



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 Health Products Regulatory Authority, 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 necrotizing 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 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**

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: [www.hpra.ie](http://www.hpra.ie); E-mail: [medsafety@hpra.ie](mailto:medsafety@hpra.ie).

Adverse reaction reports should also be reported to the company contacts listed in Table 1, for applicable products.

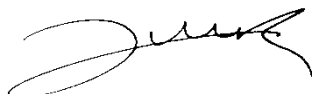
### **Company contact point**

Table 1 provides a list of Companies, their concerned products and contact points. Healthcare professionals should report adverse drug reactions to the respective marketing authorisation holder.



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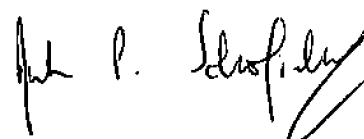
**Dr Jad El Khoury**  
Medical Director

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(Ireland) DAC,  
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**Dr Juliet Roberts**  
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**Dr J Paul Schofield**  
Medical Director

Napp Pharmaceuticals  
Limited,  
Cambridge Science Park,  
Milton Road,  
Cambridge, CB4 0AB  
United Kingdom

Table 1: Contact details for the Marketing Authorisation Holders for reporting adverse drug reactions

<b>Product Name (active substance)</b>	<b>Marketing Authorisation Holder</b>	<b>Local Representative</b>	<b>Email Contact</b>	<b>Phone Number</b>
Forxiga 5 mg film coated tablets Forxiga 10 mg film coated tablets (Dapagliflozin)	AstraZeneca AB SE-151 85 Södertälje Sweden	AstraZeneca Pharmaceuticals (Ireland) DAC, Block B, Liffey Valley Office Campus, Dublin 22	Medical.informationUK@astrazeneca.com	1800 800 899
Xigduo 5 mg/850 mg film coated tablets Xigduo 5 mg/1,000 mg film coated tablets (Dapagliflozin/Metformin)	AstraZeneca AB SE-151 85 Södertälje Sweden	AstraZeneca Pharmaceuticals (Ireland) DAC, Block B, Liffey Valley Office Campus, Dublin 22	Medical.informationUK@astrazeneca.com	1800 800 899
Jardiance ▼ 10 mg film-coated tablets Jardiance ▼ 25 mg film-coated tablets (Empagliflozin)	Boehringer Ingelheim International GmbH <sup>1</sup>	Boehringer Ingelheim Ireland Limited  Eli Lilly and Company (Ireland) Limited	Boehringer Ingelheim Limited: medinfo@dbl.boehringer-ingelheim.com  Eli Lilly and Company Limited: medinfo_ukhub@lilly.com	Boehringer Ingelheim Limited: 01 295 9620 or +44 1344 742579  Eli Lilly and Company Limited: +44 (0)1256 315 000
Synjardy ▼ 5 mg/850 mg film-coated tablets Synjardy ▼ 5 mg/1,000 mg film-coated tablets Synjardy ▼ 12.5 mg/850 mg film-coated tablets Synjardy ▼ 12.5 mg/1,000 mg film-coated tablets	Boehringer Ingelheim International GmbH <sup>2</sup>	Boehringer Ingelheim Ireland Limited  Eli Lilly and Company (Ireland) Limited	Boehringer Ingelheim Limited: medinfo@dbl.boehringer-ingelheim.com  Eli Lilly and Company Limited: medinfo_ukhub@lilly.com	Boehringer Ingelheim Limited: 01 295 9620 or +44 1344 742579  Eli Lilly and Company Limited: +44 (0)1256

(Empagliflozin/ metformin)				315 000
Invokana 100 mg film-coated tablets  Invokana 300 mg film-coated tablets  (canagliflozin)	Janssen-Cilag International NV	Mundipharma Pharmaceuticals Limited  Millbank House, Arkle Road  Sandyford  IRL-Dublin 18	medicalinforma tion@mundipha rma.ie	+353 1 2063800
Vokanamet 50 mg/850 mg film-coated tablets  Vokanamet 50 mg/1000 mg film-coated tablets  Vokanamet 150 mg/850 mg film-coated tablets  Vokanamet 150 mg/1000 mg film-coated tablets  (canagliflozin and metformin hydrochloride)	Janssen-Cilag International NV	Mundipharma Pharmaceuticals Limited  Millbank House, Arkle Road  Sandyford  IRL-Dublin 18	medicalinforma tion@mundipha rma.ie	+353 1 2063800
Steglatro ▼ (ertugliflozin)  Steglujan ▼ (ertugliflozin/sitagliptin)  Segluromet ▼ (ertugliflozin/metformin hydrochloride)	Merck Sharp & Dohme B.V.  Merck Sharp & Dohme B.V.  Merck Sharp & Dohme B.V.	Merck Sharp & Dohme Ireland (Human Health) Limited	medinfo_irelan d@merck.com	
<p><sup>1</sup>Jardiance tablets are co-promoted by Boehringer Ingelheim Limited and Eli Lilly and Company Limited  <sup>2</sup>Synjardy tablets are co-promoted by Boehringer Ingelheim Limited and Eli Lilly and Company Limited</p>				

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. Details of how to report can be found in the section call for reporting.