MDR-TB Drug Toxicity in the UK

BTS MDR-TB Clinical Advice Service

Supplemental Report 2021

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This work forms part of the BTS Respiratory Quality Improvement activities. We work with our members, healthcare professionals from other specialties, and patients and carers to improve standards of care for people with respiratory diseases, and to support those who provide that care.

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INTRODUCTION

When clinicians enter case details into the BTS MDR-TB CAS they enter full details of the drugs received by patients since diagnosis. This includes the dates individual drugs were started and stopped, as well as the reasons for ceasing treatment.

The treatment of drug resistant tuberculosis is highly complex, with drug regimens frequently subject to change due to a range of factors. These include new sensitivity information becoming available, issues with drug-drug interactions, and a range of different adverse events. With limited drug treatment options available patients are often treated with drugs which have a tendency to be poorly tolerated.

It is essential that the complexities of drug treatment are understood as fully as possible. This will help ensure patients receive effective treatment regimens, and also that clinicians are better able to monitor for potential side-effects (and cease treatment with specific drugs where necessary).

This supplemental report provides a detailed breakdown of reasons for ceasing treatment with each drug, and is intended to act as a reference guide for likely adverse reactions which may be encountered when treating drug resistant tuberculosis. This report should be read in conjunction with the BTS MDR-TB CAS Annual Report 2021.

PART 1 –Reasons for Ceasing Individual TB Drugs

The information presented in this report relates to patients with known or suspected XDR/MDR-TB, entered into the BTS MDR-TB CAS site from January 2018 to June 2021 unless otherwise stated.

Aggregate data have been used here, but over the period covered by the main BTS MDR-TB Clinical Advice Service Annual Report 2021 (July 2020 to the end of June 2021) the drugs which were most frequently included in the regimen at entry onto the Service were: linezolid (Lzd), clofazimine (Cfz), pyrazinamide (Z) and bedaquiline (Bdq).

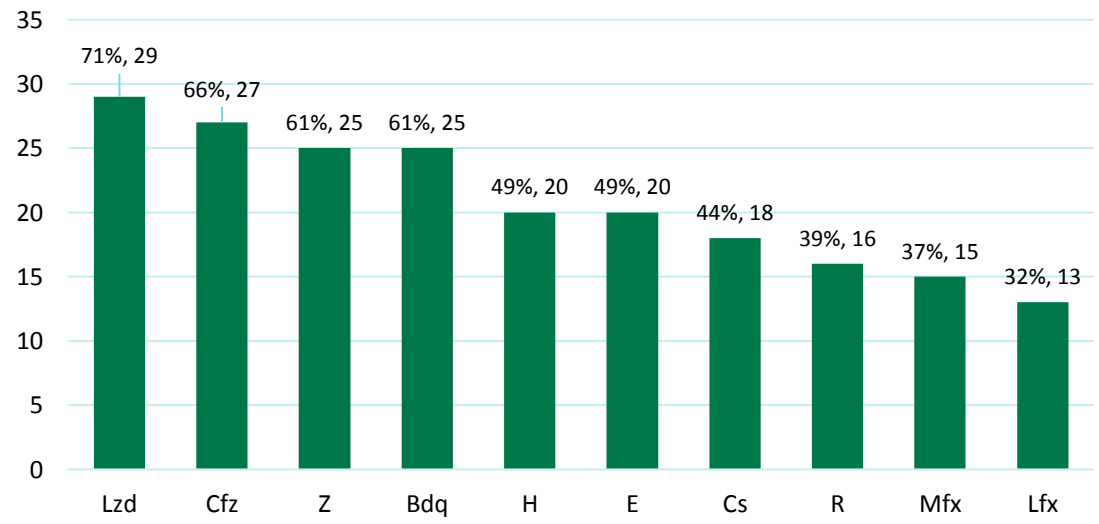


Figure 1: Ten most frequently used drugs at entry onto the Service
This chart shows the ten most frequently used drugs at entry onto the BTS MDR-TB CAS from July 2020 to June 2021, for cases of known or suspected XDR or MDR-TB only (n = 41).

Where an individual drug was removed from a patient's drug regimen, the most frequently reported reason for the change in medication was that a new drug sensitivity had become available. This was particularly true of ethionamide, where the only reported reason for ceasing treatment was a new sensitivity.

New sensitivity information was also a leading cause of ceasing treatment with each of rifampicin (68% of cases where the drug was ceased), isoniazid (67%), ethambutol (51%) and pyrazinamide (37%), as well as prothionamide (13%), moxifloxacin (9%), and cycloserine and bedaquiline (4% each).

Key Points

- The most common reason for ceasing treatment with a drug was new sensitivity information becoming available
- Potential or actual drug interactions were a common cause of ceasing treatment with delamanid, capreomycin and moxifloxacin
- Although fewer patients were treated with rifabutin, imipenem/cilastatin or rifapentine, these drugs were well tolerated and were not 'lost' from any regimens

A range of different drug toxicities were reported, with thirteen different categories listed. A full guide to adverse events is given in Part 2 of this supplemental report.

Potential or actual drug interactions resulted in treatment being ceased with each of delamanid (14% of cases where the drug was ceased), moxifloxacin (12%), capreomycin (8%), cycloserine (7%), clofazimine (6%), bedaquiline (4%) and linezolid (3%).

Although few patients received rifabutin (8), imipenem/cilastatin (1) or rifapentine (1), it is worth noting that no patients were reported to have 'lost' these drugs from their regimens. The indication that rifabutin in particular may be both well tolerated and reliable is promising for patients who are unable to tolerate rifampicin (such as patients with HIV/AIDS).

Figure 2 (page 7) displays a breakdown of clinician-reported reasons for ceasing the first treatment session with each drug.

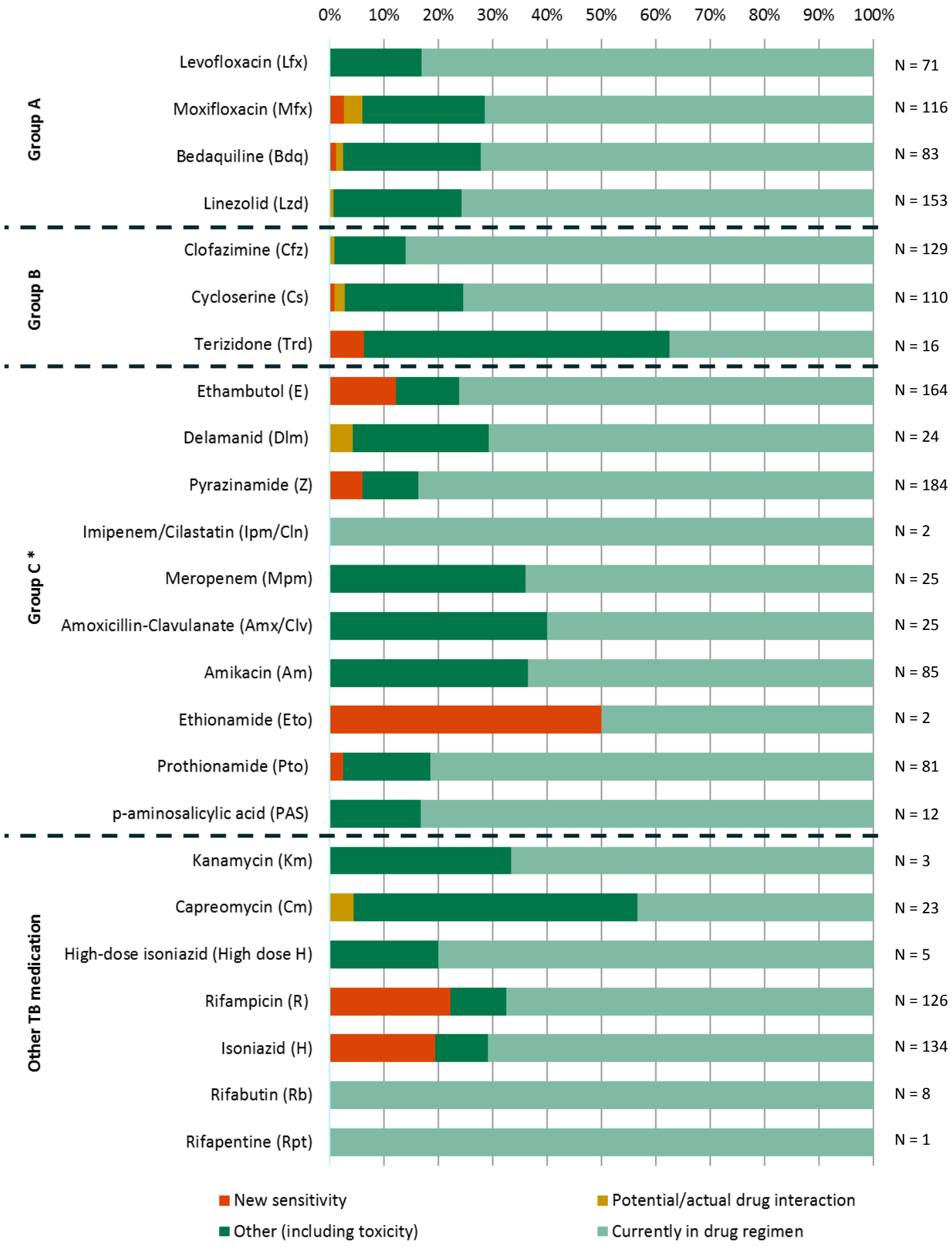


Figure 2: Reasons for Ceasing Treatment with Each Drug

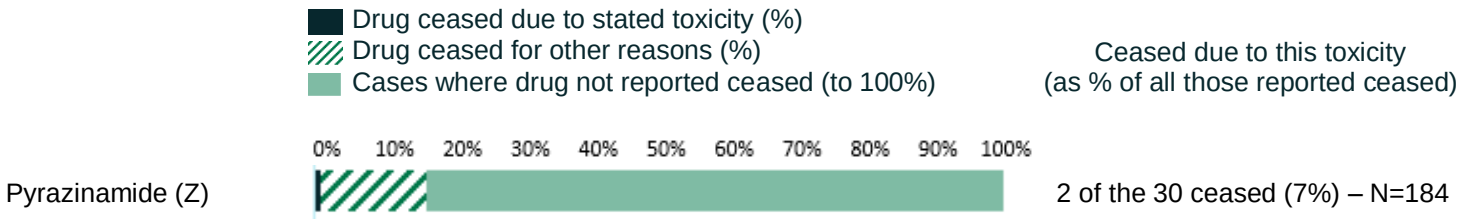
This figure shows the clinician-reported reasons for ceasing the first treatment session with each drug, for all cases of known or suspected XDR/MDR-TB entered into the BTS MDR-TB CAS from January 2018 to June 2021.

PART 2 – Adverse Reaction Guide

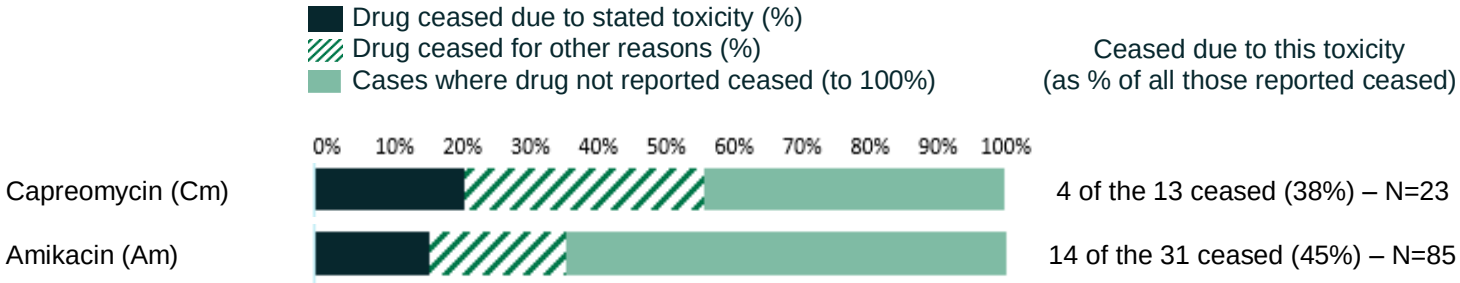
The figures included in this guide give an overview of reported drug toxicity for cases of XDR, MDR and suspected MDR-TB from January 2018 to June 2021. Bars represent total cases where each drug was given (100%) with proportions shown for cases ceased due to the stated toxicity (navy) or other reasons (striped).

BTS does not provide detailed information or advice regarding the use and monitoring of specific drugs. For overall details of adverse events and drug monitoring recommendations for each drug, as well as information on dosing, drug level monitoring and more, please visit the TB Drug Monographs site (http://www.tbdrugmonographs.co.uk/).

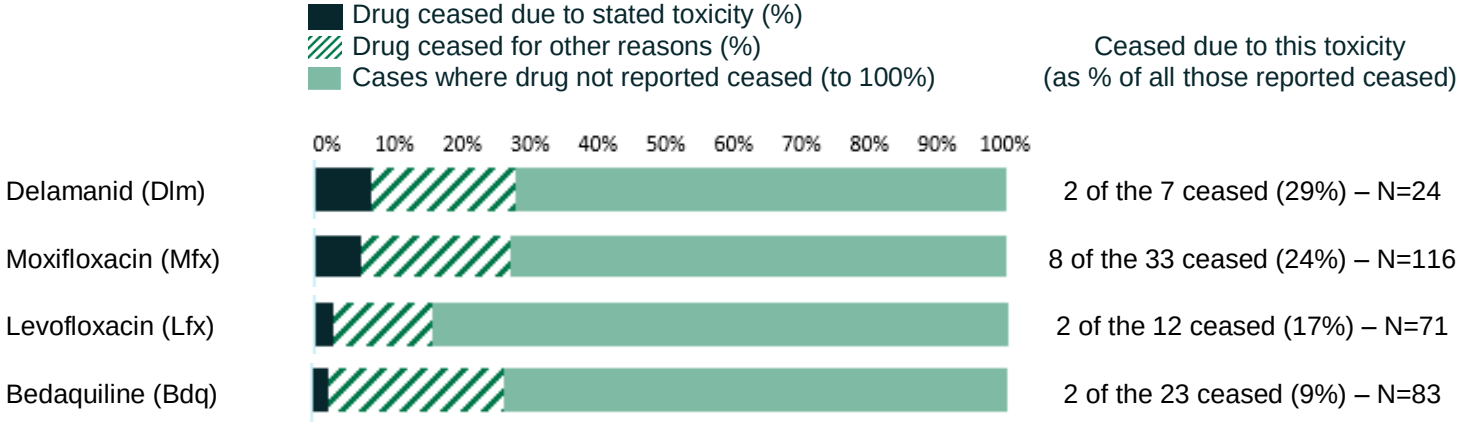
2.1 ARTHRALGIA



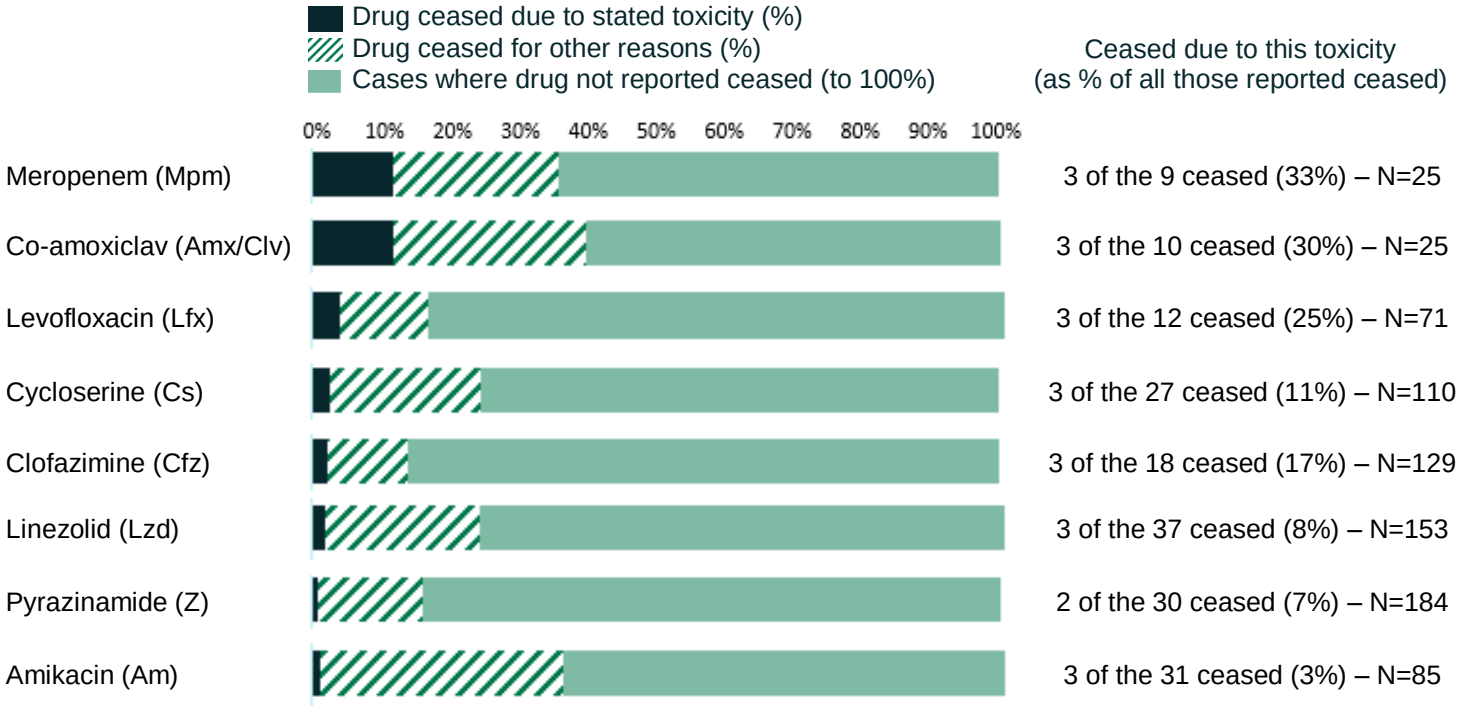
2.2 AUDIOLOGICAL REACTION



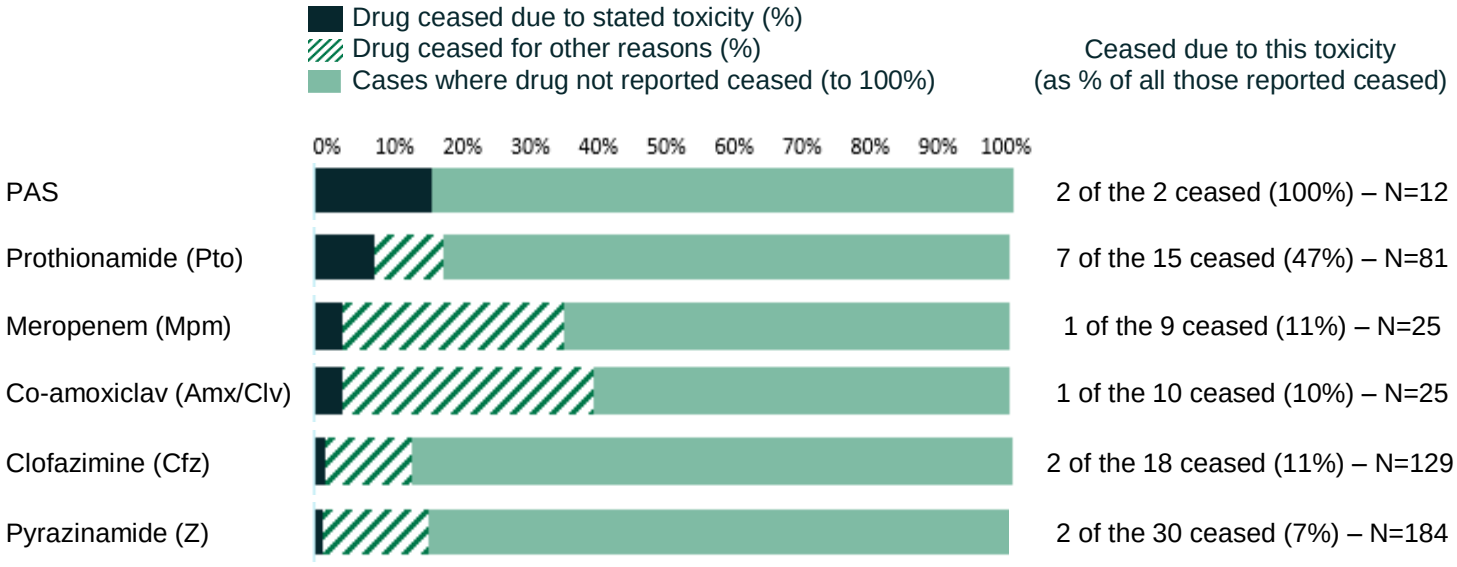
2.3 CARDIOVASCULAR REACTION



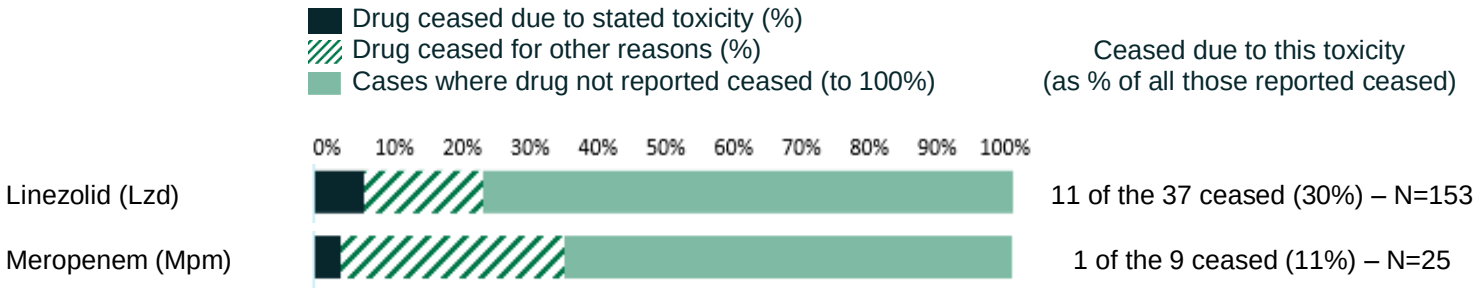
2.4 DERMATOLOGICAL REACTION



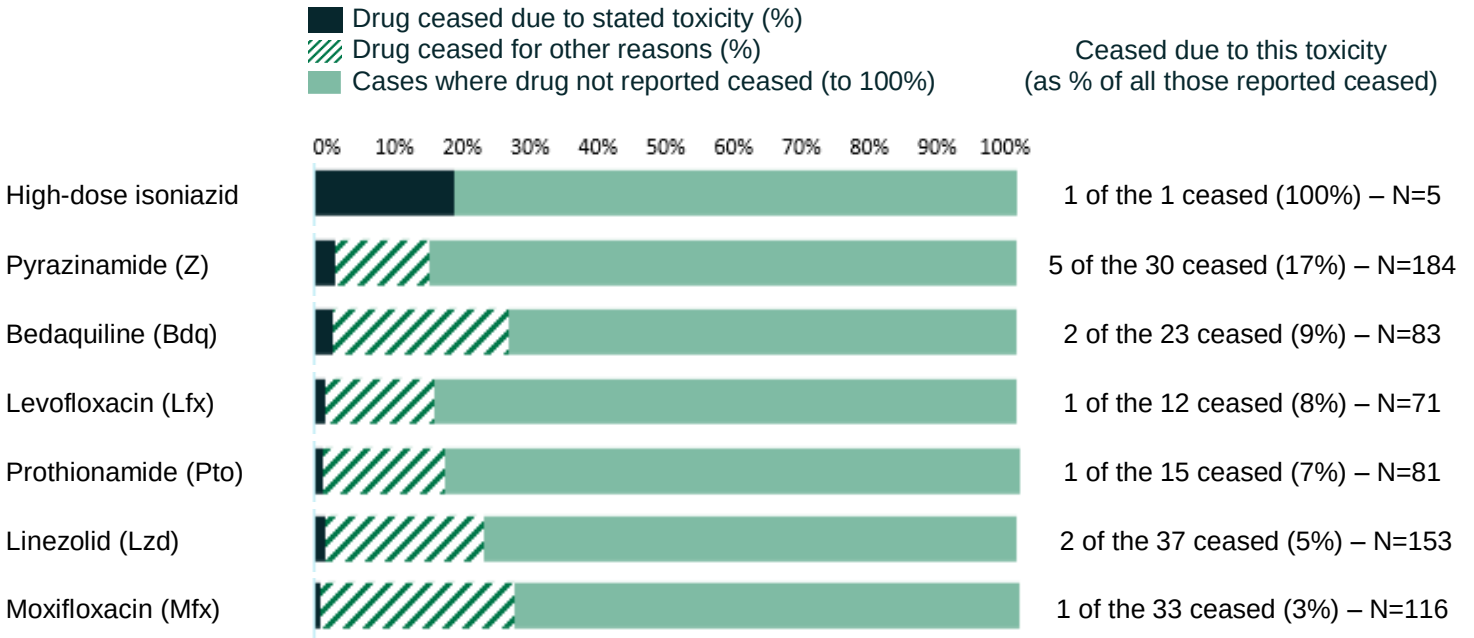
2.5 GASTROINTESTINAL REACTION



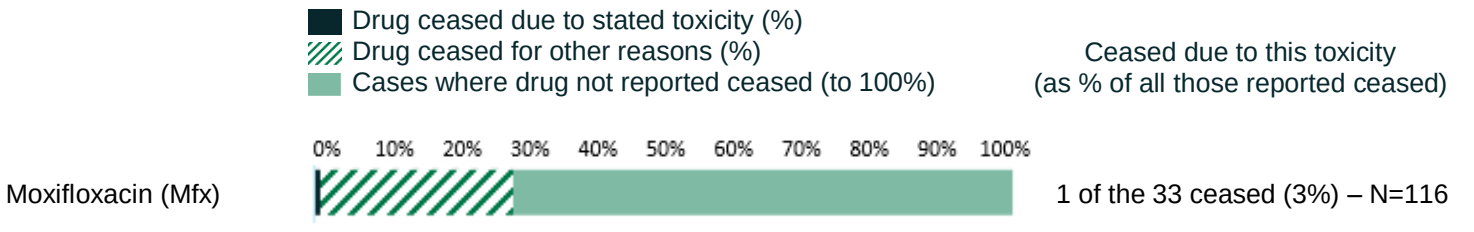
2.6 HAEMATOLOGICAL REACTION



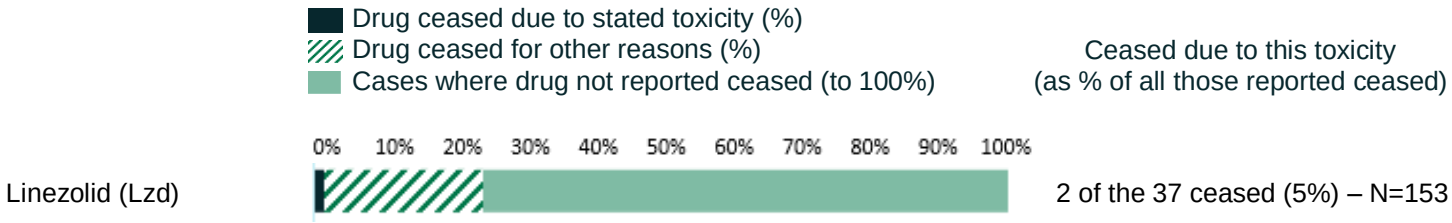
2.7 HEPATIC REACTION



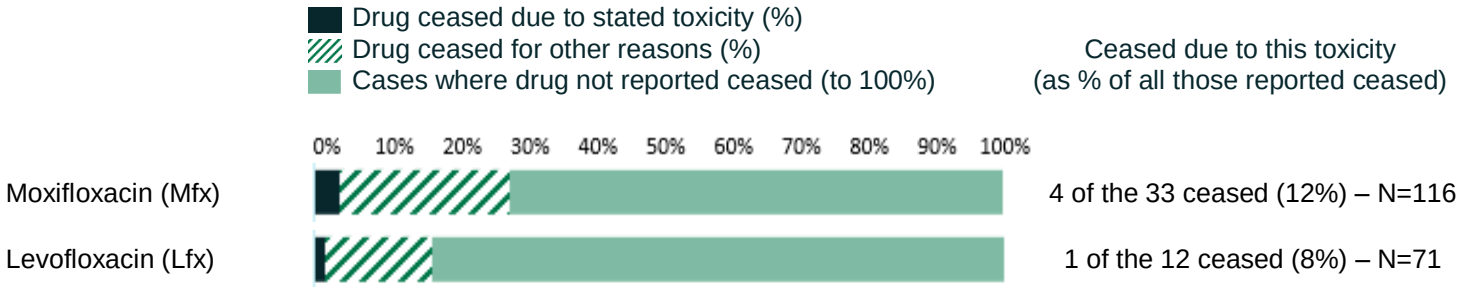
2.8 IMMUNOLOGICAL REACTION



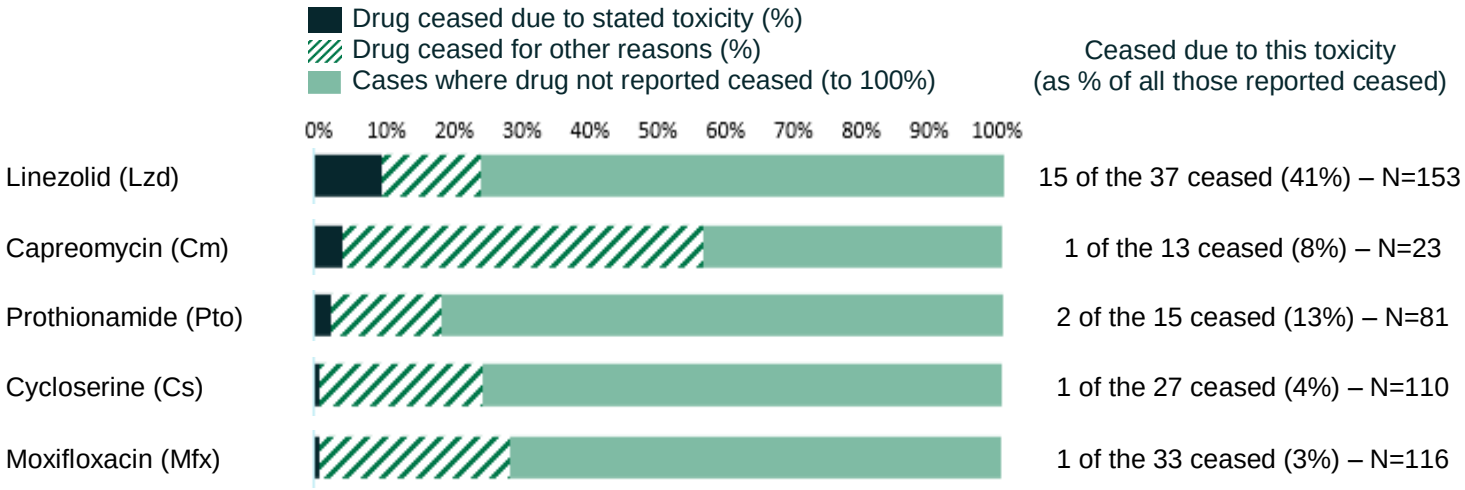
2.9 METABOLIC REACTION



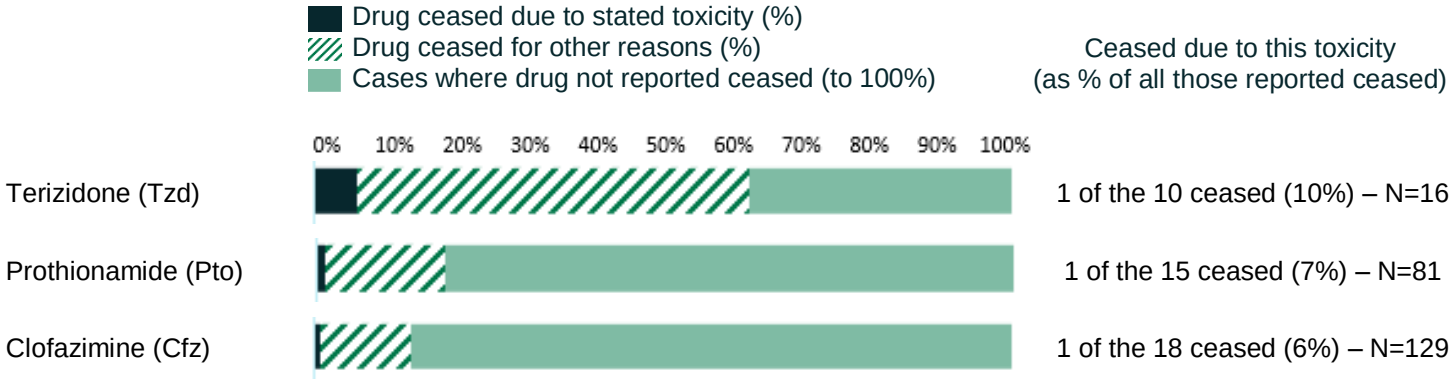
2.10 MUSCULOSKELETAL REACTION



2.11 NEUROLOGICAL REACTION



2.12 PSYCHIATRIC REACTION



2.13 RENAL REACTION