

Appendix 1 (as supplied by author)

Process for exclusion of drugs with exclusive adult uses

In order to include only drugs that are relevant to pediatrics in this study, we completed a careful review of pediatric relevancy of all the drugs that were newly approved over the period of our study. Pediatric relevancy was determined by reviewing therapeutic indications for non-oncology drugs, and molecular targets for oncology drugs. We reviewed oncology drugs by their molecular target, because although adult oncology diseases are mostly dissimilar to any pediatric cancer, their targeted agents can be applicable to cancers in children as described by the United States FDA.²⁰

We reviewed all non-oncology drugs approved through the period of our study by their individual indications (Supplement 1). We observed that 99% (140 of 142) of non-oncology drugs with only adult indications were approved for conditions that potentially overlap with therapeutic uses in children. Even for the conditions that conventionally are thought of as diseases of adults, we found evidence for their early-onset form as diseases of childhood. After review of the individual indications, we excluded two non-oncology drugs indicated for adult specific conditions: bazedoxifene/conjugated estrogens for treatment of moderate to severe vasomotor symptoms associated with menopause, and rivastigmine for symptomatic treatment of patients with mild to moderately severe dementia of the Alzheimer's type.

We reviewed all the oncology drugs for their molecular target (Supplement 2). From 57 oncology drugs approved during the period of study only for adults, we

observed 54 had molecular targets that were listed as candidate pediatric molecular targets by the FDA²⁰ and deemed substantially relevant to the growth or progression of a pediatric cancer. We therefore excluded the three oncology drugs which had non-pediatric relevant molecular targets: degarelix (GnRH receptor antagonist), abiraterone (androgen biosynthesis inhibitor) and enzalutamide (androgen receptor signaling inhibitor).