Appendix. Medications for the Treatment of Non–Small Cell Lung Cancer

Generic (Brand)	Mechanism of action	Toxicities	Place in therapy		Comments
			ASCO Guidelines	NCCN Guidelines	
Cytotoxic chemotherapy					
Antimetabolites					
Gemcitabine (Gemzar)	Gemcitabine is metabolized to diphosphate (dFdCDP) and triphosphate (dFdCTP) nucleotides. dFdCTP competes with dCTP for incorporation into DNA. dFdCDP inhibits ribonucleotide reductase resulting in reductions of dCTP allowing for incorporation of dFdCTP into DNA (self-potentiation).	Myelosuppression, N/V, flu-like syndrome, rash, hepatic transaminitis, pulmonary toxicity	First-line for SCC (in combination)	• Neoadjuvant or adjuvant therapy (in combination) • First-line for SCC and NSCC: PS 0–1 combination therapy; PS 2 combination or monotherapy • Continuation maintenance or subsequent therapy for SCC and NSCC	• Superior efficacy for cisplatin/gemcitabine in squamous histology compared with cisplatin/pemetrexed • Increased toxicity with infusion time > 60 minutes

Note. ASCO = American Society of Clinical Oncology; dFdCDP = gemcitabine diphosphate; dFdCTP = gemcitabine triphosphate; dCTP = deoxycytidine triphosphate; N/V = nausea/vomiting; SCC = squamous cell carcinoma; NSCC = nonsquamous cell carcinoma; PS = performance status; NSAIDs = non-steroidal anti-inflammatory drugs; CrCl = creatinine clearance; RT = radiation therapy; KRAS = Kirsten rat sarcoma viral oncogene; IV = intravenous; ALK = anaplastic lymphoma kinase; RET = rearranged during transfection; IGF-1R = insulin-like growth factor 1 receptor; ILD = interstitial lung disease; GI = gastrointestinal; NSCLC = non–small cell lung cancer; BRAF = v-Raf murine sarcoma viral oncogene homolog B; HFSR = hand-foot skin reaction; EGFR = epidermal growth factor receptor; HER = human epidermal growth factor receptor; TKI = tyrosine kinase inhibitor; P-gp = p-glycoprotein; MAPK = mitogen-activated protein kinase; VEGFR = vascular endothelial growth factor receptor; REMS = risk evaluation and mitigation strategy; mAb = monoclonal antibody; IgG1 = immunoglobulin G 1; FDA = Food and Drug Administration; PD-1 = programmed cell death protein 1; PD-L1 = programmed cell death ligand 1; irAEs = immune-related adverse events; TPS = tumor proportion score. Information from Masters et al. (2015); Bezjak et al. (2015); NCCN (2017); Pisters et al. (2007).

[a]Agents that are not FDA-approved for NSCLC but are included in the guidelines.

Compiled by Lisa Cordes, PharmD, BCACP, BCOP
From National Institutes of Health, Bethesda, Maryland
Author's disclosures of potential conflicts of interest are found at the end of this article.
Correspondence to: Lisa Cordes, PharmD, BCACP, BCOP, National Institutes of Health, 10 Center Drive, Room 1C240, Bethesda, MD 20892. E-mail: lisa.cordes@nih.gov
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Appendix. Medications for the Treatment of Non–Small Cell Lung Cancer

Generic (Brand)	Mechanism of action	Toxicities	Place in therapy: ASCO Guidelines	Place in therapy: NCCN Guidelines	Comments
Antimetabolites (cont.)					
Pemetrexed (Alimta)	Inhibits multiple folate-dependent enzymes involved in biosynthesis of thymidine and purine nucleotides	Myelosuppression, stomatitis, rash, N/V, fatigue	• First-line for NSCC (in combination) • Continuation/switch maintenance or second-line for NSCC	• Neoadjuvant or adjuvant therapy in NSCC (in combination) • First-line for NSCC: PS 0–1 combination therapy; PS 2 combination or monotherapy • Continuation/switch maintenance or subsequent therapy for NSCC • Concurrent chemo/RT for NSCC (in combination)	• NOT indicated for SCC • Superior efficacy and reduced toxicity for cisplatin/pemetrexed in nonsquamous histology compared with cisplatin/gemcitabine • Use caution with NSAIDs and mild to moderate renal insufficiency (CrCl 45-79 mL/min) • Folic acid and vitamin B12 must be administered to decrease the risk of severe myelosuppression • Premedicate with dexamethasone to decrease cutaneous reactions

Note. ASCO = American Society of Clinical Oncology; dFdCDP = gemcitabine diphosphate; dFdCTP = gemcitabine triphosphate; dCTP = deoxycytidine triphosphate; N/V = nausea/vomiting; SCC = squamous cell carcinoma; NSCC = nonsquamous cell carcinoma; PS = performance status; NSAIDs = non-steroidal anti-inflammatory drugs; CrCl = creatinine clearance; RT = radiation therapy; KRAS = Kirsten rat sarcoma viral oncogene; IV = intravenous; ALK = anaplastic lymphoma kinase; RET = rearranged during transfection; IGF-1R = insulin-like growth factor 1 receptor; ILD = interstitial lung disease; GI = gastrointestinal; NSCLC = non–small cell lung cancer; BRAF = v-Raf murine sarcoma viral oncogene homolog B; HFSR = hand-foot skin reaction; EGFR = epidermal growth factor receptor; HER = human epidermal growth factor receptor; TKI = tyrosine kinase inhibitor; P-gp = p-glycoprotein; MAPK = mitogen-activated protein kinase; VEGFR = vascular endothelial growth factor receptor; REMS = risk evaluation and mitigation strategy; mAb = monoclonal antibody; IgG1 = immunoglobulin G 1; FDA = Food and Drug Administration; PD-1 = programmed cell death protein 1; PD-L1 = programmed cell death ligand 1; irAEs = immune-related adverse events; TPS = tumor proportion score. Information from Masters et al. (2015); Bezjak et al. (2015); NCCN (2017); Pisters et al. (2007).

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Appendix. Medications for the Treatment of Non–Small Cell Lung Cancer

Generic (Brand)	Mechanism of action	Toxicities	Place in therapy		Comments
			ASCO Guidelines	NCCN Guidelines	
Microtubule-targeting agents					
Docetaxel (Taxotere)	Binds to free tubulin and promotes assembly of microtubules while simultaneously inhibiting their disassembly	Myelosuppression, fluid retention, alopecia, peripheral neuropathy, rash, hypersensitivity reaction	• First-line for SCC and NSCC (in combination) • Second-line for SCC and NSCC • Maintenance for SCC and NSCC	• Neoadjuvant or adjuvant therapy (in combination) • First-line for SCC and NSCC: PS 0–1 combination therapy; PS 2 combination or monotherapy • Subsequent therapy for SCC and NSCC • Switch maintenance for SCC	• Avoid use with hepatic impairment • Premedicate with dexamethasone
Paclitaxel-conventional (Taxol is a synonym)	Promotes assembly of microtubules, stabilizes existing microtubules by preventing depolymerization	Myelosuppression, hypersensitivity reaction, peripheral neuropathy, alopecia, mucositis	• First-line for SCC and NSCC (in combination) • Option for concurrent chemo/RT therapy (in combination with carboplatin)	• Neoadjuvant or adjuvant therapy (in combination) for cisplatin-ineligible patients • First-line for SCC and NSCC: PS 0–1 combination therapy; PS 2 combination or monotherapy • Concurrent or sequential chemo/RT therapy (in combination)	• Premedicate with dexamethasone, diphenhydramine, and an H2 antagonist

Note. ASCO = American Society of Clinical Oncology; dFdCDP = gemcitabine diphosphate; dFdCTP = gemcitabine triphosphate; dCTP = deoxycytidine triphosphate; N/V = nausea/vomiting; SCC = squamous cell carcinoma; NSCC = nonsquamous cell carcinoma; PS = performance status; NSAIDs = non-steroidal anti-inflammatory drugs; CrCl = creatinine clearance; RT = radiation therapy; KRAS = Kirsten rat sarcoma viral oncogene; IV = intravenous; ALK = anaplastic lymphoma kinase; RET = rearranged during transfection; IGF-1R = insulin-like growth factor 1 receptor; ILD = interstitial lung disease; GI = gastrointestinal; NSCLC = non–small cell lung cancer; BRAF = v-Raf murine sarcoma viral oncogene homolog B; HFSR = hand-foot skin reaction; EGFR = epidermal growth factor receptor; HER = human epidermal growth factor receptor; TKI = tyrosine kinase inhibitor; P-gp = p-glycoprotein; MAPK = mitogen-activated protein kinase; VEGFR = vascular endothelial growth factor receptor; REMS = risk evaluation and mitigation strategy; mAb = monoclonal antibody; IgG1 = immunoglobulin G 1; FDA = Food and Drug Administration; PD-1 = programmed cell death protein 1; PD-L1 = programmed cell death ligand 1; irAEs = immune-related adverse events; TPS = tumor proportion score. Information from Masters et al. (2015); Bezjak et al. (2015); NCCN (2017); Pisters et al. (2007).

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Appendix. Medications for the Treatment of Non–Small Cell Lung Cancer

Generic (Brand)	Mechanism of action	Toxicities	Place in therapy		Comments
			ASCO Guidelines	NCCN Guidelines	
Microtubule-targeting agents (cont.)					
Nab-paclitaxel (Abraxane)	Albumin-bound paclitaxel nanoparticle; promotes assembly of microtubules, stabilizes existing microtubules by preventing depolymerization	Myelosuppression, peripheral neuropathy, alopecia, mucositis	First-line SCC (in combination)	First-line for SCC and NSCC: PS 0–1 combination therapy; PS 2 combination or monotherapy	• May be substituted for paclitaxel or docetaxel for patients who experience hypersensitivity reactions or who have contraindication to premedications • Associated with lower risk of hypersensitivity reactions compared with conventional paclitaxel
Vinblastine[a]	Binds tubulin and inhibits microtubule formation	Myelosuppression, mucositis, neurotoxicity, constipation, alopecia	Not included in the guidelines	Concurrent or sequential chemo/RT therapy (in combination)	• Vesicant • For IV use only (fatal if given by other routes)
Vinorelbine (Navelbine)	Binds tubulin and inhibits microtubule formation	Myelosuppression, mucositis, neurotoxicity, constipation, alopecia	• Adjuvant therapy (in combination with cisplatin) • First-line for SCC and NSCC (in combination)	• Neoadjuvant or adjuvant therapy (in combination) • First-line for SCC and NSCC (in combination)	• *KRAS* mutations predict a lack of benefit from platinum/vinorelbine chemotherapy • Vesicant • For IV use only (fatal if given intrathecally)

Note. ASCO = American Society of Clinical Oncology; dFdCDP = gemcitabine diphosphate; dFdCTP = gemcitabine triphosphate; dCTP = deoxycytidine triphosphate; N/V = nausea/vomiting; SCC = squamous cell carcinoma; NSCC = nonsquamous cell carcinoma; PS = performance status; NSAIDs = non-steroidal anti-inflammatory drugs; CrCl = creatinine clearance; RT = radiation therapy; KRAS = Kirsten rat sarcoma viral oncogene; IV = intravenous; ALK = anaplastic lymphoma kinase; RET = rearranged during transfection; IGF-1R = insulin-like growth factor 1 receptor; ILD = interstitial lung disease; GI = gastrointestinal; NSCLC = non–small cell lung cancer; BRAF = v-Raf murine sarcoma viral oncogene homolog B; HFSR = hand-foot skin reaction; EGFR = epidermal growth factor receptor; HER = human epidermal growth factor receptor; TKI = tyrosine kinase inhibitor; P-gp = p-glycoprotein; MAPK = mitogen-activated protein kinase; VEGFR = vascular endothelial growth factor receptor; REMS = risk evaluation and mitigation strategy; mAb = monoclonal antibody; IgG1 = immunoglobulin G 1; FDA = Food and Drug Administration; PD-1 = programmed cell death protein 1; PD-L1 = programmed cell death ligand 1; irAEs = immune-related adverse events; TPS = tumor proportion score. Information from Masters et al. (2015); Bezjak et al. (2015); NCCN (2017); Pisters et al. (2007).
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Appendix. Medications for the Treatment of Non–Small Cell Lung Cancer

Generic (Brand)	Mechanism of action	Toxicities	Place in therapy		Comments
			ASCO Guidelines	NCCN Guidelines	
Topoisomerase inhibitor					
Etoposide[a] (Toposar)	Topoisomerase II inhibitor resulting in DNA strand breaks	Myelosuppression, N/V, alopecia, mucositis, infusion-related hypotension	• Option for large cell neuroendocrine carcinoma (in combination with platinum) • Option for concurrent chemo/RT therapy (in combination with cisplatin)	• Neoadjuvant or adjuvant therapy (in combination) • First-line for SCC and NSCC (in combination) • Concurrent chemo/RT therapy (in combination)	Etoposide phosphate (Etopophos) is a prodrug of etoposide formulated without polysorbate 80. Equivalent doses should be used when converting etoposide to etoposide phosphate.
Alkylating agents					
Carboplatin[a] (Paraplatin is a synonym)	Covalently binds to DNA; produces interstrand DNA cross-links	Myelosuppression (primarily thrombocytopenia), hypersensitivity reactions at higher cumulative doses, N/V	• First-line for SCC and NSCC (in combination) • Option for concurrent chemo/RT therapy (in combination with paclitaxel)	• Neoadjuvant or adjuvant therapy (in combination) for cisplatin-ineligible patients • First-line for SCC and NSCC (in combination) • Concurrent or sequential chemo/RT therapy (in combination)	Calvert formula most commonly used for dosing
Cisplatin[a]	Covalently binds to DNA bases, disrupting DNA function; binds two adjacent guanines on the same DNA strand producing intrastrand cross-links	Nephrotoxicity, electrolyte wasting, severe N/V, neuropathy, ototoxicity	• Adjuvant therapy (in combination) • First-line for SCC and NSCC (in combination) • Option for concurrent chemo/RT therapy (in combination with etoposide)	• Neoadjuvant or adjuvant therapy (in combination) • First-line for SCC and NSCC (in combination), PS 0–1 • Concurrent or sequential chemo/RT therapy (in combination)	• Avoid or adjust dose in renal impairment • Aggressive hydration and antiemetics required • Verify doses exceeding 100 mg/m^2 per cycle to avoid inadvertent dosing errors

Note. ASCO = American Society of Clinical Oncology; dFdCDP = gemcitabine diphosphate; dFdCTP = gemcitabine triphosphate; dCTP = deoxycytidine triphosphate; N/V = nausea/vomiting; SCC = squamous cell carcinoma; NSCC = nonsquamous cell carcinoma; PS = performance status; NSAIDs = non-steroidal anti-inflammatory drugs; CrCl = creatinine clearance; RT = radiation therapy; KRAS = Kirsten rat sarcoma viral oncogene; IV = intravenous; ALK = anaplastic lymphoma kinase; RET = rearranged during transfection; IGF-1R = insulin-like growth factor 1 receptor; ILD = interstitial lung disease; GI = gastrointestinal; NSCLC = non–small cell lung cancer; BRAF = v-Raf murine sarcoma viral oncogene homolog B; HFSR = hand-foot skin reaction; EGFR = epidermal growth factor receptor; HER = human epidermal growth factor receptor; TKI = tyrosine kinase inhibitor; P-gp = p-glycoprotein; MAPK = mitogen-activated protein kinase; VEGFR = vascular endothelial growth factor receptor; REMS = risk evaluation and mitigation strategy; mAb = monoclonal antibody; IgG1 = immunoglobulin G 1; FDA = Food and Drug Administration; PD-1 = programmed cell death protein 1; PD-L1 = programmed cell death ligand 1; irAEs = immune-related adverse events; TPS = tumor proportion score. Information from Masters et al. (2015); Bezjak et al. (2015); NCCN (2017); Pisters et al. (2007).

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Appendix. Medications for the Treatment of Non–Small Cell Lung Cancer

Generic (Brand)	Mechanism of action	Toxicities	Place in therapy		Comments
			ASCO Guidelines	NCCN Guidelines	
Targeted therapy (small molecule)					
ALK inhibitors					
Alectinib (Alecensa)	Tyrosine kinase inhibitor targeting ALK and RET	Fatigue, bradycardia, hepatotoxicity, constipation, edema, myalgias, ILD/ pneumonitis	Not included in the guidelines	*ALK*-positive NSCLC following progression on or intolerance to crizotinib	• Demonstrated activity in *ALK*-positive tumors resistant to crizotinib • Administer with food • CYP3A4 and CYP2C9 drug interactions • Available through specialty pharmacies and distributors
Brigatinib (Alunbrig)	Tyrosine kinase inhibitor targeting ALK, ROS1, IGF-1R, FLT-3	Nausea, diarrhea, fatigue, cough, headache, ILD/ pneumonitis, hypertension, bradycardia, visual disturbances, pancreatic enzyme elevation, creatine phosphokinase elevation, hyperglycemia			
Ceritinib (Zykadia)	Tyrosine kinase inhibitor targeting ALK, IGF-1R, InsR, ROS1	GI toxicity, fatigue, QT prolongation, hepatotoxicity, pancreatitis, ILD/ pneumonitis, bradycardia, hyperglycemia	Second-line for *ALK*-positive NSCLC after crizotinib	*ALK*-positive NSCLC following progression on or intolerance to crizotinib	• Demonstrated activity in *ALK*-positive tumors resistant to crizotinib • Administer on an empty stomach • CYP3A4 and CYP2C9 drug interactions

Note. ASCO = American Society of Clinical Oncology; dFdCDP = gemcitabine diphosphate; dFdCTP = gemcitabine triphosphate; dCTP = deoxycytidine triphosphate; N/V = nausea/vomiting; SCC = squamous cell carcinoma; NSCC = nonsquamous cell carcinoma; PS = performance status; NSAIDs = non-steroidal anti-inflammatory drugs; CrCl = creatinine clearance; RT = radiation therapy; KRAS = Kirsten rat sarcoma viral oncogene; IV = intravenous; ALK = anaplastic lymphoma kinase; RET = rearranged during transfection; IGF-1R = insulin-like growth factor 1 receptor; ILD = interstitial lung disease; GI = gastrointestinal; NSCLC = non–small cell lung cancer; BRAF = v-Raf murine sarcoma viral oncogene homolog B; HFSR = hand-foot skin reaction; EGFR = epidermal growth factor receptor; HER = human epidermal growth factor receptor; TKI = tyrosine kinase inhibitor; P-gp = p-glycoprotein; MAPK = mitogen-activated protein kinase; VEGFR = vascular endothelial growth factor receptor; REMS = risk evaluation and mitigation strategy; mAb = monoclonal antibody; IgG1 = immunoglobulin G 1; FDA = Food and Drug Administration; PD-1 = programmed cell death protein 1; PD-L1 = programmed cell death ligand 1; irAEs = immune-related adverse events; TPS = tumor proportion score. Information from Masters et al. (2015); Bezjak et al. (2015); NCCN (2017); Pisters et al. (2007).

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Appendix. Medications for the Treatment of Non–Small Cell Lung Cancer

Generic (Brand)	Mechanism of action	Toxicities	Place in therapy		Comments
			ASCO Guidelines	NCCN Guidelines	
ALK inhibitors (cont.)					
Crizotinib (Xalkori)	Tyrosine kinase inhibitor targeting ALK, HGFR, c-MET, ROS1, RON	N/V, diarrhea, fatigue, visual disturbances edema, QT prolongation; bradycardia, dizziness, neuropathy, hepatotoxicity, ILD/pneumonitis	• First-line for *ALK*-positive NSCLC • First-line for *ROS*-positive NSCLC	• First-line for *ALK*-positive NSCLC • First-line for *ROS*-positive NSCLC • Data to support use in high level MET amplification or MET exon 14 skipping mutation	• CYP3A4 drug interactions • Available through specialty pharmacies
BRAF inhibitors					
Dabrafenib[a] (Tafinlar)	Inhibits mutated forms of BRAF kinases, including *BRAF* V600E	Papilloma, arthralgia, fatigue, headache, HFSR, pyrexia, rash, cardiomyopathy, hyperglycemia, new primary malignancies	Not included in the guidelines	Data to support use in *BRAF* V600E mutations (with or without trametinib)	• Administer on an empty stomach • CYP3A4 and CYP2C8 interactions
Vemurafenib[a] (Zelboraf)	Inhibits mutated forms of BRAF kinases, including *BRAF* V600E	Arthralgia, fatigue, QT prolongation, dermatologic toxicity, hepatotoxicities, renal impairment, new primary malignancies	Not included in the guidelines	Data to support use in *BRAF* V600E mutations	• Advise patients to avoid sun exposure • CYP3A4 and CYP1A2 interactions • Available through specialty pharmacies

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Generic (Brand)	Mechanism of action	Toxicities	Place in therapy		Comments
			ASCO Guidelines	NCCN Guidelines	
EGFR pathway inhibitors					
Afatinib (Gilotrif)	Covalently binds to the kinase domains of EGFR (ErbB1), HER2 (ErbB2), and HER4 (ErbB4)	Diarrhea, dermatologic toxicity, N/V, ILD, hepatotoxicity	First-line for *EGFR*-positive NSCLC	• First-line for *EGFR*-positive NSCLC • May be considered in combination with cetuximab after progression on an EGFR TKI in *EGFR*-positive NSCLC • Data to support use in *HER2* mutations	• Administer on an empty stomach • P-gp inhibitor interaction
Erlotinib (Tarceva)	Reversibly inhibits the kinase activity of EGFR; higher affinity for EGFR exon 19 deletion or exon 21 (L858R) mutations than for wild type	Rash, diarrhea, anorexia, fatigue, N/V, renal impairment, hepatotoxicity, ocular disorders	• First-line for *EGFR*-positive NSCLC • Second-line for SCC and NSCC • Third-line for SCC and NSCC	First-line for *EGFR*-positive NSCLC	• Administer on an empty stomach • If clinically appropriate, supportive care should be attempted before a dose reduction to manage erlotinib-related rash • CYP3A4 and CYP1A2 interaction • Consider dose adjustment for concurrent cigarette smoking • Drugs that increase gastric pH decrease erlotinib concentrations

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Appendix. Medications for the Treatment of Non–Small Cell Lung Cancer

Generic (Brand)	Mechanism of action	Toxicities	Place in therapy		Comments
			ASCO Guidelines	NCCN Guidelines	
EGFR pathway inhibitors (cont.)					
Gefitinib (Iressa)	Reversibly inhibits the kinase activity of EGFR; higher affinity for EGFR exon 19 deletion or exon 21 (L858R) mutations than for wild type	Dermatologic toxicity, diarrhea, ILD, hepatotoxicity, ocular disorders	• First-line for *EGFR*-positive NSCLC • Second-line for SCC and NSCC	First-line for *EGFR*-positive NSCLC	• CYP3A4 interactions • Avoid drugs affecting gastric pH
Osimertinib (Tagrisso)	Irreversible inhibitor of EGFR, specifically T790M, L858R, and exon 19 deletion	Dermatologic toxicity, QT prolongation, ILD, diarrhea, cardiomyopathy	Not included in the guidelines	Subsequent therapy (following progression on EGFR TKI therapy) if T790M-positive	• Confirm T790M-mutation status prior to treatment initiation • CYP3A4 interactions • Available through specialty pharmacies and distributors
MEK inhibitor					
Trametinib[a] (Mekinist)	Reversibly inhibits MEK1 and 2	Diarrhea, dermatologic toxicity, ocular toxicity, lymphedema, thromboembolism, hyperglycemia	Not included in the guidelines	Data to support use in combination with dabrafenib for *BRAF* V600E mutations	• Use of trametinib and dabrafenib in combination allows for greater inhibition of the MAPK pathway • Administer on an empty stomach • Store capsules in refrigerator

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Generic (Brand)	Mechanism of action	Toxicities	Place in therapy		Comments
			ASCO Guidelines	NCCN Guidelines	
Multikinase inhibitors					
Cabozantinib[a] (Cabometyx)	Inhibits tyrosine kinase activity of multiple kinases including VEGFR, MET, ROS1, RET, TYRO3, MER, KIT, TRKB, FLT-3, and TIE-3	Diarrhea, HFSR, hair/skin hypopigmentation, fatigue, N/V, decreased weight/appetite, hypertension, GI perforations, hemorrhage, thromboembolism	Not included in the guidelines	Data to support use in *RET* rearrangements	• Administer on an empty stomach • CYP3A4 interactions • Available through specialty pharmacies
Vandetanib[a] (Caprelsa)	Inhibits tyrosine kinase activity of multiple kinases including EGFR, VEGFR, RET, BRK, and TIE2	Diarrhea, hypertension, N/V, headache, dermatologic toxicity, ILD, QT prolongation, and torsades de pointes	Not included in the guidelines	Data to support use in *RET* rearrangements	• Prescribers and pharmacies must be certified with the REMS program to prescribe or dispense • CYP3A4 interactions • Avoid concurrent use of QT-prolonging agents
Targeted therapy (monoclonal antibodies)					
EGFR inhibitors					
Cetuximab[a] (Erbitux)	Recombinant chimeric IgG1 mAb; binds to EGFR and competitively inhibits EGF and other ligands	Infusion reactions, dermatologic toxicity, headache, diarrhea, hypomagnesemia, cardiopulmonary arrest	Not included in the guidelines	May be considered in combination with afatinib after progression on an EGFR TKI in *EGFR*-positive NSCLC	• If clinically appropriate, supportive care should be attempted before a dose reduction to manage cetuximab-related rash • Premedicate with H1 antagonist

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Appendix. Medications for the Treatment of Non–Small Cell Lung Cancer

Generic (Brand)	Mechanism of action	Toxicities	Place in therapy		Comments
			ASCO Guidelines	NCCN Guidelines	
EGFR inhibitors (cont.)					
Necitumumab (Portrazza)	Recombinant human IgG1 mAb; binds to EGFR	Infusion reactions, dermatologic toxicity, thromboembolism, cardiopulmonary arrest, hypomagnesemia	Not included in the guidelines	FDA approved for metastatic squamous NSCLC in combo with cisplatin/gemcitabine but removed from the NCCN guidelines due to toxicity, cost, and limited improvement in efficacy when compared with cisplatin/ gemcitabine	Increased toxicity and mortality in nonsquamous NSCLC
HER2 inhibitors					
Trastuzumab (Herceptin)	Humanized IgG1 kappa mAb; binds to extracellular domain of HER2	Infusion reactions, cardiomyopathy, headache, chills, exacerbation of chemo-induced neutropenia	Not included in the guidelines	Data to support use in *HER2* mutations	• Avoid concurrent administration with anthracyclines because of cardiotoxicity • Do NOT substitute trastuzumab for or with ado-trastuzumab emtansine

Note. ASCO = American Society of Clinical Oncology; dFdCDP = gemcitabine diphosphate; dFdCTP = gemcitabine triphosphate; dCTP = deoxycytidine triphosphate; N/V = nausea/vomiting; SCC = squamous cell carcinoma; NSCC = nonsquamous cell carcinoma; PS = performance status; NSAIDs = non-steroidal anti-inflammatory drugs; CrCl = creatinine clearance; RT = radiation therapy; KRAS = Kirsten rat sarcoma viral oncogene; IV = intravenous; ALK = anaplastic lymphoma kinase; RET = rearranged during transfection; IGF-1R = insulin-like growth factor 1 receptor; ILD = interstitial lung disease; GI = gastrointestinal; NSCLC = non–small cell lung cancer; BRAF = v-Raf murine sarcoma viral oncogene homolog B; HFSR = hand-foot skin reaction; EGFR = epidermal growth factor receptor; HER = human epidermal growth factor receptor; TKI = tyrosine kinase inhibitor; P-gp = p-glycoprotein; MAPK = mitogen-activated protein kinase; VEGFR = vascular endothelial growth factor receptor; REMS = risk evaluation and mitigation strategy; mAb = monoclonal antibody; IgG1 = immunoglobulin G 1; FDA = Food and Drug Administration; PD-1 = programmed cell death protein 1; PD-L1 = programmed cell death ligand 1; irAEs = immune-related adverse events; TPS = tumor proportion score. Information from Masters et al. (2015); Bezjak et al. (2015); NCCN (2017); Pisters et al. (2007).

[a]Agents that are not FDA-approved for NSCLC but are included in the guidelines.

Appendix. Medications for the Treatment of Non–Small Cell Lung Cancer

Generic (Brand)	Mechanism of action	Toxicities	Place in therapy		Comments
			ASCO Guidelines	NCCN Guidelines	
VEGF inhibitors					
Bevacizumab (Avastin)	Recombinant humanized IgG1 mAb; binds VEGF preventing its association with receptors	GI perforation, impaired wound healing, hypertension, proteinuria, hemorrhage, thromboembolism, infusion reactions	Addition of bevacizumab to carboplatin/paclitaxel in NSCC in patients with PS 0–1 and no contraindication to therapy	• First-line for NSCC (in combination), PS 0–1 • Continuation maintenance for NSCC	• Not recommended for squamous cell NSCLC or with recent history of hemoptysis • Discontinue at least 28 days prior to elective surgery and do not resume for at least 28 days after surgery and until the surgical wound is fully healed
Ramucirumab (Cyramza)	Recombinant human IgG1 mAb; binds VEGFR2 blocking binding of VEGFR ligands	GI perforation, impaired wound healing, diarrhea, hypertension, infusion reactions, proteinuria, hemorrhage, thromboembolic events, thyroid dysfunction	Not included in the guidelines	Subsequent therapy for SCC and NSCC (in combination with docetaxel)	• Hold prior to surgery
Immunotherapy (monoclonal antibodies)					
PD-1 inhibitors					
Nivolumab (Opdivo)	Human IgG4 mAb; binds to PD-1 receptor blocking the binding of PD-L1 and PD-L2, which releases the PD-1 pathway–mediated inhibition of the immune response	Fatigue, rash, irAEs, musculoskeletal pain, arthralgia, pyrexia, diarrhea	The ASCO Update Committee awaits additional data on adverse events before full incorporation into the guidelines	Subsequent therapy for SCC and NSCC	Treat irAEs with corticosteroids

Note. ASCO = American Society of Clinical Oncology; dFdCDP = gemcitabine diphosphate; dFdCTP = gemcitabine triphosphate; dCTP = deoxycytidine triphosphate; N/V = nausea/vomiting; SCC = squamous cell carcinoma; NSCC = nonsquamous cell carcinoma; PS = performance status; NSAIDs = non-steroidal anti-inflammatory drugs; CrCl = creatinine clearance; RT = radiation therapy; KRAS = Kirsten rat sarcoma viral oncogene; IV = intravenous; ALK = anaplastic lymphoma kinase; RET = rearranged during transfection; IGF-1R = insulin-like growth factor 1 receptor; ILD = interstitial lung disease; GI = gastrointestinal; NSCLC = non–small cell lung cancer; BRAF = v-Raf murine sarcoma viral oncogene homolog B; HFSR = hand-foot skin reaction; EGFR = epidermal growth factor receptor; HER = human epidermal growth factor receptor; TKI = tyrosine kinase inhibitor; P-gp = p-glycoprotein; MAPK = mitogen-activated protein kinase; VEGFR = vascular endothelial growth factor receptor; REMS = risk evaluation and mitigation strategy; mAb = monoclonal antibody; IgG1 = immunoglobulin G 1; FDA = Food and Drug Administration; PD-1 = programmed cell death protein 1; PD-L1 = programmed cell death ligand 1; irAEs = immune-related adverse events; TPS = tumor proportion score. Information from Masters et al. (2015); Bezjak et al. (2015); NCCN (2017); Pisters et al. (2007).

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Appendix. Medications for the Treatment of Non–Small Cell Lung Cancer

Generic (Brand)	Mechanism of action	Toxicities	Place in therapy		Comments
			ASCO Guidelines	NCCN Guidelines	
PD-1 inhibitors (cont.)					
Pembrolizumab (Keytruda)	Humanized IgG4 kappa mAb; binds to PD-1 receptor blocking the binding of PD-L1 and PD-L2, which releases the PD-1 pathway–mediated inhibition of the immune response	Fatigue, rash, irAEs, nausea, diarrhea	Not included in the guidelines	• First-line for PD-L1 expression positive (≥ 50%) and *EGFR*, *ALK*, *ROS1* negative or unknown • Subsequent therapy for SCC and NSCC with PD-L1 expression ≥ 1%	• Treat irAEs with corticosteroids • Per FDA labeling » TPS ≥ 50% for first-line therapy » TPS ≥ 1% for subsequent therapy
PD-L1 inhibitor					
Atezolizumab (Tecentriq)	Humanized IgG1 kappa mAb; binds to PD-L1 and blocks its interaction with PD-1 and B7.1 receptors, which releases the PD-L1/PD-1–mediated inhibition of the immune response	Fatigue, rash, irAEs, pyrexia, nausea	Not included in the guidelines	Subsequent therapy for SCC and NSCC	Treat irAEs with corticosteroids

Note. ASCO = American Society of Clinical Oncology; dFdCDP = gemcitabine diphosphate; dFdCTP = gemcitabine triphosphate; dCTP = deoxycytidine triphosphate; N/V = nausea/vomiting; SCC = squamous cell carcinoma; NSCC = nonsquamous cell carcinoma; PS = performance status; NSAIDs = non-steroidal anti-inflammatory drugs; CrCl = creatinine clearance; RT = radiation therapy; KRAS = Kirsten rat sarcoma viral oncogene; IV = intravenous; ALK = anaplastic lymphoma kinase; RET = rearranged during transfection; IGF-1R = insulin-like growth factor 1 receptor; ILD = interstitial lung disease; GI = gastrointestinal; NSCLC = non–small cell lung cancer; BRAF = v-Raf murine sarcoma viral oncogene homolog B; HFSR = hand-foot skin reaction; EGFR = epidermal growth factor receptor; HER = human epidermal growth factor receptor; TKI = tyrosine kinase inhibitor; P-gp = p-glycoprotein; MAPK = mitogen-activated protein kinase; VEGFR = vascular endothelial growth factor receptor; REMS = risk evaluation and mitigation strategy; mAb = monoclonal antibody; IgG1 = immunoglobulin G 1; FDA = Food and Drug Administration; PD-1 = programmed cell death protein 1; PD-L1 = programmed cell death ligand 1; irAEs = immune-related adverse events; TPS = tumor proportion score. Information from Masters et al. (2015); Bezjak et al. (2015); NCCN (2017); Pisters et al. (2007).

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Disclosure

The author has no potential conflicts of interest to disclose.

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