Trust Pharmacy Team

IIF Audit Protocols

Version	Date	Author	Rationale
1.0	04/11/2022	Eleanor Barnes	Document creation. Distributed to all staff.
1.1	13/01/2023	Eleanor Barnes	Completion of CVD-06 protocol. Distributed to all staff

Contents

Aim

The aim of this document is to provide a structure to deliver quality improvement audits to positively influence the pharmacy-focussed Investment and Impact Fund indicators to all practices.

Scope

For all registered pharmacy technicians, registered pharmacists, provisionally registered pharmacists, foundation year pharmacy technicians, and foundation year pharmacists working in the Trust Primary Care Pharmacy Team.

Review

March 2023

SMR-01A Patients at risk of harm from due to medication errors to receive an SMR

Background

If in any doubt at any stage, refer to a senior member of staff.

Data Collection Form

Insert this information into Excel with an exported CSV from SystmOne

Patient Name	DOB	Age	Drug and dose	Indication	Initiating specialty	Start date	Intended course length	Date of last review	Last review done by?	Documented plan for ongoing tx?	Other	Action	Comments

Summary

SMR-01A Patients at risk of harm from due to medication errors to receive an SMR

Practice .....

Pharmacy Technician .....

Pharmacist .....

Authorising GP .....

Date Audit Completed .....

Re-audit date .....

Information sent to LCP ☐

SMR-01B Patients who are severely frail to receive an SMR

Background

If in any doubt at any stage, refer to a senior member of staff.

Data Collection Form

Insert this information into Excel with an exported CSV from SystmOne

Patient Name	DOB	Age	Drug and dose	Indication	Initiating specialty	Start date	Intended course length	Date of last review	Last review done by?	Documented plan for ongoing tx?	Other	Action	Comments

Summary

SMR-01B Patients who are severely frail to receive an SMR

Practice .....

Pharmacy Technician .....

Pharmacist .....

Authorising GP .....

Date Audit Completed .....

Re-audit date .....

Information sent to LCP ☐

SMR-01C Patients taking potentially addictive pain medication to receive an SMR

Background

If in any doubt at any stage, refer to a senior member of staff.

Data Collection Form

Insert this information into Excel with an exported CSV from SystmOne

Patient Name	DOB	Age	Drug and dose	Indication	Initiating specialty	Start date	Intended course length	Date of last review	Last review done by?	Documented plan for ongoing tx?	Other	Action	Comments

Summary

SMR-01C Patients taking potentially addictive pain medication to receive an SMR

Practice .....

Pharmacy Technician .....

Pharmacist .....

Authorising GP .....

Date Audit Completed .....

Re-audit date .....

Information sent to LCP ☐

SMR-01D Patients over 18y who are permanently resident in a care institution to receive an SMR

Background

If in any doubt at any stage, refer to a senior member of staff.

Data Collection Form

Insert this information into Excel with an exported CSV from SystmOne

Patient Name	DOB	Age	Drug and dose	Indication	Initiating specialty	Start date	Intended course length	Date of last review	Last review done by?	Documented plan for ongoing tx?	Other	Action	Comments

Summary

SMR-01D Patients over 18y who are permanently resident in a care institution to receive an SMR

Practice .....

Pharmacy Technician .....

Pharmacist .....

Authorising GP .....

Date Audit Completed .....

Re-audit date .....

Information sent to LCP ☐

SMR-02A Patients over 18y taking Non-Steroidal Anti-Inflammatory Drug and Oral Anticoagulant

Background

Indicator Specifics

Percentage of patients aged 18 years or over prescribed both a Non-Steroidal Anti-Inflammatory Drug (NSAID) and an oral anticoagulant in the 3 months to 1 April 2022, who in the 3 months to 1 April 2023 were either

(i) no longer prescribed an NSAID or
(ii) prescribed a gastroprotective in addition to both an NSAID and an oral anticoagulant

Anticoagulation treatment reduces the risk of stroke by about two-thirds (NICE CKS). Anticoagulation is achieved using either warfarin or Direct-acting Oral Anticoagulants (DOACs).

DOACs are now more widely used than warfarin, with 9.3 million prescriptions in 2018.

This number is set to increase with NHS England's new DOAC framework agreement which will allow the NHS to treat between 440,000 to 620,000 (50% - 72%) additional patients, with the aim of improving outcomes for patients while reducing current and future growth in spend.

Intelligence from the National Reporting and Learning System (NRLS) suggests that anticoagulants are linked to more deaths and severe harm errors than any other medicine. The use of anticoagulants is widespread with 18 million prescriptions issued in 2018.

The most frequent serious adverse event associated with DOACs is a major bleed. The most common modifiable causes of major bleeds associated with DOACs are:

- Co-prescription of DOAC and a gastro-toxic drug such as a NSAID (affecting an estimated 13,000 patients), or antiplatelets (affecting an estimated 22,000 patients)
- An unintentional prescribed overdose of a DOAC (affecting an estimated 155,200 patients).

The Orbit II-AF Registry found that 1 in 25 patients who were taking the incorrect dose of DOAC suffered a major bleed (affecting an estimated 155,200 people). To prevent people being prescribed an overdose, the patient's renal function must be regularly monitored (generally once or twice a year) and the dose adjusted based on their creatinine levels and body weight.

Nonsteroidal anti-inflammatory drugs (NSAIDs) have analgesic, antipyretic and, at higher doses, anti-inflammatory actions. NSAIDs inhibit prostaglandin synthesis by reversibly inhibiting cyclo-oxygenase (COX) enzymes — the two main types of COX enzyme are COX-1 and COX-2, which have different physiological functions. COX-1 produces prostaglandins that help to maintain gastric mucosal integrity and platelet-initiated blood clotting. Inhibition is thought to be responsible for gastrointestinal toxicity. COX-2 produces prostaglandins that mediate pain and inflammation. Inhibition is thought to be responsible for the anti-inflammatory action of NSAIDs. NSAIDs vary in

how selective they are for COX-1 and COX-2 pathways and the degree of selectivity for COX-1 relative to COX-2 can be used to classify NSAIDs:

Standard NSAIDs are nonselective NSAIDs (inhibiting both COX-1 and COX-2), and include ibuprofen, indometacin, mefenamic acid, and naproxen. Diclofenac, etodolac, meloxicam, and nabumetone, are also nonselective NSAIDs, but are thought to have a preference for COX-2. Coxibs are COX-2 specific NSAIDs and include celecoxib and etoricoxib.

When prescribing an NSAID, individual risk factors for adverse effects should be considered and include any contraindications, drug interactions, medical history, and any monitoring requirements. If an NSAID is indicated, the lowest effective dose should be used for the shortest possible duration.

For people with:

- Severe heart failure
    - NSAIDs should be avoided.
- Mild, moderate, or severe heart failure
    - COX-2 inhibitors, diclofenac, and high-dose ibuprofen (2400 mg or more daily) should be avoided.
- Mild to moderate heart failure
    - a standard NSAID should be prescribed (but not diclofenac or high-dose ibuprofen), and the person should be monitored closely.
    - Ibuprofen up to 1200 mg daily, or naproxen up to 1000 mg daily, should be first-line options.
- Ischaemic heart disease, cerebrovascular disease, or peripheral arterial disease,
    - ibuprofen up to 1200 mg per day or naproxen up to 1000 mg daily, should be first-line options.
    - COX-2 inhibitors, diclofenac, and high-dose ibuprofen are contraindicated.
- Severe renal impairment (estimated glomerular filtration rate [eGFR] less than 30 mL/minute/1.73 m2),
    - ideally NSAIDs should be avoided.
    - If an NSAID is used, the person should be monitored closely.
- Risk factors for cardiovascular disease and all elderly people,
    - ibuprofen up to 1200 mg per day or naproxen up to 1000 mg daily should be prescribed.
- Uncontrolled hypertension (blood pressure persistently above 140/90 mmHg),
    - etoricoxib and high-dose ibuprofen should be avoided.
- To prevent GI adverse effects associated with NSAIDs:
    - An alternative analgesic should be considered.
    - Prescribing more than one NSAID at a time should be avoided.
    - Concomitant use of an NSAID with low-dose aspirin should be avoided

Short-acting NSAIDs (such as ibuprofen) should be used in preference to long-acting formulations (such as naproxen). Coxibs are associated with a reduction in the risk of GI symptoms and complications compared with standard NSAIDs, but they do not eliminate the risk of GI adverse

effects. Selectivity for COX-2 represents a continuum, and COX-2 inhibitors can therefore be ranked based on their relative COX-2 vs COX-1 selectivity, with etoricoxib more selective than celecoxib.

Proton pump inhibitors (PPIs) are well tolerated and effective at reducing the GI risks associated with NSAIDs and reduce the risks to a similar level as using a coxib alone.

The combination of selective COX-2 inhibitors plus PPIs provides the best gastrointestinal protection, followed by selective COX-2 inhibitors alone, and thirdly by nonselective NSAIDs plus PPIs.

Options for gastroprotective drugs to prescribe with standard NSAIDs also include misoprostol or a histamine$_2$–receptor antagonist, but a PPI is the preferred choice.

SMR-02 encourages the identification of people at significant risk of gastric bleed with the aim of reducing that risk by either

(i) stopping prescribing of the (combination of) medications that is causing the increased risk or,
(ii) where this is not possible, prescribing a gastroprotective medication to reduce the risk.

Licensed doses of proton pump inhibitors used for gastroprotection for people who require continued NSAID treatment

Proton Pump Inhibitor	**Dose for NSAID prophylaxis**
Lansoprazole	15–30 mg once daily
Omeprazole	20 mg once daily
Esomeprazole	20 mg once daily
Pantoprazole	20 mg once daily

PPIs should be prescribed with caution to people:

- At risk of osteoporosis — the person should maintain an adequate intake of calcium and vitamin D, and if necessary, be given additional bone-sparing therapy.
- At risk of hypomagnesaemia — if possible, magnesium levels should be checked before starting PPI therapy and intermittently during long-term treatment, for example if the person is prescribed drugs that can cause hypomagnesaemia, such as digoxin and diuretics.

Adverse effects of proton pump inhibitors (PPIs) are usually mild and reversible. Adverse effects include headache, diarrhoea, nausea, vomiting, abdominal pain, constipation, and dizziness.

- Less common adverse effects include dry mouth, peripheral oedema, sleep disturbance, fatigue, paraesthesia, arthralgia, myalgia, pruritus, and rash.
- Rare or very rare adverse effects include:
    - Subacute cutaneous lupus erythematosus (SCLE), which can occur weeks, months, or years after exposure to a PPI. If suspected discontinue the PPI and seek specialist advice if needed [MHRA, 2015].
    - Severe cutaneous adverse reactions (SCARs) including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS) and acute generalized have been reported very rarely and rarely with omeprazole treatment.
    - Taste disturbance, hepatitis, jaundice, depression, confusion, hallucinations, hyponatraemia, leucopenia, leucocytosis, pancytopenia, thrombocytopenia, visual disturbances, sweating, photophobia, and alopecia.

Long-term PPI treatment may be associated with uncommon, serious adverse effects such as:

- Hypomagnesaemia — symptoms include muscle twitching, tremors, vomiting, fatigue, and loss of appetite. Case reports after one year of PPI therapy, but may occur after 3 months. This usually improves after magnesium replacement therapy and discontinuation of the PPI [MHRA, 2012].
- Increased risk of fractures — especially when used at high doses for over a year in the elderly [MHRA, 2012].
- Clostridium difficile infection — because of decreasing gastric acidity.
- Rebound acid hypersecretion syndrome — may occur after stopping long-term PPI therapy, although this may be more a theoretical risk than clinical phenomenon.

Possible drug interactions with proton pump inhibitors (PPIs) include:

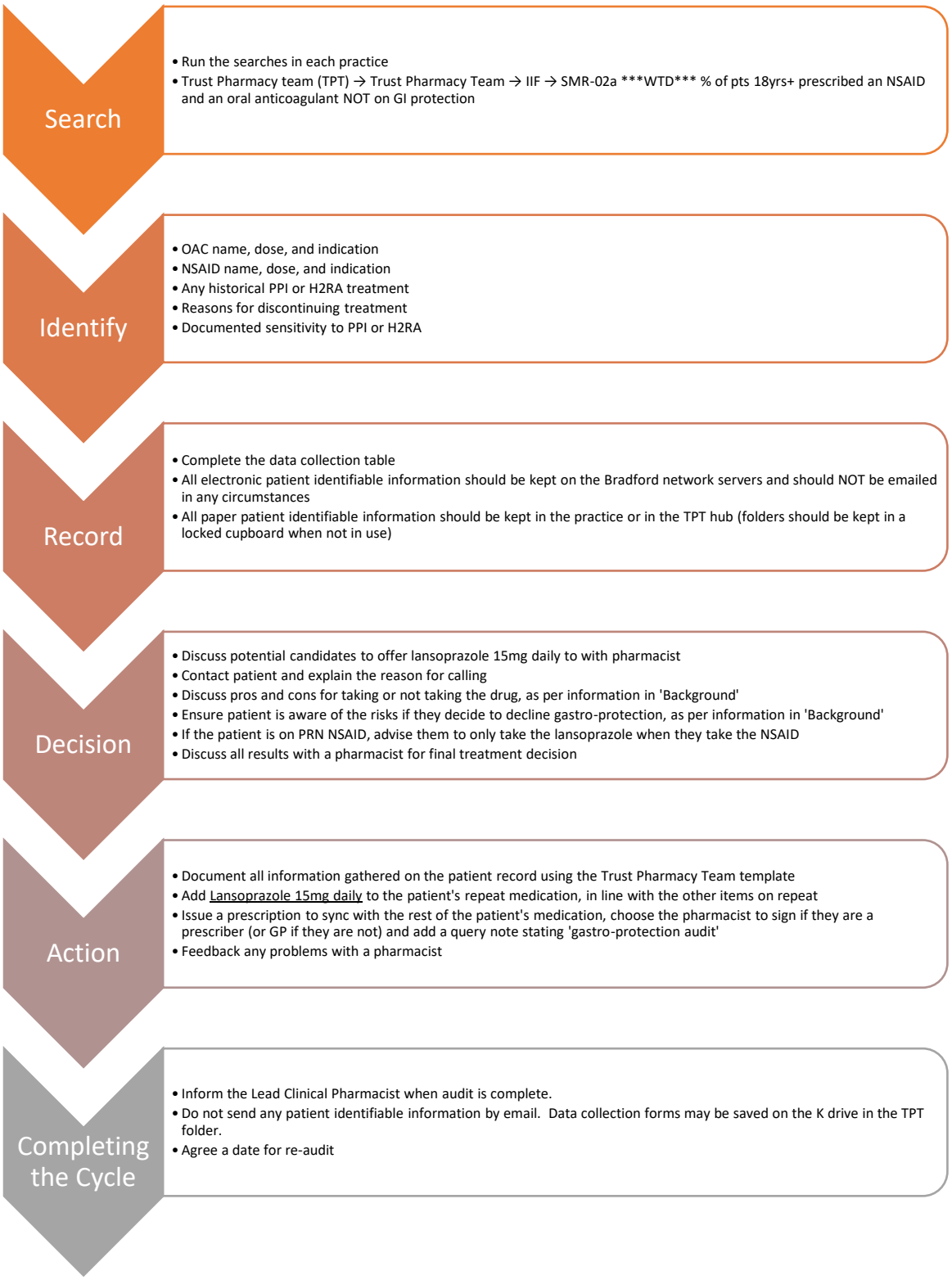
- Digoxin — PPIs may cause a small rise in serum digoxin levels (although not considered clinically significant). The manufacturer of lansoprazole suggests that digoxin levels should be monitored if lansoprazole is started or stopped.
- Warfarin — PPIs can occasionally enhance the effects of warfarin. The international normalized ratio (INR) should be monitored in people taking warfarin if omeprazole, pantoprazole, or esomeprazole is started or stopped.
- Methotrexate — PPIs possibly reduce excretion of methotrexate, leading to an increased risk of methotrexate toxicity.
- Phenytoin — omeprazole and esomeprazole can occasionally enhance the effects of phenytoin. The manufacturers recommend that people taking phenytoin are carefully monitored if omeprazole or esomeprazole is started or stopped.
- Azole antifungals — the absorption of ketoconazole or itraconazole may be reduced during PPI treatment. Dose adjustment of the antifungal drug may be required during long-term PPI treatment.

- Clopidogrel — omeprazole and esomeprazole reduce the antiplatelet effect of clopidogrel, and concomitant use should be avoided. The other PPIs may also reduce the efficacy of clopidogrel, and this risk should be weighed against the potential benefit of the PPI [MHRA, 2010].
- Protease inhibitors — PPIs can significantly affect plasma levels of some protease inhibitor drugs, including:
    - Atazanavir — concurrent use of PPIs and atazanavir is not recommended as the absorption of atazanavir may be affected by a PPI (due to changes in gastric acidity). This may lead to a reduced plasma concentration of atazanavir which may affect its efficacy. If concurrent use is necessary, seek specialist advice.
    - Saquinavir — plasma concentration of saquinavir may be increased by PPI treatment, leading to increased risk of adverse effects.
    - Tipranavir — concurrent use with omeprazole or esomeprazole is not recommended, as tipranavir may reduce the plasma concentration of the PPI. If concurrent use is necessary, seek specialist advice.

Further resources:

- CKS Atrial Fibrillation
- Off-Label Dosing of Non-Vitamin K Antagonist Oral Anticoagulants and Adverse Outcomes
- DOACs: reminder of bleeding risk, including availability of reversal agents (MHRA Drug Safety Update)
- CKS. NSAIDs – prescribing issues

If in any doubt at any stage, refer to a senior member of staff.



Data Collection Form

Insert this information into Excel with an exported CSV from SystmOne

A	B	C	D	E	F	G	H	I	J
Patient Name	Age	OAC name and dose	Indication for OAC	NSAID name and dose	Indication for NSAID	History of GI protection? If none, skip column J	Reason for stopping?	Sensitivity to GI protection?	Recommendation

K	L	M	N	O
Information given to pt?	Concerns raised by pt?	Confirmation of tx by pharmacist (Give detail of tx)	Added to rpt and rx issued?	Comments

Summary

SMR-02A Patients over 18y taking Non-Steroidal Anti-Inflammatory Drug and Oral Anticoagulant

Practice .....

Pharmacy Technician .....

Pharmacist .....

Authorising GP .....

Date Audit Completed .....

Re-audit date .....

Information sent to LCP ☐

SMR-02B Patients over 65y taking a Non-Steroidal Anti-Inflammatory Drug

Background

Indicator Specifics

Percentage of patients aged 65 years or over prescribed a Non-Steroidal Anti-Inflammatory Drug (NSAID) and not an oral anticoagulant in the 3 months to 1 April 2022, who in the 3 months to 1 April 2023 were either

(i) no longer prescribed an NSAID or
(ii) prescribed a gastroprotective in addition to an NSAID

Nonsteroidal anti-inflammatory drugs (NSAIDs) have analgesic, antipyretic and, at higher doses, anti-inflammatory actions. NSAIDs inhibit prostaglandin synthesis by reversibly inhibiting cyclo-oxygenase (COX) enzymes — the two main types of COX enzyme are COX-1 and COX-2, which have different physiological functions. COX-1 produces prostaglandins that help to maintain gastric mucosal integrity and platelet-initiated blood clotting. Inhibition is thought to be responsible for gastrointestinal toxicity. COX-2 produces prostaglandins that mediate pain and inflammation. Inhibition is thought to be responsible for the anti-inflammatory action of NSAIDs. NSAIDs vary in how selective they are for COX-1 and COX-2 pathways and the degree of selectivity for COX-1 relative to COX-2 can be used to classify NSAIDs:

Standard NSAIDs are nonselective NSAIDs (inhibiting both COX-1 and COX-2), and include ibuprofen, indometacin, mefenamic acid, and naproxen. Diclofenac, etodolac, meloxicam, and nabumetone, are also nonselective NSAIDs, but are thought to have a preference for COX-2. Coxibs are COX-2 specific NSAIDs and include celecoxib and etoricoxib.

When prescribing an NSAID, individual risk factors for adverse effects should be considered and include any contraindications, drug interactions, medical history, and any monitoring requirements. If an NSAID is indicated, the lowest effective dose should be used for the shortest possible duration.

For people with:

- Severe heart failure
    - NSAIDs should be avoided.
- Mild, moderate, or severe heart failure
    - COX-2 inhibitors, diclofenac, and high-dose ibuprofen (2400 mg or more daily) should be avoided.
- Mild to moderate heart failure
    - a standard NSAID should be prescribed (but not diclofenac or high-dose ibuprofen), and the person should be monitored closely.
    - Ibuprofen up to 1200 mg daily, or naproxen up to 1000 mg daily, should be first-line options.

- Ischaemic heart disease, cerebrovascular disease, or peripheral arterial disease,
    - ibuprofen up to 1200 mg per day or naproxen up to 1000 mg daily, should be first-line options.
    - COX-2 inhibitors, diclofenac, and high-dose ibuprofen are contraindicated.
- Severe renal impairment (eGFR less than 30 mL/minute/1.73 m^2),
    - ideally NSAIDs should be avoided.
    - If an NSAID is used, the person should be monitored closely.
- Risk factors for cardiovascular disease and all elderly people,
    - ibuprofen up to 1200 mg per day or naproxen up to 1000 mg daily should be prescribed.
- Uncontrolled hypertension (blood pressure persistently above 140/90 mmHg),
    - etoricoxib and high-dose ibuprofen should be avoided.
- To prevent GI adverse effects associated with NSAIDs:
    - An alternative analgesic should be considered.
    - Prescribing more than one NSAID at a time should be avoided.
    - Concomitant use of an NSAID with low-dose aspirin should be avoided

Short-acting NSAIDs (such as ibuprofen) should be used in preference to long-acting formulations (such as naproxen).

Coxibs are associated with a reduction in the risk of GI symptoms and complications compared with standard NSAIDs, but they do not eliminate the risk of GI adverse effects. Selectivity for COX-2 represents a continuum, and COX-2 inhibitors can therefore be ranked based on their relative COX-2 vs COX-1 selectivity, with etoricoxib more selective than celecoxib.

Proton pump inhibitors (PPIs) are well tolerated and effective at reducing the GI risks associated with NSAIDs and reduce the risks to a similar level as using a coxib alone.

The combination of selective COX-2 inhibitors plus PPIs provides the best gastrointestinal protection, followed by selective COX-2 inhibitors alone, and thirdly by nonselective NSAIDs plus PPIs.

Options for gastroprotective drugs to prescribe with standard NSAIDs also include misoprostol or a $histamine_2$–receptor antagonist, but a PPI is the preferred choice.

SMR-02 encourages the identification of people at significant risk of gastric bleed with the aim of reducing that risk by either

(i) stopping prescribing of the (combination of) medications that is causing the increased risk or,

(ii) where this is not possible, prescribing a gastroprotective medication to reduce the risk.

Licensed doses of proton pump inhibitors used for gastroprotection for people who require continued NSAID treatment

Proton Pump Inhibitor	Dose for NSAID prophylaxis
Lansoprazole	15–30 mg once daily
Omeprazole	20 mg once daily
Esomeprazole	20 mg once daily
Pantoprazole	20 mg once daily

PPIs should be prescribed with caution to people:

- At risk of osteoporosis — the person should maintain an adequate intake of calcium and vitamin D, and if necessary, be given additional bone-sparing therapy.
- At risk of hypomagnesaemia — if possible, magnesium levels should be checked before starting PPI therapy and intermittently during long-term treatment, for example if the person is prescribed drugs that can cause hypomagnesaemia, such as digoxin and diuretics.

Adverse effects of proton pump inhibitors (PPIs) are usually mild and reversible. Adverse effects include headache, diarrhoea, nausea, vomiting, abdominal pain, constipation, and dizziness.

- Less common adverse effects include dry mouth, peripheral oedema, sleep disturbance, fatigue, paraesthesia, arthralgia, myalgia, pruritus, and rash.
- Rare or very rare adverse effects include:
    - Subacute cutaneous lupus erythematosus (SCLE), which can occur weeks, months, or years after exposure to a PPI. If suspected discontinue the PPI and seek specialist advice if needed [MHRA, 2015].
    - Severe cutaneous adverse reactions (SCARs) including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS) and acute generalized have been reported very rarely and rarely with omeprazole treatment.
    - Taste disturbance, hepatitis, jaundice, depression, confusion, hallucinations, hyponatraemia, leucopenia, leucocytosis, pancytopenia, thrombocytopenia, visual disturbances, sweating, photophobia, and alopecia.

Long-term PPI treatment may be associated with uncommon, serious adverse effects such as:

- Hypomagnesaemia — symptoms include muscle twitching, tremors, vomiting, fatigue, and loss of appetite. Case reports after one year of PPI therapy, but may occur after 3 months. This usually improves after magnesium replacement therapy and discontinuation of the PPI [MHRA, 2012].
- Increased risk of fractures — especially when used at high doses for over a year in the elderly [MHRA, 2012].
- Clostridium difficile infection — because of decreasing gastric acidity.
- Rebound acid hypersecretion syndrome — may occur after stopping long-term PPI therapy, although this may be more a theoretical risk than clinical phenomenon.

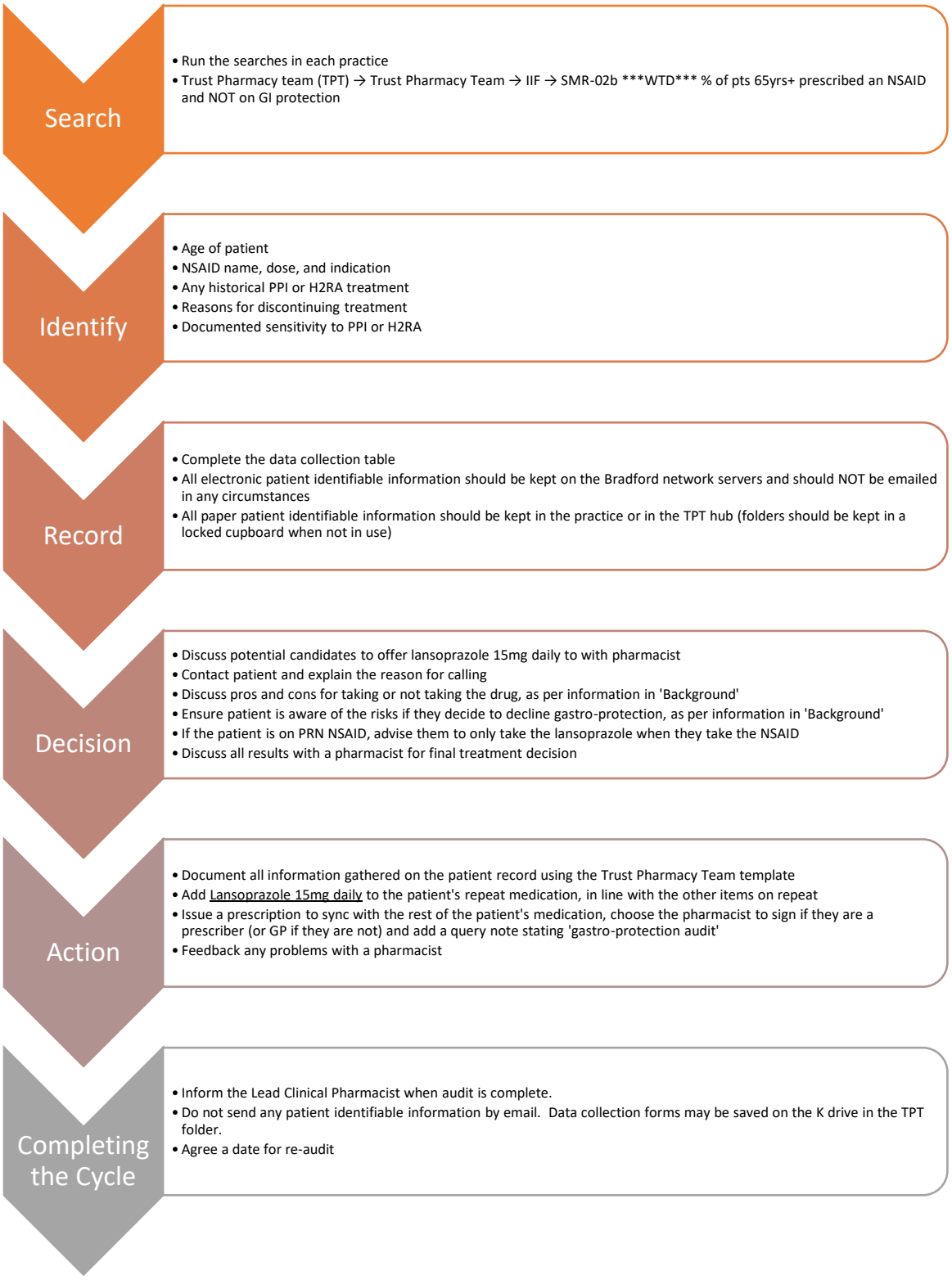
Possible drug interactions with proton pump inhibitors (PPIs) include:

- Digoxin — PPIs may cause a small rise in serum digoxin levels (although not considered clinically significant). The manufacturer of lansoprazole suggests that digoxin levels should be monitored if lansoprazole is started or stopped.
- Warfarin — PPIs can occasionally enhance the effects of warfarin. The international normalized ratio (INR) should be monitored in people taking warfarin if omeprazole, pantoprazole, or esomeprazole is started or stopped.
- Methotrexate — PPIs possibly reduce excretion of methotrexate, leading to an increased risk of methotrexate toxicity.
- Phenytoin — omeprazole and esomeprazole can occasionally enhance the effects of phenytoin. The manufacturers recommend that people taking phenytoin are carefully monitored if omeprazole or esomeprazole is started or stopped.
- Azole antifungals — the absorption of ketoconazole or itraconazole may be reduced during PPI treatment. Dose adjustment of the antifungal drug may be required during long-term PPI treatment.
- Clopidogrel — omeprazole and esomeprazole reduce the antiplatelet effect of clopidogrel, and concomitant use should be avoided. The other PPIs may also reduce the efficacy of clopidogrel, and this risk should be weighed against the potential benefit of the PPI [MHRA, 2010].
- Protease inhibitors — PPIs can significantly affect plasma levels of some protease inhibitor drugs, including:
    - Atazanavir — concurrent use of PPIs and atazanavir is not recommended as the absorption of atazanavir may be affected by a PPI (due to changes in gastric acidity). This may lead to a reduced plasma concentration of atazanavir which may affect its efficacy. If concurrent use is necessary, seek specialist advice.
    - Saquinavir — plasma concentration of saquinavir may be increased by PPI treatment, leading to increased risk of adverse effects.
    - Tipranavir — concurrent use with omeprazole or esomeprazole is not recommended, as tipranavir may reduce the plasma concentration of the PPI. If concurrent use is necessary, seek specialist advice.

Further resources:

- CKS. NSAIDs – prescribing issues

If in any doubt at any stage, refer to a senior member of staff.



Data Collection Form

Insert this information into Excel with an exported CSV from SystmOne

A	B	C	D	E	F	G	H
Patient Name	Age	NSAID name and dose	Indication for NSAID	History of GI protection? If none, skip column E	Reason for stopping?	Sensitivity to GI protection?	Recommendation

I	J	K	L	M
Information given to pt?	Concerns raised by pt?	Confirmation of tx by pharmacist (Give detail of tx)	Added to rpt and rx issued?	Comments

Summary

SMR-02B Patients over 65y taking a Non-Steroidal Anti-Inflammatory Drug

Practice .....

Pharmacy Technician .....

Pharmacist .....

Authorising GP .....

Date Audit Completed .....

Re-audit date .....

Information sent to LCP ☐

SMR-02C Patients over 18y taking an Oral Anticoagulant and Antiplatelet

Background

Indicator Specifics

Percentage of patients aged 18 years or over prescribed both an oral anticoagulant and an anti-platelet in the 3 months to 1 April 2022, who in the 3 months to 1 April 2023 were either

(i) no longer prescribed an anti-platelet or
(ii) prescribed a gastroprotective in addition to both an oral anticoagulant and an antiplatelet.

Anticoagulation treatment reduces the risk of stroke by about two-thirds (NICE CKS). Anticoagulation is achieved using either warfarin or Direct-acting Oral Anticoagulants (DOACs).

DOACs are now more widely used than warfarin, with 9.3 million prescriptions in 2018.

This number is set to increase with NHS England's new DOAC framework agreement which will allow the NHS to treat between 440,000 to 620,000 (50% - 72%) additional patients, with the aim of improving outcomes for patients while reducing current and future growth in spend.

Intelligence from the National Reporting and Learning System (NRLS) suggests that anticoagulants are linked to more deaths and severe harm errors than any other medicine. The use of anticoagulants is widespread with 18 million prescriptions issued in 2018.

The most frequent serious adverse event associated with DOACs is a major bleed. The most common modifiable causes of major bleeds associated with DOACs are:

- Co-prescription of DOAC and a gastro-toxic drug such as a NSAID (affecting an estimated 13,000 patients), or antiplatelets (affecting an estimated 22,000 patients)
- An unintentional prescribed overdose of a DOAC (affecting an estimated 155,200 patients).

The Orbit II-AF Registry found that 1 in 25 patients who were taking the incorrect dose of DOAC suffered a major bleed (affecting an estimated 155,200 people). To prevent people being prescribed an overdose, the patient's renal function must be regularly monitored (generally once or twice a year) and the dose adjusted based on their creatinine levels and body weight.

Antiplatelet treatment is drug treatment that decreases platelet aggregation and inhibit thrombus formation in the arterial circulation.

Four main types of antiplatelet drugs are available:

- Aspirin — this irreversibly inhibits cyclo-oxygenase and blocks the production of thromboxane.
- Clopidogrel, prasugrel and ticagrelor — these are thienopyridines. They inhibit the binding of adenosine diphosphate to its platelet receptor; this is thought to inhibit platelet aggregation by blocking activation of the glycoprotein IIb/IIIa pathway.
- Dipyridamole — this has both antiplatelet and vasodilatory properties. It inhibits uptake of adenosine into erythrocytes, platelets, and endothelial cells, resulting in an increased extracellular concentration of adenosine, which is a potent inhibitor of platelet activation and aggregation. It may also act by inhibiting the breakdown of cyclic guanosine monophosphate.
- Glycoprotein IIb/IIIa inhibitors (for example, abciximab, eptifibatide, and tirofiban) block the binding of fibrinogen to glycoprotein IIb/IIIa receptors on the platelet. They are given intravenously in secondary care and are not discussed in this topic.

The main indications for antiplatelets are:

- The primary prevention of atherothrombotic events in people who are at high risk.
- The secondary prevention of atherothrombotic events in people with acute coronary syndrome (ACS), angina, peripheral arterial disease (PAD), and atrial fibrillation (AF) (although anticoagulants are usually used).
- The secondary prevention of cardiovascular events in people after myocardial infarction (MI), stent implantation, stroke or transient ischaemic attack (TIA).
- The prevention of atherothrombotic events in people undergoing percutaneous coronary intervention (PCI).

Antiplatelets should not be prescribed routinely for the primary prevention of cardiovascular disease, however, they may be considered in people at high risk of stroke or myocardial infarction.

Antiplatelet treatment for secondary prevention of CVD should be prescribed for people with:

- Angina — aspirin 75 mg. Clopidogrel 75 mg daily should be considered for people unable to take aspirin.
- AF — dual antiplatelet therapy (DAPT) of aspirin 75 mg daily plus clopidogrel 75 mg daily may be suitable for people who are unable or unwilling to take anticoagulants.
- ACS which is medically managed — aspirin 75 mg daily plus ticagrelor 90 mg twice a day for 12 months.
- PCI for people with ACS — aspirin 75 mg in combination with either ticagrelor 90 mg twice a day, or prasugrel 10 mg daily. Clopidogrel 75 mg daily should be prescribed if prasugrel or ticagrelor are unsuitable.
- PCI in people with stable coronary artery disease — aspirin 75 mg daily plus clopidogrel 75 mg daily. Ticagrelor or prasugrel may be considered instead of clopidogrel where appropriate.

- ACS who are undergoing coronary artery bypass grafting (CABG) — aspirin 75 mg in combination with ticagrelor 90 mg twice a day, or prasugrel 10 mg daily. Clopidogrel 75 mg daily should be prescribed if prasugrel or ticagrelor are not suitable.
- Stroke, or TIA — clopidogrel 75 mg daily is the preferred antiplatelet. Modified-release dipyridamole (200 mg twice a day) should be prescribed with combined with aspirin 75 mg if clopidogrel is unsuitable.
- PAD, or multivascular disease — clopidogrel 75 mg daily is the preferred antiplatelet. Aspirin 75 mg alone should be prescribed if clopidogrel is unsuitable.
- People already receiving anticoagulation therapy may have been advised to continue their existing treatment with the addition of aspirin or clopidogrel, depending on their risk of bleeding and the type of medical/surgical treatment received. Dosages and any necessary titrations should have been detailed in the management plan received from the treating specialist.

SMR-02 encourages the identification of people at significant risk of gastric bleed with the aim of reducing that risk by either

(iii) stopping prescribing of the (combination of) medications that is causing the increased risk or,

(iv) where this is not possible, prescribing a gastroprotective medication to reduce the risk.

If the person has a high risk of GI adverse effects (for example, bleeding) and is taking low-dose aspirin alone, or in combination with ticagrelor or prasugrel, co-prescribe a proton pump inhibitor (PPI), such as lansoprazole, omeprazole, or pantoprazole, for gastroprotection.

If the person has a high risk of GI adverse effects (for example, bleeding) and is taking clopidogrel alone, or in combination with low-dose aspirin, co-prescribe a PPI, except omeprazole or esomeprazole, or consider prescribing an H2-receptor antagonist, e.g., famotidine (avoid cimetidine).

Licensed doses of proton pump inhibitors used for gastroprotection for people who require continued NSAID treatment

Proton Pump Inhibitor	**Dose for NSAID prophylaxis**
Lansoprazole	15–30 mg once daily
Omeprazole	20 mg once daily
Esomeprazole	20 mg once daily
Pantoprazole	20 mg once daily

PPIs should be prescribed with caution to people:

- At risk of osteoporosis — the person should maintain an adequate intake of calcium and vitamin D, and if necessary, be given additional bone-sparing therapy.
- At risk of hypomagnesaemia — if possible, magnesium levels should be checked before starting PPI therapy and intermittently during long-term treatment, for example if the person is prescribed drugs that can cause hypomagnesaemia, such as digoxin and diuretics.

Adverse effects of proton pump inhibitors (PPIs) are usually mild and reversible. Adverse effects include headache, diarrhoea, nausea, vomiting, abdominal pain, constipation, and dizziness.

- Less common adverse effects include dry mouth, peripheral oedema, sleep disturbance, fatigue, paraesthesia, arthralgia, myalgia, pruritus, and rash.
- Rare or very rare adverse effects include:
    - Subacute cutaneous lupus erythematosus (SCLE), which can occur weeks, months, or years after exposure to a PPI. If suspected discontinue the PPI and seek specialist advice if needed [MHRA, 2015].
    - Severe cutaneous adverse reactions (SCARs) including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS) and acute generalized have been reported very rarely and rarely with omeprazole treatment.
    - Taste disturbance, hepatitis, jaundice, depression, confusion, hallucinations, hyponatraemia, leucopenia, leucocytosis, pancytopenia, thrombocytopenia, visual disturbances, sweating, photophobia, and alopecia.

Long-term PPI treatment may be associated with uncommon, serious adverse effects such as:

- Hypomagnesaemia — symptoms include muscle twitching, tremors, vomiting, fatigue, and loss of appetite. Case reports after one year of PPI therapy but may occur after 3 months. This usually improves after magnesium replacement therapy and discontinuation of the PPI [MHRA, 2012].
- Increased risk of fractures — especially when used at high doses for over a year in the elderly [MHRA, 2012].
- Clostridium difficile infection — because of decreasing gastric acidity.
- Rebound acid hypersecretion syndrome — may occur after stopping long-term PPI therapy, although this may be more a theoretical risk than clinical phenomenon.

Possible drug interactions with proton pump inhibitors (PPIs) include:

- Digoxin — PPIs may cause a small rise in serum digoxin levels (although not considered clinically significant). The manufacturer of lansoprazole suggests that digoxin levels should be monitored if lansoprazole is started or stopped.
- Warfarin — PPIs can occasionally enhance the effects of warfarin. The international normalized ratio (INR) should be monitored in people taking warfarin if omeprazole, pantoprazole, or esomeprazole is started or stopped.

- Methotrexate — PPIs possibly reduce excretion of methotrexate, leading to an increased risk of methotrexate toxicity.
- Phenytoin — omeprazole and esomeprazole can occasionally enhance the effects of phenytoin. The manufacturers recommend that people taking phenytoin are carefully monitored if omeprazole or esomeprazole is started or stopped.
- Azole antifungals — the absorption of ketoconazole or itraconazole may be reduced during PPI treatment. Dose adjustment of the antifungal drug may be required during long-term PPI treatment.
- Clopidogrel — omeprazole and esomeprazole reduce the antiplatelet effect of clopidogrel, and concomitant use should be avoided. The other PPIs may also reduce the efficacy of clopidogrel, and this risk should be weighed against the potential benefit of the PPI [MHRA, 2010].
- Protease inhibitors — PPIs can significantly affect plasma levels of some protease inhibitor drugs, including:
    - Atazanavir — concurrent use of PPIs and atazanavir is not recommended as the absorption of atazanavir may be affected by a PPI (due to changes in gastric acidity). This may lead to a reduced plasma concentration of atazanavir which may affect its efficacy. If concurrent use is necessary, seek specialist advice.
    - Saquinavir — plasma concentration of saquinavir may be increased by PPI treatment, leading to increased risk of adverse effects.
    - Tipranavir — concurrent use with omeprazole or esomeprazole is not recommended, as tipranavir may reduce the plasma concentration of the PPI. If concurrent use is necessary, seek specialist advice.

Further resources:

- CKS Atrial Fibrillation
- Off-Label Dosing of Non-Vitamin K Antagonist Oral Anticoagulants and Adverse Outcomes
- DOACs: reminder of bleeding risk, including availability of reversal agents (MHRA Drug Safety Update)
- CKS. Antiplatelet treatment in CVD

If in any doubt at any stage, refer to a senior member of staff.

Data Collection Form

Insert this information into Excel with an exported CSV from SystmOne

A	B	C		D		E	F	G	H
Patient Name	Age	OAC name and dose	Indication for OAC	Antiplatelet name and dose	Indication for antiplatelet	History of GI protection? If none, skip column E	Reason for stopping?	Sensitivity to GI protection?	Recommendation

I	J	K	L	M
Information given to pt?	Concerns raised by pt?	Confirmation of tx by pharmacist (Give detail of tx)	Added to rpt and rx issued?	Comments

Summary

SMR-02C Patients over 18y taking an oral anticoagulant and antiplatelet

Practice .....

Pharmacy Technician .....

Pharmacist .....

Authorising GP .....

Date Audit Completed .....

Re-audit date .....

Information sent to LCP ☐

SMR-02D Patients over 18y taking Dual Antiplatelets

Background

Indicator Specifics

Percentage of patients aged 18 years or over prescribed aspirin and another anti-platelet in the 3 months to 1 April 2022, who in the 3 months to 1 April 2023 were either

(i) no longer prescribed aspirin and/or no longer prescribed an antiplatelet or
(ii) prescribed a gastroprotective in addition to both aspirin and another antiplatelet.

Antiplatelet treatment is drug treatment that decreases platelet aggregation and inhibit thrombus formation in the arterial circulation.

Four main types of antiplatelet drugs are available:

- Aspirin — this irreversibly inhibits cyclo-oxygenase and blocks the production of thromboxane.
- Clopidogrel, prasugrel and ticagrelor — these are thienopyridines. They inhibit the binding of adenosine diphosphate to its platelet receptor; this is thought to inhibit platelet aggregation by blocking activation of the glycoprotein IIb/IIIa pathway.
- Dipyridamole — this has both antiplatelet and vasodilatory properties. It inhibits uptake of adenosine into erythrocytes, platelets, and endothelial cells, resulting in an increased extracellular concentration of adenosine, which is a potent inhibitor of platelet activation and aggregation. It may also act by inhibiting the breakdown of cyclic guanosine monophosphate.
- Glycoprotein IIb/IIIa inhibitors (for example, abciximab, eptifibatide, and tirofiban) block the binding of fibrinogen to glycoprotein IIb/IIIa receptors on the platelet. They are given intravenously in secondary care and are not discussed in this topic.

The main indications for antiplatelets are:

- The primary prevention of atherothrombotic events in people who are at high risk.
- The secondary prevention of atherothrombotic events in people with acute coronary syndrome (ACS), angina, peripheral arterial disease (PAD), and atrial fibrillation (AF) (although anticoagulants are usually used).
- The secondary prevention of cardiovascular events in people after myocardial infarction (MI), stent implantation, stroke, or transient ischaemic attack (TIA).
- The prevention of atherothrombotic events in people undergoing percutaneous coronary intervention (PCI).

Antiplatelets should not be prescribed routinely for the primary prevention of cardiovascular disease, however, they may be considered in people at high risk of stroke or myocardial infarction.

Antiplatelet treatment for secondary prevention of CVD should be prescribed for people with:

- Angina — aspirin 75 mg. Clopidogrel 75 mg daily should be considered for people unable to take aspirin.
- AF — dual antiplatelet therapy (DAPT) of aspirin 75 mg daily plus clopidogrel 75 mg daily may be suitable for people who are unable or unwilling to take anticoagulants.
- ACS which is medically managed — aspirin 75 mg daily plus ticagrelor 90 mg twice a day for 12 months.
- PCI for people with ACS — aspirin 75 mg in combination with either ticagrelor 90 mg twice a day, or prasugrel 10 mg daily. Clopidogrel 75 mg daily should be prescribed if prasugrel or ticagrelor are unsuitable.
- PCI in people with stable coronary artery disease — aspirin 75 mg daily plus clopidogrel 75 mg daily. Ticagrelor or prasugrel may be considered instead of clopidogrel where appropriate.
- ACS who are undergoing coronary artery bypass grafting (CABG) — aspirin 75 mg in combination with ticagrelor 90 mg twice a day, or prasugrel 10 mg daily. Clopidogrel 75 mg daily should be prescribed if prasugrel or ticagrelor are not suitable.
- Stroke, or TIA — clopidogrel 75 mg daily is the preferred antiplatelet. Modified-release dipyridamole (200 mg twice a day) should be prescribed with combined with aspirin 75 mg if clopidogrel is unsuitable.
- PAD, or multivascular disease — clopidogrel 75 mg daily is the preferred antiplatelet. Aspirin 75 mg alone should be prescribed if clopidogrel is unsuitable.

SMR-02 encourages the identification of people at significant risk of gastric bleed with the aim of reducing that risk by either

(v) stopping prescribing of the (combination of) medications that is causing the increased risk or,

(vi) where this is not possible, prescribing a gastroprotective medication to reduce the risk.

If the person has a high risk of GI adverse effects (for example, bleeding) and is taking low-dose aspirin alone, or in combination with ticagrelor or prasugrel, co-prescribe a proton pump inhibitor (PPI), such as lansoprazole, omeprazole, or pantoprazole, for gastroprotection.

If the person has a high risk of GI adverse effects (for example, bleeding) and is taking clopidogrel alone, or in combination with low-dose aspirin, co-prescribe a PPI, except omeprazole or esomeprazole, or consider prescribing an H2-receptor antagonist, e.g., famotidine (avoid cimetidine).

Licensed doses of proton pump inhibitors used for gastroprotection for people who require continued NSAID treatment

Proton Pump Inhibitor	Dose for NSAID prophylaxis
Lansoprazole	15–30 mg once daily
Omeprazole	20 mg once daily
Esomeprazole	20 mg once daily
Pantoprazole	20 mg once daily

PPIs should be prescribed with caution to people:

- At risk of osteoporosis — the person should maintain an adequate intake of calcium and vitamin D, and if necessary, be given additional bone-sparing therapy.
- At risk of hypomagnesaemia — if possible, magnesium levels should be checked before starting PPI therapy and intermittently during long-term treatment, for example if the person is prescribed drugs that can cause hypomagnesaemia, such as digoxin and diuretics.

Adverse effects of proton pump inhibitors (PPIs) are usually mild and reversible. Adverse effects include headache, diarrhoea, nausea, vomiting, abdominal pain, constipation, and dizziness.

- Less common adverse effects include dry mouth, peripheral oedema, sleep disturbance, fatigue, paraesthesia, arthralgia, myalgia, pruritus, and rash.
- Rare or very rare adverse effects include:
    - Subacute cutaneous lupus erythematosus (SCLE), which can occur weeks, months, or years after exposure to a PPI. If suspected discontinue the PPI and seek specialist advice if needed [MHRA, 2015].
    - Severe cutaneous adverse reactions (SCARs) including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS) and acute generalized have been reported very rarely and rarely with omeprazole treatment.
    - Taste disturbance, hepatitis, jaundice, depression, confusion, hallucinations, hyponatraemia, leucopenia, leucocytosis, pancytopenia, thrombocytopenia, visual disturbances, sweating, photophobia, and alopecia.

Long-term PPI treatment may be associated with uncommon, serious adverse effects such as:

- Hypomagnesaemia — symptoms include muscle twitching, tremors, vomiting, fatigue, and loss of appetite. Case reports after one year of PPI therapy but may occur after 3 months. This usually improves after magnesium replacement therapy and discontinuation of the PPI [MHRA, 2012].
- Increased risk of fractures — especially when used at high doses for over a year in the elderly [MHRA, 2012].
- Clostridium difficile infection — because of decreasing gastric acidity.
- Rebound acid hypersecretion syndrome — may occur after stopping long-term PPI therapy, although this may be more a theoretical risk than clinical phenomenon.

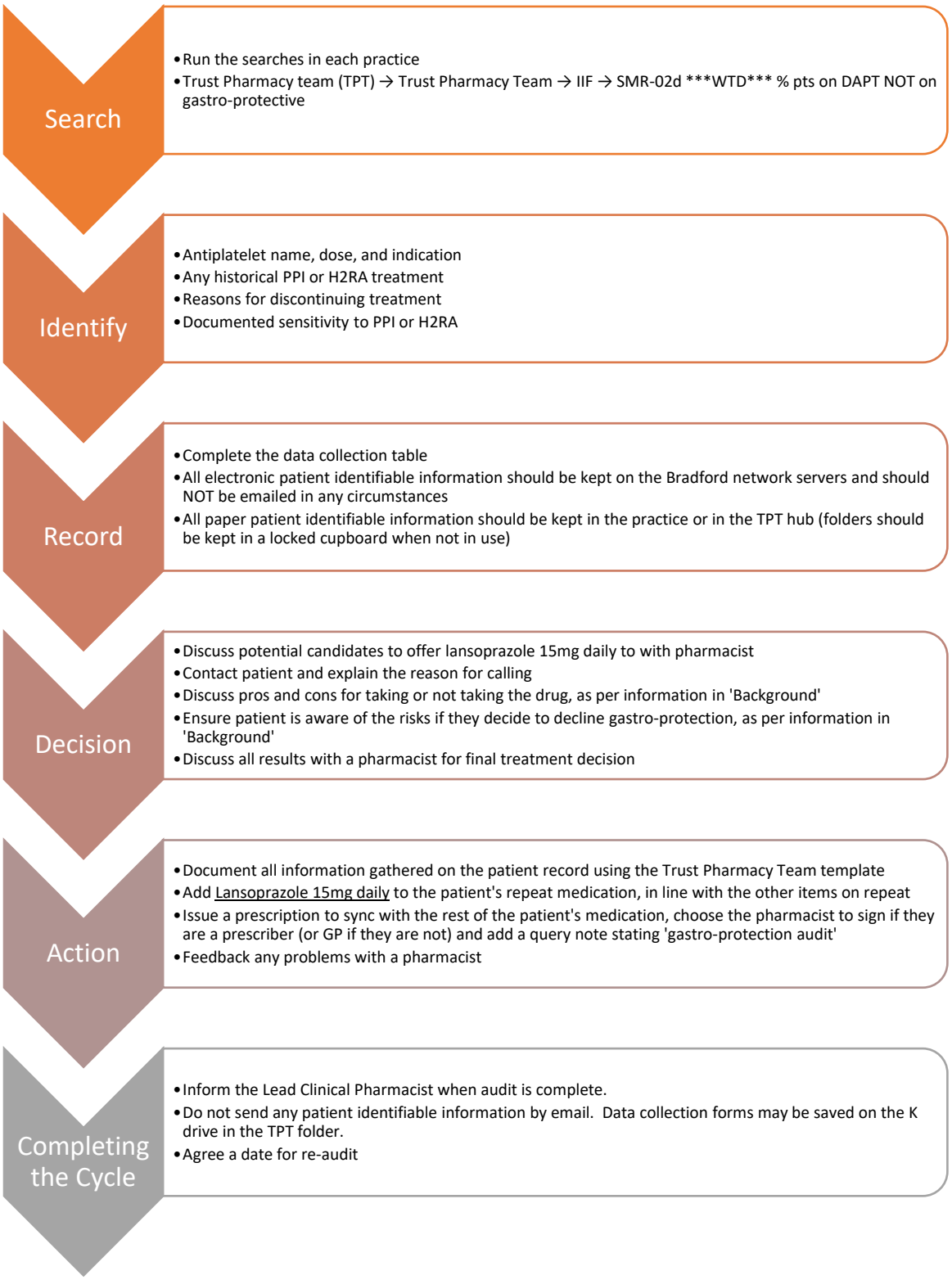
Possible drug interactions with proton pump inhibitors (PPIs) include:

- Digoxin — PPIs may cause a small rise in serum digoxin levels (although not considered clinically significant). The manufacturer of lansoprazole suggests that digoxin levels should be monitored if lansoprazole is started or stopped.
- Warfarin — PPIs can occasionally enhance the effects of warfarin. The international normalized ratio (INR) should be monitored in people taking warfarin if omeprazole, pantoprazole, or esomeprazole is started or stopped.
- Methotrexate — PPIs possibly reduce excretion of methotrexate, leading to an increased risk of methotrexate toxicity.
- Phenytoin — omeprazole and esomeprazole can occasionally enhance the effects of phenytoin. The manufacturers recommend that people taking phenytoin are carefully monitored if omeprazole or esomeprazole is started or stopped.
- Azole antifungals — the absorption of ketoconazole or itraconazole may be reduced during PPI treatment. Dose adjustment of the antifungal drug may be required during long-term PPI treatment.
- Clopidogrel — omeprazole and esomeprazole reduce the antiplatelet effect of clopidogrel, and concomitant use should be avoided. The other PPIs may also reduce the efficacy of clopidogrel, and this risk should be weighed against the potential benefit of the PPI [MHRA, 2010].
- Protease inhibitors — PPIs can significantly affect plasma levels of some protease inhibitor drugs, including:
    - Atazanavir — concurrent use of PPIs and atazanavir is not recommended as the absorption of atazanavir may be affected by a PPI (due to changes in gastric acidity). This may lead to a reduced plasma concentration of atazanavir which may affect its efficacy. If concurrent use is necessary, seek specialist advice.
    - Saquinavir — plasma concentration of saquinavir may be increased by PPI treatment, leading to increased risk of adverse effects.
    - Tipranavir — concurrent use with omeprazole or esomeprazole is not recommended, as tipranavir may reduce the plasma concentration of the PPI. If concurrent use is necessary, seek specialist advice.

Further resources:

- CKS. Antiplatelet treatment in CVD

If in any doubt at any stage, refer to a senior member of staff.



Data Collection Form

Insert this information into Excel with an exported CSV from SystmOne

A	B	C	D	E	F	G	H	I	J
Patient Name	Age	Antiplatelet 1 name and dose	Antiplatelet 2 name and dose	Indication for dual antiplatelet therapy	Documented stop date	History of GI protection? If none, skip column E	Reason for stopping?	Sensitivity to GI protection?	Recommendation

	K	L	M	N
Information given to pt?	Concerns raised by pt?	Confirmation of tx by pharmacist (Give detail of tx)	Added to rpt and rx issued?	Comments

Summary

SMR-02D P**atients over 18y taking dual antiplatelets**

Practice .....

Pharmacy Technician .....

Pharmacist .....

Authorising GP .....

Date Audit Completed .....

Re-audit date .....

Information sent to LCP ☐

SMR-03 Patients taking a DOAC with a renal test, weight, creatinine clearance and confirmation of changed or unchanged dose

Background

Indicator Specifics

Percentage of patients prescribed a direct oral anti-coagulant, who received a renal function test and a recording of their weight and Creatinine Clearance Rate, along with a recording that their DOAC dose was either changed or confirmed (not changed).

Anticoagulation treatment reduces the risk of stroke by about two-thirds (NICE CKS). Anticoagulation is achieved using either warfarin or Direct-acting Oral Anticoagulants (DOACs).

DOACs are now more widely used than warfarin, with 9.3 million prescriptions in 2018.

This number is set to increase with NHS England's new DOAC framework agreement which will allow the NHS to treat between 440,000 to 620,000 (50% - 72%) additional patients, with the aim of improving outcomes for patients while reducing current and future growth in spend.

Intelligence from the National Reporting and Learning System (NRLS) suggests that anticoagulants are linked to more deaths and severe harm errors than any other medicine. The use of anticoagulants is widespread with 18 million prescriptions issued in 2018.

The most frequent serious adverse event associated with DOACs is a major bleed. The most common modifiable causes of major bleeds associated with DOACs are:

- Co-prescription of DOAC and a gastro-toxic drug such as a NSAID (affecting an estimated 13,000 patients), or antiplatelets (affecting an estimated 22,000 patients)
- An unintentional prescribed overdose of a DOAC (affecting an estimated 155,200 patients).

The Orbit II-AF Registry found that 1 in 25 patients who were taking the incorrect dose of DOAC suffered a major bleed (affecting an estimated 155,200 people). To prevent people being prescribed an overdose, the patient's renal function must be regularly monitored (generally once or twice a year) and the dose adjusted based on their creatinine levels and body weight.

SMR-03 supports the dose optimisation of DOACs based on current renal function, with the aim of reducing the risk of unintentionally prescribed overdoses.

The most frequent serious adverse event associated with DOACs is a major bleed. The most common modifiable causes of major bleeds associated with DOACs are:

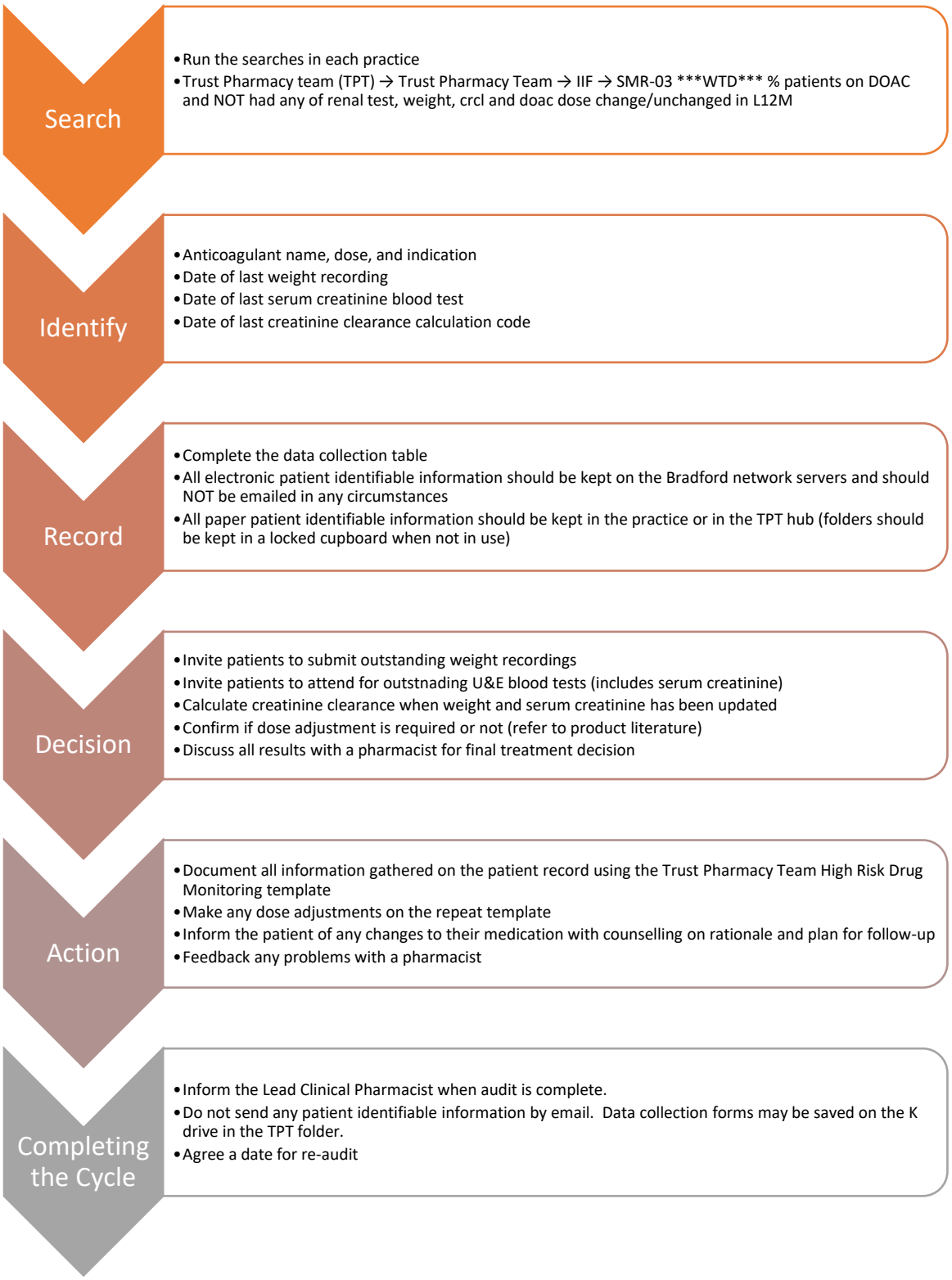
- Co-prescription of DOAC and a gastro-toxic drug such as a non-steroidal anti-inflammatory drug (NSAID), aspirin and/or anti-platelets (affecting an estimated 12,500 patients)
- An unintentional prescribed overdose (affecting an estimated 155,200 patients).

The Orbit II-AF Registry found that 1 in 25 patients on the incorrect dose of DOAC suffered a major bleed. To prevent people being prescribed an overdose, patient renal function must be regularly monitored (generally once or twice a year) and the dose adjusted based on creatinine levels and weight.

Further resources:

- CKS Atrial Fibrillation
- Off-Label Dosing of Non-Vitamin K Antagonist Oral Anticoagulants and Adverse Outcomes
- DOACs: reminder of bleeding risk, including availability of reversal agents (MHRA Drug Safety Update)

If in any doubt at any stage, refer to a senior member of staff.



Data Collection Form

Insert this information into Excel with an exported CSV from SystmOne

A	B	C	D	E	F	G	H	I	M	N
Patient Name	Age	Anticoagulant name and dose	Indication for anticoagulant	Date of last weight	Date of last serum creatinine	Date of last creatinine clearance	New creatinine clearance	Recommendation	Rpt template updated (if applicable)	Comments

J	K	L
Confirmation of dose by pharmacist (Give detail of new dose)	Information given to pt?	Concerns raised by pt?

Summary

SMR-03 Patients taking a DOAC with a renal test, weight, creatinine clearance and confirmation of changed or unchanged dose

Practice .....

Pharmacy Technician .....

Pharmacist .....

Authorising GP .....

Date Audit Completed .....

Re-audit date .....

Information sent to LCP ☐

RESP-01 Patients with asthma regularly prescribed an inhaled corticosteroid

Background

Percentage of patients on the QOF Asthma Register who were regularly prescribed* an inhaled corticosteroid over the previous 12 months

*22/23: 3 or more ICS prescriptions; 23/24 onwards: 5 or more ICS inhalers

Further Resources

If in any doubt at any stage, refer to a senior member of staff.

Data Collection Form

Insert this information into Excel with an exported CSV from SystmOne

A	B	C	D	E	F	G	H
Patient Name	DOB	Age	Date DAPT started	Initiating specialty	Indication for DAPT	Intended duration of DAPT	Has the duration exceeded the intent? (Y/N)

I	J	K	L	M	N
Is there a stop date documented on the prescription?	Is there a history of GI bleed (If yes, when and what?)	Are there any risk factors for bleeding	GI protective medication?	Any other comments	Decision

Summary

RESP-01 Patients with asthma regularly prescribed an inhaled corticosteroid

Practice .....

Pharmacy Technician .....

Pharmacist .....

Authorising GP .....

Date Audit Completed .....

Re-audit date .....

Information sent to LCP ☐

RESP-02 Patients with asthma who have had 6 or more SABA inhalers prescriptions

Background

Percentage of patients on the QOF Asthma Register who received six or more SABA inhaler prescriptions* over the previous 12 months

*From 23/24: who were prescribed 6 or more SABA inhalers

Further Resources

If in any doubt at any stage, refer to a senior member of staff.

Data Collection Form

Insert this information into Excel with an exported CSV from SystmOne

A	B	C	D	E	F	G
Patient Name	DOB	Age	Information sent by SMS (Y/N)	Information sent by letter (Y/N)	Information sent by another method (Y/N)	Comments

Summary

RESP-02 Patients with asthma who have had 6 or more SABA inhalers prescriptions

Practice .....

Pharmacy Technician .....

Pharmacist .....

Authorising GP .....

Date Audit Completed .....

Re-audit date .....

Information sent to LCP ☐

ES-01 Patients using environmentally unsustainable inhalers

Background

Metered Dose Inhaler (MDI) prescriptions as a percentage of all non-salbutamol inhaler prescriptions issued on or after 1/10/21

Further Resources

If in any doubt at any stage, refer to a senior member of staff.

Data Collection Form

Insert this information into Excel with an exported CSV from SystmOne

A	B	C	D	E	F	G
Patient Name	DOB	Age	Information sent by SMS (Y/N)	Information sent by letter (Y/N)	Information sent by another method (Y/N)	Comments

Summary

ES-01 Patients using environmentally unsustainable inhalers

Practice .....

Pharmacy Technician .....

Pharmacist .....

Authorising GP .....

Date Audit Completed .....

Re-audit date .....

Information sent to LCP ☐

CVD-03 Patients aged 25-84y with CVD risk >20% currently on a statin

Background

Percentage of patients aged between 25 and 84 years inclusive and with a CVD risk score (QRISK2 or 3) greater than 20 percent, who are currently treated with statins

Further Resources

If in any doubt at any stage, refer to a senior member of staff.

Data Collection Form

Insert this information into Excel with an exported CSV from SystmOne

A	B	C	D	E	F	G
Patient Name	DOB	Age	Information sent by SMS (Y/N)	Information sent by letter (Y/N)	Information sent by another method (Y/N)	Comments

Summary

CVD-03 Patients aged 25-84y with CVD risk >20% currently on a statin

Practice .....

Pharmacy Technician .....

Pharmacist .....

Authorising GP .....

Date Audit Completed .....

Re-audit date .....

Information sent to LCP ☐

CVD-05 Patients with AF and high CHADS-VASc score prescribed anticoagulant

Background

Percentage of patients on the QOF Atrial Fibrillation register and with a CHA2DS2-VASc score of 2 or more (1 or more for patients that are not female), who were prescribed a direct-acting oral anticoagulant (DOAC), or, where a DOAC was declined or clinically unsuitable, a Vitamin K antagonist.

Further Resources

If in any doubt at any stage, refer to a senior member of staff.

Data Collection Form

Insert this information into Excel with an exported CSV from SystmOne

A	B	C	D	E	F	G
Patient Name	DOB	Age	Information sent by SMS (Y/N)	Information sent by letter (Y/N)	Information sent by another method (Y/N)	Comments

Summary

CVD-05 Patients with AF and high CHADS-VASc score prescribed anticoagulant

Practice .....

Pharmacy Technician .....

Pharmacist .....

Authorising GP .....

Date Audit Completed .....

Re-audit date .....

Information sent to LCP ☐

CVD-06 Patients with AF on DOAC currently taking edoxaban

Background

Indicator Specifics

> Number of patients that are currently prescribed Edoxaban, as a percentage of patients on the QOF Atrial Fibrillation register with a CHA2DS2-VASc score of 2 or more (1 or more for patients that are not female) and who are currently prescribed a direct-acting oral anticoagulant (DOAC)Number of patients that are currently prescribed Edoxaban, as a percentage of patients on the QOF Atrial Fibrillation register with a CHA2DS2-VASc score of 2 or more (1 or more for patients that are not female) and who are currently prescribed a direct-acting oral anticoagulant (DOAC).

DOACs are the highest spend medicines category in primary care, costing the NHS in England over £500m per annum. If patient numbers grow and no action, annual expenditure is expected to more than double. In 2021, NHSEI completed a transparent and compliant national procurement to give all DOAC suppliers an opportunity to update their value proposition to the NHS. All suppliers who responded to the procurement have been awarded national framework agreements, effective from 1 January 2022 to 31 March 2024.

Daiichi Sankyo offered the most significant discount for their product, edoxaban. Overall, the NHS can now treat significantly more patients using edoxaban than any other DOAC, where clinically appropriate. In line with NG196, practices may achieve against this indicator by prescribing edoxaban to patients who are newly diagnosed with AF. NICE also supports affordability being considered as a differentiation between drugs.

It is important that switching patients who are currently prescribed a different brand of DOAC to edoxaban is done in a clinically appropriate way and as the result of a shared decision-making conversation. To emphasise this, this indicator excludes anyone who is prescribed warfarin because DOACs are contraindicated or because they have declined to switch.

Edoxaban is a direct oral factor 10a inhibitor and is licensed for the prevention of stroke and systemic embolism in patients with non-valvular AF and the treatment and prevention of DVT and PE. Edoxaban is not structurally like apixaban and rivaroxaban and so cross-over of side-effects is unlikely.

Edoxaban has been shown to be as clinically effective as other DOACs for the treatment of AF. No trials have directly compared the DOACs to each other; all the trials look at individual DOACs compared to warfarin, and all are slightly different, so none are not directly comparable. Edoxaban was found to be non-inferior to warfarin for both the 30mg and 60mg dose if the most appropriate dose of edoxaban is given.

In older patients edoxaban has been shown to be as safe as warfarin in terms of major bleeding at both the 30mg and 60mg dose.

Contraindications (DOACs)

- Hypersensitivity to the active substance or to any of the excipients

- Clinically significant active bleeding
- Co-morbidity conveying significant risk of major bleeding such as:
    - Current or recent gastrointestinal (GI) ulceration
    - Malignant neoplasms at high risk of bleeding
    - Recent brain or spinal injury or surgery
    - Recent ophthalmic surgery
    - Recent intracranial haemorrhage
    - Suspected or diagnosed oesophageal varices, arteriovenous malformations, vascular aneurysms or major intraspinal or intracerebral vascular abnormalities
- Valvular AF e.g., mechanical heart valve, moderate to severe mitral stenosis
- Hepatic disease associated with coagulopathy and clinically relevant bleeding risk
- Renal impairment – creatinine clearance <15ml/min
- Concomitant treatment with any other anticoagulants except under the circumstances of switching therapy to or from edoxaban
- Pregnancy. Women of child-bearing potential should avoid becoming pregnant during treatment
- Breastfeeding
- Uncontrolled severe hypertension

Contra-indications (edoxaban specific)

- Weight >120kg
- Percutaneous coronary intervention within last 12m
- Creatinine clearance >95ml/min – the ENGAGE AF-TIMI study showed a lower efficacy of edoxaban in patients with a creatinine clearance above 95ml/min. This was only found in patients treated with edoxaban for AF and is not relevant in the VTE population. Patients with a high creatinine clearance should be offered rivaroxaban first line.

Caution in:

- Mild or moderate hepatic impairment
- ALT or AST >2x ULN
- Total bilirubin ≥1.5x ULN
- Patients on P-gp inducers (rifampicin, phenytoin, carbamazepine, phenobarbital, St. John's Wort)
- Patients on other medicines that increase the risk of bleeding
    - Antiplatelets, SSRIs, NSAIDs
    - Review regularly and consider PPI where concurrent use cannot be avoided

Interactions

- Antiplatelets, NSAIDs, SSRIs, steroids
    - Increased risk of bleeding, avoid where possible. Review regularly and consider GI protection
    - Apixaban or dabigatran 110mg BD may be more suitable where GI bleed risk increased
- Dronedarone, ciclosporin, ketoconazole, erythromycin
    - Reduce dose to 30mg OD or consider alternative

- Antiretrovirals
    - Check Liverpool HIV Drug Interaction Checker or discuss with specialist
- Itraconazole, rifampicin, phenytoin, carbamazepine, phenobarbitone, St John's Wort, antivirals
    - Discuss with specialist, may need warfarin

Posology

Edoxaban dosing is based on kidney function, body weight and the use of concomitant medicines. The standard dose is 60mg once daily. The reduced dose of 30mg daily should only prescribed if:

- creatinine clearance is less than 50ml/min,
- the patient weighs <60kg, or
- the patient is also on ciclosporin, erythromycin, ketoconazole or dronedarone.

If the patient is not eligible for reduced dose edoxaban and bleeding risk is a concern, other DOACs where a dose reduction is indicated (i.e., apixaban or dabigatran) may be preferred.

Administration

Edoxaban should be swallowed whole with or without food; rivaroxaban must be taken with a large meal. If not, efficacy is reduced by up to 30%. Patients who do not eat large meal may be better suited to edoxaban rather than rivaroxaban.

Tablets may be crushed and mixed with water or apple puree for administration to people with swallowing difficulties. They may also be crushed and suspended in water to be flushed down a gastric tube.

Side Effects

Edoxaban is generally well tolerated but may be associated with rashes, bruising, bleeding, and anaemia as seen with all anticoagulants. Other common effects include dizziness, headaches, and gastrointestinal upset. These are usually mild and/or transient. Edoxaban may be trialled if the patient has had side effects with other DOACs as they are not structurally similar, and crossover of side effects is unlikely.

Monitoring

- Adherence review every 3 months (ideally, or 6 months at least)
- Review of adverse effects (specifically bleeding/anaemia) every 3 months (ideally, or 6 months at least)
- Review ORBIT-AF regularly (TPT suggests review at each re-authorisation). A score of 3+ indicates a high risk of bleeding; edoxaban should be used in caution, with regular review.
- LFTs every 12 months. Increase the frequency of testing if patient has intercurrent illness which may affect renal or hepatic function
- FBC every 12 months
- Weight with every blood test (to calculate creatinine clearance accurately)
- U&Es:
    - CrCl > 60ml/min, check U&Es every 12 months
    - CrCl 30-59ml/min, or patient is 75y+, or patient is fragile, check U&Es every 6 months
    - CrCl 15-29ml/min, check U&Es every 3 months

Actual body weight should be used to calculate creatinine clearance for DOAC dosing in all patients under 120kg (remove the height from the SystmOne calculator). If there is any uncertainty, MDCalc should be used to ensure accuracy.

DO NOT use eGFR to calculate DOAC doses.

Any decision to start of change therapy must be a shared decision made with the patient and/or carer. Patients should be informed of the reason for prescribing, the benefits and risks, and the implications of therapy (e.g., regular monitoring). When discussing the benefits and risks of anticoagulation and the available drugs, use clinical risk profiles and personal preferences to guide treatment choices. Discuss with the person that:

- For most people the benefit of anticoagulation outweighs the bleeding risk.
- For people with an increased risk of bleeding, the benefit of anticoagulation may not always outweigh the bleeding risk, and careful monitoring of bleeding risk is important.

Benefits

Patients with AF are five times more likely to have a stroke. Strokes due to AF tend to be more serious, with more damage to the brain and worse long-term effects resulting in 2 out of every 5 patients dying, another 2 going into a care home and only 1 going home; approximately 20% of all strokes are caused by AF.

Anticoagulation reduces the risk of stroke by preventing clot formation during periods of AF (due to blood stasis). Table 1 shows the CHA_2DS_2-VASc scoring system. Table 2 shows the % chance of a patient experiencing a stroke in 1 year depending on CHADS-VASc score.

C	Congestive heart failure	1 point
H	History of hypertension	1 point
A	Age	75+ – 2 points 65-74 – 1 point
D	History of diabetes	1 point
S	History of stroke, TIA, thromboembolism	2 points
Va	History of vascular disease (including prior MI, peripheral artery disease, or aortic plaque)	1 point
Sc	Sex category	Female – 1 point

Table 1

CHA_2DS_2VASc score	Risk of ischaemic stroke at 1y	Risk of stroke/TIA/embolic event at 1y
0	0.2%	0.3%
1	0.6%	0.9%
2	2.2%	2.9%
3	3.2%	4.6%
4	4.8%	6.7%
5	7.2%	10.0%
6	9.7%	13.6%
7	11.2%	15.7%
8*	10.8%	15.2%
9	12.2%	17.4%

Table 2 - *risk is lower due to the lower chance of patients still being alive at 1y. The original evidence had a small number of patients in this group and so further research is required to find the true risk.

Risks

Excessive bleeding remains the most pertinent risk for any oral anticoagulant and patients should be counselled sufficiently on their personalised risk using the ORBIT-AF scoring system (see Tables 3 and 4 below).

ORBIT score	Bleeds per 100 patient-years
0	1.7
1	2.3
2	2.9
3	4.7
4	6.8
5	9.0
6	12.3
7	14.9

Table 3

ORBIT score	Risk group	Bleeds per 100 patient-years
0-2	Low	2.4
3	Medium	4.7
4-7	High	8.1

Table 4

GI bleed risk may be mitigated using an acid suppressing agent (e.g., H2 receptor antagonist, or proton pump inhibitor) and low doses of these drugs in patients with no GI symptoms are sufficient. Patients with medium to high ORBIT score should be offered GI protection therapy.

There is currently no reversal agent for edoxaban; if the patient experiences a major bleeding event requiring admission, they will receive symptomatic support (e.g., fluid replacement, transfusion). Evidence is showing that the use of prothrombin complex can be an effective way to stop edoxaban-related bleeding within an hour. If major bleeding is a clinical concern, dabigatran is a better

alternative due to the availability of a full antidote. If gastrointestinal bleeding is a significant clinical concern, a reversal agent for GI bleeding is available for apixaban and rivaroxaban.

Switching from DOAC to edoxaban

TPC have decided to only switch patients on rivaroxaban to edoxaban:

- Rivaroxaban and edoxaban are both taken once daily,
- Rivaroxaban has previously been first line therapy due to familiarity in prescribing in the DVT pathway and so large numbers of patients use this locally,
- Practices do not wish to switch more patients than is necessary to meet the indicator threshold.

Switching from another DOAC may be done by simply stopping the old DOAC and starting edoxaban at the time the next dose is due. This may be done at the end of a supply of the old DOAC or, if the patient is likely to become confused, straight away while ensuring adequate disposal of any leftover medicines.

Patients should also be offered a follow up conversation at 3-6 weeks after the switch to check compliance and side-effects. A reminder of the next blood test should also be given at this follow-up.

If a patient refuses a switch, this should be clearly documented in the clinical notes with appropriate Snomed codes applied to the record:

Description	Snomed code	READ code
Edoxaban declined	1443911000000106	No equivalent
DOAC (direct-acting oral anticoagulant) contraindicated	912841000000100	XabEn
DOAC (direct-acting oral anticoagulant) declined	912661000000103	XabEe
DOAC (direct-acting oral anticoagulant) not indicated	912881000000108	XabEp
DOAC (direct-acting oral anticoagulant) not tolerated	912861000000104	XabEo

Further Resources

- West Yorkshire Health and Care Partnership and NHS West Yorkshire Integrated Care Board Edoxaban training presentation

Edoxaban_training.pptx

- West Yorkshire Health and Care Partnership and NHS West Yorkshire Integrated Care Board Quick Reference Sheet

Edoxaban_quick_reference_prescribing_gui

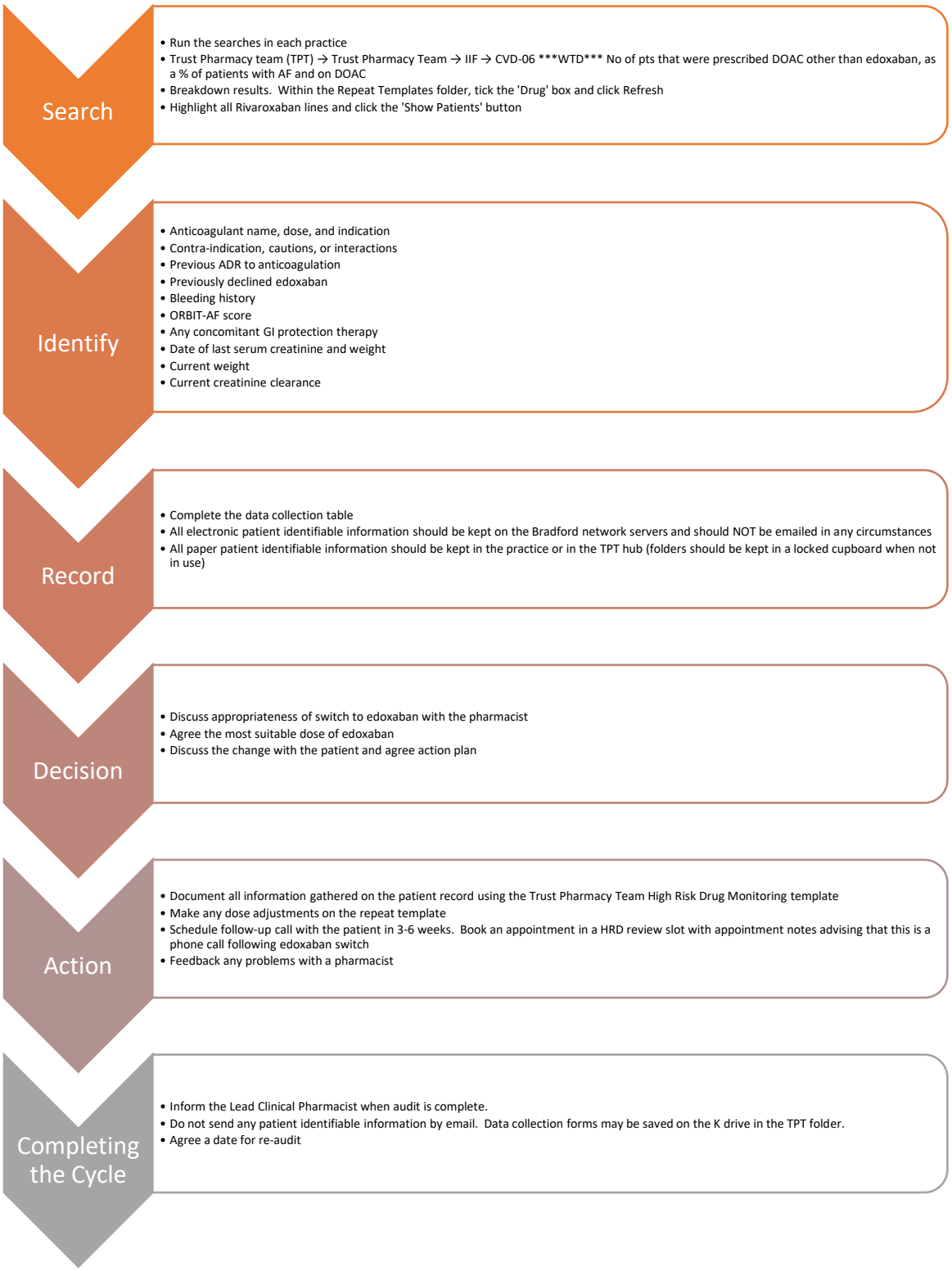
- Edoxaban Summary of Product Characteristics
- Lixiana Prescribing Guide (Daiichi Sankyo)
- Lixiana Patient Alert Care (Daiichi Sankyo)
- Specialist Pharmacy Service Drug Monitoring
- MDCalc Creatinine clearance calculator
- MDCalc CHADS-VASc risk calculator
- CKS Management of AF
- AF Association
- Stroke Association

References

Lip, G.Y., Frison, L., Halperin, J.L. and Lane, D.A. (2010) Identifying patients at high risk for stroke despite anticoagulation: a comparison of contemporary stroke risk stratification schemes in an anticoagulated atrial fibrillation cohort. Stroke 41(12), 2731-2738.

O'Brien, E.C., Simon, D.N., Thomas, L.E. et al. (2015) The ORBIT bleeding score: a simple bedside score to assess bleeding risk in atrial fibrillation. European Heart Journal 36(46), 3258-3264.

If in any doubt at any stage, refer to a senior member of staff.



Data Collection Form

Insert this information into Excel with an exported CSV from SystmOne

A	B	C	D	E	F	G	H	I	J
Patient Name	DOB	Age	Anticoagulant name & dose	Indication	Contra-indications	Cautions	Interactions	Previous ADR	Previously declined

K	L	M	N	O	P	Q	R	S	T	U
Bleeding history	ORBIT-AF score	Current GI protection tx	Date of last serum creatinine	Date of last weight	Current weight	Current CrCl	Decision	Action	Follow-up booked on DATE?	Comments

Example SMS

The Department of Health has asked all GP practices to review its anticoagulation prescribing. Changes in the cost of these drugs means that we must look at changing some people's medicines so we can release funding to provide medicines and care to more patients. We have looked at your records and it is safe for us to change your rivaroxaban to EDOXABAN. This medicine works in the same way, is taken once a day, and provides the same protection from stroke as rivaroxaban. If you do not want us to make this change, please reply to this message. You can find more information on edoxaban at this link. If you have any questions or concerns, please get in touch with our reception team.

https://api.heartrhythmalliance.org/files/download/aada88bb131e465f2090fb3721144163

Summary

CVD-06 Patients with AF on DOAC currently taking edoxaban

Practice .....

Pharmacy Technician .....

Pharmacist .....

Authorising GP .....

Date Audit Completed .....

Re-audit date .....

Information sent to LCP ☐