismodegib | Skin | For the treatment of adult patients with histologically confirmed metastatic basal cell carcinoma or with locally advanced basal cell carcinoma inappropriate for surgery or radiotherapy |
| 5-Mar-14 | Arsenic trioxide | Hematology | For patients who were refractory to or relapsed from previous treatment and newly diagnosed APL patients who have received no prior treatment |
| 8-Jul-15 | Siltuximab | Hematology | For the treatment of patients with multicentric Castleman's disease (MCD) who are human immunodeficiency virus (HIV)-negative and human herpes virus-8 (HHV-8)-negative |
| 8-Jul-15 | Adesleukin | Skin | Administered intra-lesionally, for the treatment of in-transit metastasis from melanoma in patients who have failed or are not candidates for surgery or other treatments |
| 18-Apr-16 | Blinatumomab | Hematology | For the treatment of patients with Philadelphia chromosome-negative relapsed or refractory B precursor acute lymphoblastic leukemia (ALL) |
| 17-Apr-17 | Vandetanib | Head/Neck/Thyroid | For the treatment of symptomatic and or progressive MTC in adult patients with unresectable locally advanced or metastatic disease |
| 8-Sep-17 | Blinatumomab | Hematology | For the treatment of pediatric patients with Ph- relapsed or refractory B-precursor ALL |
| 18-Sep-17 | Blinatumomab | Hematology | For the treatment of adult patients with Ph- relapsed or refractory B-precursor ALL, including those that have had one prior line of therapy |

aDate refers to the date which the drug received a notice to implement from pCODR.