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Overlapping and non-overlapping indications for checkpoint inhibitors in the US.

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Background: Since the first checkpoint inhibitor was approved in 2014, this class of cancer drug has revolutionized the treatment of several malignancies. As of January 2024, 11 checkpoint inhibitors have been approved by the US Food and Drug Administration (FDA), each with its own particular indications. We assessed the overlap of approved indications, which has implications for competition and price negotiation by payers. **Methods:** In this cross-sectional study, we evaluated the FDA-approved indications for 11 checkpoint inhibitors as of January 2024. Indications were defined by cancer tissue type (or mutation status for non-tumor-type indications), stage, and line of treatment (first-line, second-line, third-line, or fourth-or-greater-line). Non-overlapping indications were defined as those with only a single drug approved; for overlapping indications, we tabulated the number of approved drugs. **Results:** The 11 FDA-approved checkpoint inhibitors were associated with 43 distinct indications, ranging from 2 (retifanlimab, toripalimab, and tremelimumab) to 35 (pembrolizumab) indications per drug. Fifteen (43%) indications were non-overlapping. Pembrolizumab had 11 non-overlapping indications (e.g., certain breast, cervical, and urothelial cancers); all other drugs had between 0 and 2 non-overlapping indications (Table). Among the 28 overlapping indications, 15 (54%) had approvals for 2 drugs, 9 (32%) had approvals for 3 drugs, 3 (11%) had approvals for 4 drugs, and 1 (3%; non-small cell lung cancer) had approvals for 7 of the 11 drugs. **Conclusions:** Checkpoint inhibitors are FDA-approved for a total of 43 different indications, but most indications were included on the labeling of 3 or fewer drugs in this class. Over 1 in 3 indications had only 1 approved drug, most commonly pembrolizumab. This limited overlap of indications suggests that manufacturers may avoid seeking approval for indications that already have multiple approved drugs of the same class, which may decrease competition and lead to sustained high drug prices. To provide patients with better information about the checkpoint inhibitor most appropriate for their cancer, the NIH could fund, and the FDA could encourage, more direct comparative effectiveness trials. Research Sponsor: None.

Checkpoint Inhibitor	Date of First FDA Approval	# of Total Indications	# of Mon-overlapping Indications	# of Indications Overlapping with >3 Other Drugs
Ipilimumab (Yervoy)	Mar 2011	8	0	4
Pembrolizumab (Keytruda)	Sep 2014	35	11	4
Nivolumab (Opdivo)	Dec 2014	18	2	4
Atezolizumab (Tecentriq)	May 2016	7	1	2
Avelumab (Bavencio)	Mar 2017	4	0	1
Durvalumab (Imfinzi)	May 2017	5	0	1
Cemiplimab (Libtayo)	Sep 2018	4	1	1
Tremelimumab (Imjudo)	Oct 2022	2	0	1
Retifanlimab (Zynyz)	Mar 2023	2	0	0
Dostarlimab (Jemperli)	Jul 2023	4	0	1
Toripalimab (Loqtorzi)	Oct 2023	2	0	0

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