



21 January 2019

Risk of Fournier's gangrene (necrotising fasciitis of the perineum) with Sodium-Glucose-Co-Transporter 2 inhibitors (SGLT2i)

Direct Healthcare Professional Communication

Dear Healthcare Professionals,

Marketing authorisation holders of products containing SGLT2 inhibitors [Invokana (canagliflozin), Forxiga (dapagliflozin), Jardiance▼ (empagliflozin), Steglatro▼ (ertugliflozin)], in agreement with the European Medicines Agency and the Medicines and Healthcare products Regulatory Agency, would like to inform you of the following

Summary

- Post-marketing cases of Fournier's gangrene (necrotising fasciitis of the perineum) have been associated with the use of SGLT2 inhibitors
- Fournier's gangrene is a rare but serious and potentially life-threatening infection
- Uro-genital infection or perineal abscess may precede necrotising fasciitis
- Advise patients to seek urgent medical attention if they experience severe pain, tenderness, erythema, or swelling in the genital or perineal area accompanied by fever or malaise
- If Fournier's gangrene is suspected, stop the SGLT2 inhibitor and promptly start treatment (including antibiotics and surgical debridement)

Background on the safety concern

SGLT2 inhibitors are indicated for the treatment of type 2 diabetes. The following SGLT2 inhibitors are currently authorised in the EU: Edistride (dapagliflozin), Forxiga (dapagliflozin), Ebymect (dapagliflozin / metformin), Xigduo (dapagliflozin / metformin), Qtern (dapagliflozin / saxagliptin), Invokana (canagliflozin), Vokanamet (canagliflozin / metformin), Jardiance▼ (empagliflozin), Synjardy▼ (empagliflozin / metformin), Glyxambi▼ (empagliflozin / linagliptin), Steglatro▼ (ertugliflozin), Segluromet▼ (ertugliflozin / metformin) and Steglujan▼ (ertugliflozin / sitagliptin).

Cases of Fournier's gangrene have been reported across the class of SGLT2 inhibitors. Although diabetes mellitus is a risk factor for the development of Fournier's gangrene, some of the post-marketing reports are considered possibly related to the use of SGLT2 inhibitors.

Fournier's gangrene is known to occur almost exclusively in men. However, in association with SGLT2 inhibitors it was also reported in women.

The product information will be revised to list Fournier's Gangrene as an adverse reaction in section 4.8 and will also include respective warning statements in section 4.4 of the SmPC as outlined in the summary above.

Call for reporting

Please continue to report suspected adverse drug reactions (ADRs) to the MHRA through the Yellow Card Scheme.

Please report:

- all suspected ADRs that are serious or result in harm. Serious reactions are those that are fatal, life-threatening, disabling or incapacitating, those that cause a congenital abnormality or result in hospitalisation, and those that are considered medically significant for any other reason
- all suspected ADRs associated with new drugs and vaccines identified by the black triangle▼

It is easiest and quickest to report ADRs online via the Yellow Cards website - <https://yellowcard.mhra.gov.uk/> or via the Yellow Card app available from the Apple App Store or Google Play Store.

Alternatively, prepaid Yellow Cards for reporting are available by writing to FREEPOST YELLOW CARD (no other address details necessary); by emailing yellowcard@mhra.gov.uk; at the back of the British National Formulary (BNF); by telephoning the Commission on Human Medicines (CHM) free phone line: 0800-731-6789; or by downloading and printing a form from the Yellow Card website.

Adverse reactions should also be reported to the relevant company [see Table 1 for company contact details by product].

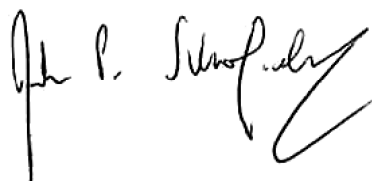
Company contact point

If you have any questions, or if you require any further information, please contact the relevant Medical Information Department [See Table 1 for company contact details by product].

Yours sincerely,



Dr Dilruwan Herath
Medical and Regulatory Affairs Director,
AstraZeneca UK



Dr J Paul Schofield
Medical Director
Napp Pharmaceuticals Limited



Dr Juliet Roberts
Medical Director UK & Ireland
Boehringer Ingelheim Limited



Dr Michael England
UK Executive Medical Director
Merck Sharp & Dohme Limited

Table 1

Product name (active ingredient)	Marketing Authorisation Holder	Local Representative
Forxiga (dapagliflozin)	AstraZeneca Pharmaceuticals	AstraZeneca Pharmaceuticals Tel no: 0800 783 0033 e-mail: medical.informationUK@astrazeneca.com
Invokana (canagliflozin)	Janssen-Cilag International NV	Napp Pharmaceuticals Ltd Tel no: 01223 424444 e-mail: medicalinformationUK@napp.co.uk
▼ Jardiance ¹ (empagliflozin)	Boehringer Ingelheim International GmbH	Boehringer Ingelheim Limited Tel no: 01344 742579 e-mail: medinfo.bra@boehringer-ingelheim.com Eli Lilly and Company Limited Telephone: 01256 315000 e-mail: medinfo_ukhub@lilly.com
Qtern (dapagliflozin/saxagliptin)	AstraZeneca Pharmaceuticals	AstraZeneca Pharmaceuticals Medical Information Tel no: 0800 783 0033 e-mail: medical.informationUK@astrazeneca.com
▼ Steglatro (ertugliflozin)	Merck Sharp & Dohme B.V.	Merck Sharp & Dohme Ltd Tel no: 01992 467272 e-mail: medicalinformationuk@merck.com
▼ Steglujan (ertugliflozin/sitagliptin)	Merck Sharp & Dohme B.V.	Merck Sharp & Dohme Ltd Tel no: 01992 467272 e-mail: medicalinformationuk@merck.com
▼ Segluromet (ertugliflozin/metformin)	Merck Sharp & Dohme B.V.	Merck Sharp & Dohme Ltd Tel no: 01992 467272 e-mail: medicalinformationuk@merck.com
▼ Synjardy ¹ (empagliflozin/ metformin)	Boehringer Ingelheim International GmbH	Boehringer Ingelheim Limited Tel no: 01344 742579 e-mail: medinfo.bra@boehringer-ingelheim.com Eli Lilly and Company Limited Telephone: 01256 315000 e-mail: medinfo_ukhub@lilly.com
Vokanamet (canagliflozin/metformin)	Janssen-Cilag International NV	Napp Pharmaceuticals Ltd Tel no: 01223 424444 e-mail: medicalinformationUK@napp.co.uk
Xigduo (dapagliflozin/metformin)	AstraZeneca Pharmaceuticals	AstraZeneca Pharmaceuticals Medical Information Tel no: 0800 783 0033 e-mail: medical.informationUK@astrazeneca.com

¹ Jardiance and Synjardy are co-promoted by Boehringer Ingelheim Limited and Eli Lilly and Company Limited